**Endoscopy F197-F198**

**FORCEFUL PNEUMATIC DILATATION FOR ACHALASIA OF THE CARDIA USING THE WITZEL BALLOON METHOD**

A.S. Mee, R. Przemilowski, L. Williams. Department of Gastroenterology, Belforte Hospital and Department of Medical Illustration Royal Berkshire Hospital Reading.

This video describes the method of forceful pneumatic balloon dilatation for achalasia of the cardia using a commercially available endoscope mounted balloon (the Witzel balloon). The balloon attains a pre-formed diameter of 40mm and can be inflated to a maximum pressure of 300mm Hg. Patients are treated as day cases on a routine endoscopy list. The procedure is carried out under intravenous sedation. Initial inflation pressures of 100mm Hg for 1 minute, 150mm Hg for 1 minute and 200mm Hg for 2 minutes are used. A post procedure chest X Ray is carried out at 4 hours. A second dilatation at higher inflation pressures is performed at 1 month if the result at review appointment is not entirely satisfactory.

Between 1985 and 1992 18 patients (14M, 4F, median age 44; range 20 - 76) with clinical and radiological evidence of achalasia have been treated.

**Results**

One patient developed a perforation which was treated conservatively. His subsequent swallowing was normal. The procedure failed in one patient who required a Heller's myotomy. Two patients underwent a second dilatation at early review. Three patients underwent a further successful dilatation after 9 months, 3 and 4 years. One elderly patient died after 5 years from a carcinoma of the oesophagus. One patient required an oesophageal resection 3 years post-dilatation for a fibrotic stricture. One patient has been lost to long-term follow up.

The procedure has, therefore, been effective in 15 of 17 (88%) patients available for long term evaluation.

**Conclusion**

The Witzel balloon technique of forceful pneumatic dilatation for achalasia is simple to perform, inexpensive and effective and should be considered as the initial approach before contemplating surgical intervention.

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**T195**

**CIRCULATING PLATELETS ARE ACTIVATED IN INFLAMMATORY BOWEL DISEASE (IBD).** CE Collins, MR Cahill, MG Macay, AC Newland, DS Rampton. Gl Science Research Unit and Dept of Haematology, Royal London Hospital, London.

Activated platelets play a role in the vascular damage associated with ischaemic heart disease and diabetes. Systemic thromboses may complicate active IBD and recent evidence suggests there is significant intestinal vascular endothelial injury in Crohn's disease. We tested the hypothesis that platelet activation contributes to the pathogenesis of IBD.

**METHODS:** We used i) flow cyrometry to quantify the platelet surface antigens P-selectin (a specific adhesion receptor for neutrophils released from alpha-granules) and GP53 (a lysosome-derived protein), both of which are expressed on activation, and ii) ELISA to measure beta-thromboglobulin (βTG), a platelet-specific protein discharged from alpha-granules on activation. Disease activity was defined according to the modified Harvey-Bradshaw index.

**RESULTS:** There was increased expression of surface markers in all IBD groups, and of βTG in active CD and inactive UC. % cells positive for specific fluorescent antibody marker, and serum βTG in IU/ml, are shown as medians (interquartile range):  

<table>
<thead>
<tr>
<th>n</th>
<th>P-selectin (GP53)</th>
<th>βTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>controls</td>
<td>32</td>
<td>1.8 (1.1-3.3)</td>
</tr>
<tr>
<td>active CD</td>
<td>19</td>
<td>4.2 (2.0-13.8)*</td>
</tr>
<tr>
<td>active UC</td>
<td>11</td>
<td>4.0 (1.6-10.7)</td>
</tr>
<tr>
<td>active UC</td>
<td>3</td>
<td>7.1 (4.1-13.0)*</td>
</tr>
<tr>
<td>active UC</td>
<td>9</td>
<td>3.5 (2.3-5.5)*</td>
</tr>
</tbody>
</table>

*p<0.05, t>p<0.01 vs healthy controls using Mann-Whitney U.

**CONCLUSION:** Platelets circulate in an activated state in IBD. This abnormality could contribute to the pathogenesis of IBD by promoting neutrophil adhesion, and by predisposing to thrombosis and infarction in the vasculature of the bowel wall and elsewhere.

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**T196**

**PLATELET ACTIVATION IN INFLAMMATORY BOWEL DISEASE.** HD Schaeubleger, M.R Uhr, AC Smith, KPH Logan, PC Gordon-Smith, J. Misiewicz. Department of Gastroenterology, Central Middlesex Hospital London NW10 7NS and 2nd Division of Haematology, St George's Hospital London SW17 0RE.

Abnormal coagulation is involved in inflammatory bowel disease (IBD). P-selectin (GP5140, CD62), a receptor mediating neutrophil adhesion on the surface of activated platelets and vascular endothelial cells, is uniquely expressed on the surface of activated platelets and vascular endothelial cells. We have investigated the contribution of activated vascular endothelium in the pathogenesis of IBD.

Twenty patients (median age 38y (15-73, range) 13 men) with either ulcerative colitis (UC) n=12, 5 active, 7 inactive) or Crohn's disease (CD n=8, 3 active, 5 inactive) were studied and compared with 9 healthy volunteers (median age 31y (23-40) 4 men). IBD was graded as active/inactive, using the Harvey-Bradshaw classification. Circulating activated platelets in venous whole blood were assessed by their expression of the membrane protein GMP140, measured semiquantitatively by flow cyrometry on a random sample of 8,000 platelets from each subject.

The percentage of circulating activated platelets was significantly increased in the IBD group as a whole compared to healthy subjects (18.8%, mean [4.2%, SEM] vs 4.3% [1.5%], P<0.001). When considered separately, patients with UC [20.5% (2.5%)] and CD [16.6% (2.2%)] had increased numbers of activated platelets compared to normals, (P<0.001). Patients with active disease, either UC or Crohn's, did not differ from those with inactive disease [22.1% (1.5%) vs 16.9% (3.7%)], P=0.23].

(Independent t-test on absolute values, converted to % for clarity)

Our finding suggest that patients with IBD show a persistent response to haemostatic and/or inflammatory tissue injury but that this does not depend upon disease activity.

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**T198**

**KATE'S VIDEO DIARY; A PATIENT'S PERSPECTIVE OF ENDOSCOPY**

Owen Epstein, Jan Cave, John Lineham

Endoscopy Unit, Royal Free Hospital NHS Trust, Pond Street London NW3 2QG

Prior to an endoscopy, most patients are given both verbal and written explanations of the procedure. The information is provided by doctors or nurses, most of whom have not themselves undergone the procedure. The information tends to focus on the safety and comfort of the examination with a simple description of the instrument and technique. This short video captures a patient's recollection of her experience of endoscopy. She remembers the outpatient department and endoscopy waiting area for its anonymous audience of fellow patients and medical students. She assimilated little of the doctor's explanation of the endoscopy but it did arouse powerful memories of morbid medical TV documentaries and 'soaps'. She remembers the anxiety provoked by visions of X-ray machines, computers, hissing machines and unfamiliar faces as she was led into the endoscopy room. Of the procedure itself, Kate remembers no more than the prick of the needle, followed by gentle sleep and a friendly cup of tea which she'd be promised. We recommend the video is shown to doctors and nurses and used to stimulate a discussion on the overall quality of the endoscopy experience for patients.

The video does not offer answers but a sample list of questions is included to help a facilitator use the video to discuss overall quality of patient care.

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Biliary F199-F204

F199

PHYSICAL CHEMISTRY AND CHELOROLESTIC (CH) CRYSTAL NUCLEATION TIME (NT) - THE MISSING LINKS IN GALLBLADDER STONE (GBS) RECURRENTNESS? Hussaini SH, Pereira SP, Kennedy C Murphy GM, Doull HS. Castoro Unit, UWS, Guy’s Campus, London.

After dissolution or removal of GBS and withdrawal of treatment, GBS reverts to being supersaturated with CH and GB hypomotility persists - factors that contribute to GBS recurrence which develops in approx 50% at 5yr. However, in vitro biliary bile acid (BA) composition in these patients, nor about the distribution of CH between vesicles, and micelles, the vesicular CH:phos-pholipid (PL) molar ratio (an index of vesicle stability) or the micrortal PT - additional factors which could be well important in predicting GBS recurrence. METHODS: Therefore, in (i) a gallstone disease group rendered stone-free (by oral BAs i 12,000 mg, or a mixture of CH:PL in one and partecutaneous cholecystectomy in one), and (ii) a non-gallstone control group of 7 (children, we obtained GB bile by US-guided fine needle aspiration and measured biliary BA composition, BA, PL and CH concentrations. CH saturation indices (CISs), vesicular CH % of total vesicular CH:PL molar ratio and CH microcrystal NTs. RESULTS: Compared dissolution clearance patients had: (i) more deoxycholic acid (DCA; 22.2±SEM 4.1% vs 12.5±1.4%; p<0.05), (ii) higher CISs (1.34±0.12 vs 0.90±0.66; p<0.02), (iii) a greater % of biliary CH in vesicles (64.7±8.2% vs 38±0.40%; p<0.001), (iv) more unstable vesicles (CH:PL ratios of 1.849±15 vs 0.540±0.30; p<0.03) and more rapid NTs (7.7±2.9 vs 20.7±3.3; p<0.02). NTs were normal (>100) in all 7 controls, of the 5 post-dissolution patients and the PCCL patient but were minutely (<50%) in the remaining 4 post-dissolution patients, all of whom remain stone-free 2-3mo after stopping oral BAs. SUMMARY/INTERPRETATION: These results confirm that after GBS dissolution/clearance GB bile becomes less supersaturated with CH, and show that it has an increased CH:PL ratio, is rich in vesicular CH and has unstable vesicles - factors which predispose to short NTs and GBS recurrence. Thus, the nucleation defect persists in some, but not all post-dissolution patients, but the value of measuring NTs in predicting GBS recurrence is, as yet, unknown.

F200

HYDROPHOBIC/HYDROPHILIC BALANCE OF PROTEINS IS A MAJOR DETERMINANT OF CHOLESTEROL CRYSTAL FORMATION IN MODEL BILE.

HA Ahmed, MA Patrini, GL Laffuer, PP Jazrawi, MA Hamdyah, TC Northfield, Department of Medicine, St George’s Hospital Medical School, London, UK.

Biliary proteins play a fundamental role in modulating nucleation of cholesterol crystals from supersaturated gallbladder bile, acting either as pro- or anti-nucleating agents. However, conflicting results have been obtained in attempts to locate specifically active proteins. Our hypothesis, therefore, was that this may be a non-specific effect of proteins, related to their secondary structure or to their overall hydrophobic/hydrophilic balance. We studied the effect of a number of "non-specific" proteins with different secondary structures on cholesterol crystal formation in model bile. The overall hydrophobic/hydrophilic protein indices were experimentally determined by measuring their retention time on a phenyl-agrose column. The potency of each protein in enhancing or inhibiting crystal formation was ranked according to the lowest protein concentration capable of significantly influencing crystal formation by comparison with control. Some of these proteins (chymotrypsin and myoglobin) significantly enhanced crystal formation, while some (apolipoproteins AI, All and B) inhibited it, and others (albumin and chymotrypsinogen) showed no effect. The different effects were not related to their secondary structure but to their hydrophobic/hydrophilic index, with the most hydrophobic proteins showing maximal pro-nucleating potency and vice versa (r=0.95, p<0.001). Pronucleating proteins enhanced, while anti-nucleating proteins inhibited, the transfer of cholesterol and phospholipid from micellar to vesicular forms. We conclude that the effect of proteins on cholesterol crystal formation is a non-specific one; and that for a mixture of proteins, it is mainly related to their overall hydrophobic/hydrophilic balance rather than to their secondary structures.

F201

BILIARY MOTILITY AND CCK LEVELS AFTER TRUNCAL VAGOTOMY

R Patankar, IS Bailey, A Sandersen, C D Johnson. University Surgical Unit, Southampton General Hospital, Southampton.

Bile stasis and an increased incidence of gallstones is observed after truncal vagotomy. Cisapride may increase contraction of the gallbladder and reduce bile stasis. Seven patients after TVP and 13 normal subjects (CTR) were studied after an overnight fast. Gallbladder volume and plasma CCK were measured before and after 15, 30, 60 and 90 minutes after a small, fatty meal. Six TVP patients and six CTR subjects were entered into a double blind, prospectively randomised, placebo controlled study of placebo/cisapride 10 mg and TVP.

CCK levels in TVP patients were higher than in controls. Baseline CCK was TVP 1.12 (0.92-2.29), CTR: 0.56 (0.31 - 1.15) p<0.01. Maximum CCK was TVP: 16.49 (9.12 - 18.04), CTR: 5.62 (2.49 - 10.84) p<0.01. Integrated CCK was TVP: 621.07 (307.5 - 864), CTR: 300.5 (160.9 - 642.9) p<0.02. Gallbladder contractility was greater in TVP patients. CCK was inhibited, or increased in all TVP patients, while TVP patients had a higher BW when taking Cisapride: 7.13 (4.19 - 15.95)mg vs placebo 5.21 (3.85 - 14.04)mg. This may be related to denervation of the gallbladder. Significant elevations of bile acids, bile salt ratios after TVP were due to decreased feedback inhibition of CCK release consequent on reduced gallbladder emptying. This may contribute to post vagotomy symptoms.

ENTERAL NUTRITION DOES NOT PROTECT AGAINST BILARY SLUDGE IN CRITICALLY ILL PATIENTS.

SM Catnach, CJ Hinds, PF Fairbrough, Dept Gastroenterology & Anaesthesia, St Bartholomew’s Hospital, West Smithfield, London EC1A 7BE.

Total parenteral nutrition and fasting are associated with the development of biliary sludge, presumably due to lack of oral nutrients leading to reduced cholecystokinin release and gallbladder stasis. Biliary sludge is common in patients in intensive care, many of whom are fed parenterally. The effect of continuous infusion of oral nutrients on gallbladder motility has however been little studied, and it is not known whether such feeding regimes are associated with the formation of biliary sludge. We have therefore prospectively studied 18 patients (13 men), median age 60 years (range18-76), admitted to the intensive care unit (ICU) who were fasted for a median of 2 days (range 1-5) and then fed enterally. Five patients (30%) received enteral nutrition (EN) (1) while on parenteral nutrition (PN), or (2) while receiving intravenous ninitine. Patients received either 21 of Entera (8 patients) or 2Cal (7 patients) daily or 11 Entera (3 patients) in a 6 hourly cycle of 5 hours infusion, 1 hour rest, repeated 4 times daily. All patients were ventilated and received muscle relaxants intravenously. 13 patients were sedated with intravenous morphine by infusion and 3 patients with subarachnodal haemorrhage received intravenous midazolam. Ultrasound scans of the gallbladder were obtained on the day of admission to ICU and daily thereafter until discharge or death. Median length of stay on ICU was 7 days (range 2-37). One patient had gallstones and another had sludge on admission to ICU. Ten of 18 (56%) patients developed sludge after a median of 2 days (range 2-70), at least one risk factor for sludge formation (2 abdominal surgery, 7 head injury or neurosurgery, 1 cardiac surgery). No patient cleared biliary sludge during the study.

We conclude that in patients on ICU enteral nutrition given continuously does not prevent the development of biliary sludge, possibly because of failure of gallbladder contraction. These patients, as well as those on parenteral nutrition, should be considered for prophylactic regimes to prevent biliary sludge.
OUTCOME OF 'SALVAGE SURGERY' FOR BILE DUCT STONES

B Davidson, A Lautr, R Horton, A Burroughs, JS Dooley
Royal Free Hospital and Medical School, Pond Street, London

Endoscopic sphincterotomy (ES) is the treatment of choice for common bile duct (CBD) stones in elderly patients. For those in whom endoscopic clearance of the CBD fails the treatment options include stenting, dissolution therapy and lithotripsy. Surgery is often avoided because of the reported high morbidity and mortality in elderly patients. We reviewed the outcome of patients referred for 'salvage surgery' following failed endoscopic clearance of CBD stones.

Over a three year period 100 patients with CBD stones were referred specifically for endoscopic clearance of the CBD (median age 69 years, range 19-97). In 7 patients CBD clearance was possible without ES and in 5 patients ES was considered inappropriate (2 acute cholecystitis, one stone >50 mm, one CBD packed with stones and one Milizzi syndrome). ES was attempted in 88 and was successful in 75 (85%). Of the 13 patients failing ES or stone removal 'salvage surgery' was performed in 9 (no ES) and 4 were stented. Of patients having successful ES (n=75) 10 were referred for surgery because of incomplete CBD clearance.

Surgery was performed to achieve CBD clearance in 19 patients (8M, 11F, median age 77 years, range 47-90). Eight of the 19 had previously undergone a cholecystectomy (42%) and 17 of the 19 had biliary tract drainage pre-operatively (90%) (naso-biliary, percutaneous). The procedures performed consisted of choledocholithotomy in all plus cholecystectomy (10), choledochoduodenostomy (7) + choledochojejunostomy (7). There were no deaths or major complications. The median total in-patient stay was 26 days (range 14-75 days) and the median post-op stay was 12 days (range 7-50).

We would conclude that open surgery can be performed safely and effectively in elderly patients in whom an endoscopic approach fails to clear CBD stones.

THE PLACE OF ENDOSCOPIC THERAPY IN BILE LEAKS POST-LAPAROSCOPIC CHOLECYSTECTOMY

Roger Barton, ARW Hatfield, B Thee, RCO Russell, Departments of Gastroenterology and Surgery, The Middlesex Hospital, Mortimer St, London, W1N 8AA

We have already had considerable experience in the endoscopic management of biliary leaks after open cholecystectomy. We now report experience with the laparoscopic management of biliary leaks following laparoscopic cholecystectomy (LC). Eighteen patients with bile leaks post-LC have been referred to our unit, which has an extensive referral practice, since May 1989. Ten were females, with 8 males, mean age 59 (24-81). ERCP was performed in all patients with a view to endoscopic therapy. Four patients had complete biliary disruption, two with clipped bile ducts and two with transections; all four had a hepatico-jejunostomy, three after an initial period of external biliary drainage. Of the remaining 14 patients, 10 had a leak from the cystic duct stump, 5 in association with CBD stones. Of the other four patients, one had a leak from the CBD, one from the right intrahepatic duct, and two from both of these ducts together; none had stones.

In four of 5 patients with retained stones, successful clearance was achieved at initial ERCP and sphincterotomy. In one the stone was impacted, a stent placed, and the stone extracted two months later after the leak had healed. In all, stents were inserted in 11 of the 14 patients (4 of 5 patients with leaks and stones, and 7 of 9 with leaks alone). In all patients with stents, the leaks healed quickly, and stents were removed within 1-3 months. In two of the three patients with sphincterotomy alone at the leak persistence, this was followed by rapid healing. This was surprising, since sphincterotomy alone, in our experience after open cholecystectomy, usually allowed leaking cystic ducts to heal. In ten of 11 patients stented, no stricture was seen to have developed at the site of the biliary leak when the stent was removed. In one patient, a long, probably ischaemic, stricture was seen at initial presentation, and remained once the leak had healed, requiring longer term stenting.

Conclusions: Biliary leaks following LC can be managed simply and effectively by endoscopic stent insertion. Leaks heal quickly without stricture formation, and surgical exploration can be avoided.
ANTIGASTRIN ANTIBODIES RAISED BY GASTRIMMUNE INHIBIT THE GROWTH OF COLORECTAL TUMOURS.

I.A. Watson, D. Michael, J.E.R. Robertson, B.T.C. Steel and Z.D. Hardcastle. Department of Surgery, University Hospital, Nottingham, UK and APhton Corp, California, USA.

Gastrin promotes the growth of colorectal tumours. An immunogen has been developed called Gastrimune in which the amino terminus of G17 is linked to diphteria toxoid (DT) and which raises specific neutralizing antibodies against G17 when administered in vivo. Two in vivo models have been developed to determine the efficacy of anti-G17 antibodies on colorectal tumour growth. The first model involved the human colorectal tumour, AP5 grown s.c. in nude mice. AP5 was derived from a primary tumour specimen and used at passage 2 from the patient. AP5 expresses gastrin receptors on 75 to 100% of the cells as detected with the anti-gastrin receptor antibody, 2CI, and has intracellular gastrin immunoreactivity on 5-25% of the cells as detected with an anti-G17 polyclonal antibody. In vitro, AP5 xenografts were significantly stimulated by G17 (10 ng/mouse/day by continuous infusion) (p=0.047) and anti human G17 antibodies raised by Gastrimune (administered IV, 0.5ml daily) significantly reduced the basal growth of AP5 xenografts by 46% when compared to treatment with anti-DT antibodies (p=0.0071).

The second model involved the rat colon line, DHDK12, which is gastrin receptor positive as shown by histological staining with the 2CI antibody. BDIX rats were immunised 3 times at 3 weekly intervals with either a rat G17-DT immunogen or a DT control immunogen prior to subcutaneous (s.c.) injection of the DHDK12 cells. Rat anti-rat G17 antibodies had previously been shown to be present in the sera of the animals by an enzyme-linked immunoabsorbant assay. Rats immunised with the G17:DT immunogen had a significantly reduced tumour burden with a mean weight of 1.18g compared to 2.44g for the control which received DT only (p=0.0453).

UKCCCR Guidelines were adhered to throughout all animal experiments.

Gastrimune may be used to raise anti-G17 antibodies in patients which may have a valuable role in the therapy of colorectal cancer.

DETECTION OF RAS MUTATIONS IN FASCAL MATERIALS FROM COLORECTAL CANCER PATIENTS


Colorectal Cancer Unit, ICRF, St Mark’s Hospital, U.K.

Mutations at codons 12 and 13 of the ras gene are an early step in carcinogenesis and they are found in about 40% of colorectal adenomas. Because of the early nature of this marker, it would be of great medical interest if it became possible to detect the presence of ras mutations in exfoliated colonic cell DNA from faecal materials such as endoscopic washings or stool specimens.

A method has been developed for extracting DNA from faecal material. Detection of human DNA was performed by PCR using primers specific for mitochondrial DNA and ras oncogene sequences. We have also investigated the presence of ras mutations in faecal samples obtained from sporadic colorectal cancer patients using an allele-specific mismatch method developed by Stork et al. (Oncogene 1991, 6: 857). Our data show that ras mutations are detected in these faecal samples at different stages of the disease. These mutations were confirmed on the corresponding tumours using the same method. These promising results represent an important stage in the development of a novel test for detecting early stages of colorectal cancer.


There has been a world-wide effort to identify patients who carry a high risk of metachronous colorectal adenomas after endoscopic polypectomy for colorectal adenomas. We prospectively reevaluated, with colonoscopy, 40 patients (21 18F,19M) who had undergone polypectomy for adenomas during a one-year period. The surveillance colonoscopy was performed two years after the index colonoscopy. All the patients underwent total colonoscopy. Positive findings after polypectomy, in order to detect missed synchronous polyps, and the colon was confirmed as clean. Patients with colon cancer were excluded. In all removed adenomas the expression for PCNA was studied (PC10 antibody was used for immunolocalisation). PCNA immunoreactivity was estimated by the intensity of nuclear staining, the percentage of positively stained dysplastic glands and the percentage of positively stained cells in selected areas. The intensity of nuclear staining was scored on a four-point scale (no staining, weak, moderate, strong). X2 test was used for statistical analysis. Among the 40 reexamined patients in 16 patients (group A), recurrent adenomas were found and in the remaining 24 patients (group B) the colon was free of polyps. A total number of 51 adenoma (25 in group A and 26 in group B) in index colonoscopies was found. Strong nuclear staining was more pronounced in group A index adenomas (9/25) compared with group B adenomas (2/26) (P<0.005). The patients of group A had adenomas with a significantly more pronounced nuclear staining compared with group B patients (P<0.01). The percentage of positively stained dysplastic glands was more pronounced in group A index adenomas compared with group B adenomas (P<0.05). The results were also statistically significant (P<0.05), between the two groups, concerning the percentage of positively stained cells. A total number of 21 metachronous adenomas was found. The intensity of nuclear staining, the percentage of positively stained dysplastic glands and the percentage of positively stained cells in the metachronous adenomas were less pronounced compared with the index adenomas of the same group. Although the number of cases is limited we may conclude that the increased PCNA expression in colonic adenomas may be a predictor for metachronous colorectal adenomas.

REGIONAL PROLIFERATIVE ACTIVITY IN THE COLON OF PATIENTS AT RISK OF HEREDITARY NON POLYPOSIS COLON CANCER (HNPPC). SE Patchett, BP Saunders, C. Harrocopus, SV Hodgson, EM Aletas, MG Farthing, Dept of Gastroenterology, St Bartholomew’s and St Mark’s Hospitals, London.

Subjects from an HNPPC kindred (Lynch type 1 and type 2) have an increased risk of developing large bowel cancer. Tumours occur at a young age and are characteristically right sided. Colonic mucosal proliferation is known to be increased in several groups of patients at risk of colon cancer. This study was performed to assess the patterns of mucosal proliferation at different sites in the colon of patients at risk of HNPPC and to determine whether a HNPPC kindred subjects. Mucosal biopsies were obtained at colonoscopy from 21 patients at risk of HNPPC (16 female, mean age 42y) and from 7 normal subjects (4 female, mean age 38y). Samples were fixed in Carnoy’s solution and stored in 70% alcohol. Following hydration, hydrolysis and staining with Schiff’s reagent, whole colonic crypts were microdissected, and crypt area and whole crypt mitotic counts (WCMC) were quantitated.

<table>
<thead>
<tr>
<th>Region</th>
<th>Caecum</th>
<th>Transverse colon</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HNPPC</td>
<td>Normal</td>
<td>HNPPC</td>
</tr>
<tr>
<td></td>
<td>11.7±0.44</td>
<td>9.4±0.29</td>
<td>8.8±0.46</td>
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<tr>
<td>WCMC</td>
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<td>AREA</td>
<td>μm&lt;sup&gt;2&lt;/sup&gt;</td>
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<td>μm&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>11.7±0.44</td>
<td>9.4±0.29</td>
<td>8.8±0.46</td>
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</table>

In HNPPC subjects, WCMC and crypt area were significantly greater in the caecum than in the transverse colon and the left colon (p<0.001). Compared to normals, WCMC in HNPPC subjects was significantly greater in the caecum only (p<0.05). A significant right to left shift was also observed in normal subjects but the percentage increase from right to left was two-fold greater in HNPPC subjects. These results confirm a proximal to distal proliferative gradient in the human colon and suggest that this may be exaggerated in HNPPC. This increased proximal proliferative rate may be a factor in the development of right-sided cancer in these patients.

Echo-planar magnetic resonance imaging of the gastrointestinal tract offers a non-invasive method to study the pathophysiology of gastrointestinal function. Our group have previously demonstrated the feasibility of prolonged GI tract imaging using EPI but correlation with conventional manometric methods has not been assessed. The aim of this study was to evaluate gastric duodenal motility measured by conventional perfused tube pressure manometry with images obtained from EPI.

Seven fasted volunteers were intubated with a 6 channel perfused tube catheter system. Four pressure ports (1 cm apart) were positioned across the antrum-pylo-duodenal segment and a further 2 in the duodenum. Motility patterns were displayed on a chart recorder and stored on an FM tape recorder. A trigger pulse from the imaging system was recorded on one channel of the chart recorder to date all data points. EPI images were obtained by highlighting the gastric lumen using 1 L of tap water as a contrast medium. 128 x 128 MBEST-images were collected at 2 sec intervals over periods of 11 min from a transaxial slice through the pylorus. Patterns of fasting upper GI motility were visualized for up to 2 hr and subjects were then fed with 500 ml of a semi-solid meal (bread) or a high fat liquid (calgon) in order to assess the effects of nutrients on motility and transit. One subject was also given cisapride (20 mg oral) to assess its effects on antroduodenal motility and gastric emptying.

Images were processed at 8 times real time to form a video loop to visualise contractions and flow across the gastro-duodenal junction. Manometric data was transferred and placed on the same time axis as the EPI images. Following the ingestion of the fatty liquid, the waterfat interface could be clearly seen in the gastric body, with preferential emptying of water. This was in keeping with theoretical and experimental considerations of fatty materials in the stomach, which are known to delay gastric emptying. Further development will offer an alternative non-invasive method of assessment of gastrointestinal motility and transit.

The DISTRIBUTION AND ACTION OF NEUROGENES IMMUNOREACTIVE FOR NITRIC OXIDE SYNTHASE IN HUMAN INTESTINE. D A Wattchow, S J H Brooks, L Kow, M Costa, D Breid and S Physiological and Surgery, and The Centre for Neuroscience, Flinders University of South Australia, Bedford Park, South Australia, and the Johns Hopkins School of Medicine (introduced by P. Prichard).

The relaxation of intestinal smooth muscle is controlled by the release of several substances from enteric neurones, one of which is nitric oxide (NO). This study has been carried out to determine the distribution of neurones immunoreactive for the synthetic enzyme for nitric oxide in human intestine and secondly, to investigate the effect of NO-nitro-L-arginine methyl ester (L-NNAME), a nitric oxide synthase inhibitor, on relaxation of human intestinal muscle strips mediated by enteric neurones.

Samples of healthy intestines taken at surgery were fixed, incubated with the antibody to nitric oxide synthase (NOS) and a secondary antibody/avidin/biotin immunoperoxidase reaction was performed. Muscle strips in either circular or longitudinal orientation were cut and placed in oxygenated Krebs solution, containing bovine (10-6 M) and guanethidine (5x10-6 M) in organ baths. Electrical field stimulation (60 V, 0.2-0.5 ms, 1-10 Hz, for 5 sec) was delivered by a pair of ring electrodes. In sections, large numbers of NOS-immunoreactive fibres were present in the circular muscle. The numbers were fewer and more variable in the longitudinal muscle layer. Many immunoreactive cell bodies and varicosities were seen in the myenteric plexus. No nerve cell bodies or fibres were seen in the mucosa, submucosa or serosa. Using the histological appearance, there were many NOS-immunoreactive cell bodies with lamellar processes. Nerve fibres were visible in the internal muscular layers as well as the myenteric ganglia. In circular muscle preparations L-NNAME abolished nerve mediated relaxations. This relaxation was reversed in most preparations by the addition of L-Arginine. In longitudinal muscle strips, L-NNAME maintained but did not abolish the relaxation and had a more variable effect.

In conclusion, in the human intestine the inhibitory motor neurones to the circular muscle fibres impregnated and utilize it as a mediator to relax the muscle. The role of the NOS-immunoreactive interneurones remains to be determined.
RELATIONSHIPS BETWEEN NEURON NUMBER AND DISTENSION RESPONSES FOLLOWING EXPERIMENTAL MYENTERIC NEUROPATHY.
A.D. Higham, F. Owen, E. Kirkman, D.G. Thompson. Departments of Medicine, NWIRC and Biological Sciences, University of Manchester, England.

Aims: To study the effects of variable myenteric nerve damage on rat jejunal motor responses to distension and relate changes to nerve cell number. Methods: Denervation was induced by serial application of 0.04 and 0.05% (w/v) Benzalkonium chloride (BAC) in 0.9% NaCl. Controls (C) received 0.9% NaCl. Distension responses (work done mg/cm) 1cm oral or anal to stimulus were recorded in vitro, 15 days later. The remaining EMG was studied. Results: The number of myenteric neurons in each preparation was determined and compared with the magnitude of the responses observed. Results: Denervation led to a 70% decrease in the number of myenteric neurons. The distension response decreased by 90% (n=6, p<0.05). In the controls, the distension response was 37±5ml; and 35±4.43±9AU, p>0.05; TTX blocked the response to distension (n=6, p<0.05) and distension was reduced by 90% (n=6, p<0.05). The response of the remaining neurons was corrected for the number of normal neurons present. Conclusions: A decrease in myenteric neurons leads to a decrease in the distension response.

SELECTIVE INHIBITION OF POST-PRANDIAL SMALL BOWEL MOTILITY IN MAN BY A SPECIFIC M3 MUSCARINIC RECEPTOR INHIBITOR. Evans, D.F. Benson ML, Williams, S., Wingate DL. Gl Science Research Unit, London Hospital Medical College, London, and *Pfizer Research Laboratories, Sandwich, Kent, UK.

We postulate that patients with functional bowel disorders with symptoms suggestive of an exaggerated motor response to meals may get relief by reduction of postprandial small bowel motor activity. A novel approach to this was tested in human volunteers. M3 selective muscarinic receptor inhibitor, equopretide to aripnone with few of its side effects.

We studied the effect of 9 days dosing of Z on proximal small bowel motility in 16 healthy men, in a prospective, randomised, placebo (P) controlled study. Duodenal jejunal motility was measured with a nasojejunal catheter (od 2.5mm) containing three micro-transducers (15 cm spacing), positioned across the ligament of Treitz. Data was recorded on a portable 2MB data logger sampling at 2 Hz for 36 hrs, with standard meals on each day. Subjects were studied twice, with an interval of 8 days between studies. 20 mg Z bid (n=8) or P (n=8) was administered before breakfast on day 2 and continued until the evening of day 10. Data was analysed manually and by computer program for periodicity, migration velocity, and incidence of phasic patterns of motility. The results were compared using analysis of variance. There was no change in any aspect of intraluminal pressure, or in the pattern of postprandial motility. Activity was significantly decreased in the control diet compared with the high fat diet.

SENSORY AND MOTOR RESPONSES TO EXPERIMENTAL DISTENSION OF THE HUMAN PROXIMAL SMALL BOWEL.
D.Covic, A.D. Higham, J. Barlow, D.G. Thompson. Department of Medicine, University of Manchester, England.

Aims: To define normal human small intestinal motor responses to graded distension and their relationship to perception, distension pressure and distension volume. Subjects: 15 normal volunteers, aged 32.5±11.5 yrs. Methods: After passing a small intestinal intubation with a multilumen manometric catheter incorporating a 4cm inflatable balloon, distensions were performed for 2.5min every 7.5min, increasing the balloon volume in 5ml increments to the maximum tolerated. Manometry was recorded 4cm above and below the balloon. Pressure and distal responses to each distension were assessed by calculating the difference between the areas under the manometric tracing before and during balloon inflations; the differences were expressed as area units (AU). Intraintestinal distension pressure and perception characteristics were assessed at each balloon volume and by subjects the protocol was repeated on a separate day. Results: Perception: sensory threshold was 25±5ml; pain threshold was 35±5ml; maximum tolerated volume was 42±12.5ml. Pressure: sensory threshold, balloon volume and pressure were closely related (mean±SD 31.0±10mg/Hg/10ml; r=0.93, p<0.01). Above this threshold, further distension did not increase pressure (mean±SD 2±4mg/Hg/10ml; r=0.78, p<0.05). Motility: below sensory threshold, both balloon volume and pressure were closely related (mean±SD 4.4±3.9AU, p<0.05). distalA=0.9±4AU, p<0.05). Above this threshold, activity increased proximally (A=17±3±3AU, p<0.05) but was unchanged distally (A=2±1.1AU, p>0.05). 14 of 15 subjects tolerated the proximal balloon activation (mean±SD 2.5±12.5ml; A=1.5±0.2AU, p<0.05) but distal balloon activation (A=1.5±4.0AU, p<0.05) and A=1.1±1AU, p<0.05 respectively). The threshold for this inhibition was 32.5±7.5ml and was unrelated to pain threshold (r=1.89, p>0.05). The repeat studies showed identical and consistent threshold and motor responses throughout distension (n=0.928, p<0.01). Conclusions: The human small intestine responds in a consistent stereotypic manner to graded distension, responses being related to the distension volume and not to the distension pressure, indicating recruitment of stretch-sensitive mechanoreceptors in their induction.

LARGE SCALE AMBULATORY STUDIES CONFIRM ABNORMAL SMALL INTESTINAL MOTILITY IN IRITRITABLE BOWEL SYNDROME. M. A. Loudon, P.K. Small, B. Waldron, D. Smith, F.C. Campbell. Department of Surgery, Ninewells Hospital, Dunbees. Scotland DDI 9SY.

Irritable bowel syndrome (IBS) is a common cause of chronic abdominal pain and irregular bowel habit. Altered gut motility may be contributory but large scale studies are lacking. We evaluated jejunal motility by 24-hour ambulatory studies, in 50 IBS patients (constipation predominant N=19, diarrhoea predominant N=31) and 15 volunteers. Meal timing and caloric intake were standardised. Symptoms were scored and stool frequency assessed. Manometric catheters, mounted with 3 solid state pressure sensors, at intervals of 12cm were positioned in the jejunum. Analysis of motility was assisted by microcomputer

Results: Pain scores were similar in both IBS groups (90±49.73)*[Constipation] vs 97±57.78*[Diarrhoea]. Mean stool frequency was 0.424 hours [Constipation], 2.24/4 hours [Diarrhoea], and 0.38/2 hours [Normal]. p<0.025*[Constipation vs Diarrhoea]. Migration of the Migrating Motor Complex (MMC) Phase III was slower in IBS [1.57±4.3 cm/min, Constipation, 3.18±5.3 cm/min, Diarrhoea] versus [3.18±5.3 cm/min, Normal]. p<0.025*[Constipation vs Normal]. Full duration of Phase II activity (as a percentage of fasting state) was greater in IBS [60% (54.4±6.3%) Constipation, 55% (47.5±6.7%) Normal]. p<0.04*[Diarrhoea] vs 49% (42-54%)*[Normal]. p<0.001*[IBS vs Normal]. Discrete cluster contractions were common in IBS [105 (45-256)* Mins/study]. Constipation, 101 (25-160)* Mins/study Diarrhoea] vs 0 (0-160)* Mins/study. Discreet contractions are common in IBS. These patterns may represent a disorder of organisation and control of small bowel motility.

Conclusion: Jejunal motility is abnormal in IBS. Irregular contractions (Phase II) activity is increased and migration of the MMC is impaired. Discrete cluster contractions are common in IBS. These patterns may represent a disorder of organisation and control of small bowel motility.

**Median (Inter-quartile range) Gastroenterology. 1983, 10, 34-1.
ASSOCIATION OF CENTRAL 5-HYDROXYTRYPTAMINE (5HT) FUNCTION IN IRRITABLE BOWEL SYNDROME

DA. Goral, PA. D (73) S, SH Medich, GW Libby, MG Farthing

Departments of Gastroenterology & Chemical Endocrinology, St. Bartholomew's Hospital, London.

Irritable bowel syndrome (IBS) may represent a disorder of the brain-gut axis. Responses of 5HT neurons in the enteric nervous system may reflect those of 5HT neurons in the central nervous system. Altered sensitivity of central 5HT receptors may be a biological marker for IBS, as it is in depression. Deacteptamocine selectively stimulates central 5HT receptors, eliciting prolactin release via the hypothalamic-pituitary axis. This prolactin response is diminished in depression. We have found this neuroendocrine challenge test to investigate central 5HT responses in 12 IBS patients (mean age 34.6 y, range 19-57, 9f), and 12 healthy control subjects (mean age 29.6 y, range 18-57, 4f).

After an overnight fast, blood was drawn for 2 baseline prolactin levels 45 min after intravenous cannulation. 30 mg deacteptamocine was given orally and prolactin levels taken hourly for 5 hr. Prolactin response was assessed by the maximum prolactin increase above baseline (Δ prolactin), and by area under the curve (AUC). All subjects underwent psychiatric assessment by structured interview and self-report questionnaires.

### Results

<table>
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<tr>
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<th>Controls</th>
<th>IBS</th>
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<tr>
<td>Baseline prolactin (mIU)</td>
<td>236.3 ± 23.1</td>
<td>224.7 ± 54.6</td>
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<tr>
<td>Δ prolactin (mIU)</td>
<td>147.8 ± 39.4</td>
<td>164.4 ± 40.4</td>
</tr>
<tr>
<td>AUC</td>
<td>1328 ± 148</td>
<td>1228 ± 167</td>
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IBS patients had greater psychological morbidity with a Hospital Anxiety & Depression scale mean score of 10 (range 2-18), compared to 5.5 (1-25) in controls (p<0.005). Beck Depression Inventory score was median 3.5 (range 0-6) in IBS, and 1 (0-17) in controls (p=0.05). Three IBS patients and one control met DSM-III-R criteria for major affective disorders.

Thus central 5HT sensitivity is not abnormal in IBS patients despite higher depression scores. This finding suggests that apparently 'depressed' IBS patients do not have this central biochemical marker of depression.

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THE EFFECT OF NICOTINE AND ITS METABOLITES ON THE DISTAL COLON


To determine the effect of nicotine on distal colonic motility 8 healthy smokers (2 M, mean age 26.5 y) were studied on 2 separate occasions in random order. On one occasion they smoked 1 cigarette containing 1.1mg nicotine over 5 min and on the second occasion they did exactly the same except the cigarette was not lit. A further 8 non-smokers (4 M, mean age 25.6 y) were investigated on 1 occasion when they chewed nicotine gum, 4mg over a 30 min period. Colonic pressure activity was measured using a water perfused tube assembly placed in the true sigmoid colon. A baseline period of 30 min was recorded, following which the cigarette was smoked or sham smoked, or the gum chewed and recordings carried on for a further 4 hr. Blood was drawn from an indwelling cannula for estimation of plasma nicotine and cotinine levels by HPLC prior to, at 15 min, and then at 30 min intervals after smoking or starting chewing. Smoking rapidly increased colonic pressure activity as measured by the colonic activity index (area under the curve) for the study segment as a whole. [615 mmHg.min, mean (49, SEM) smoking 631 mmHg.min, P=0.021] temporarily related to rising cotinine levels which plateaued at 30.24 ng/ml, mean (5.47, SEM) 90 min after the cigarette [P < 0.001 vs baseline levels of 0.27 ng/ml mean, 0.04 SEM). This was followed by profound and prolonged inhibition of pressure activity. [263 mmHg.min (34) smoking 122 ± 92 (P=0.01), P<0.001; pairing smoking, P=0.001, paired t test) and this coincided with peak plasma nicotine levels (9.97 ng/ml mean, 0.82 SEM, P < 0.001 vs baseline levels of 0.27 ng/ml mean, 0.04 SEM). These findings were in the non-smokers with an initial rise in AI [540 mmHg.min mean baseline(63, SEM) vs 751(138) during chewing, P=0.1] followed by inhibition [284(23)] for the remainder of the recording, P=0.001).

Basal nicotine and cotinine concentrations were 0.26 ng/l, mean (0.13, SEM) and 3.2 ng/l(1.5) vs peak levels of 9.11, P<0.001 vs basal for nicotine and plateau levels of 28.2(3.7), P=0.001 vs basal for cotinine. Nicotine and its metabolites profoundly affect colonic motility.

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INFLUENCE OF PSYCHIATRIC MORBIDITY ON SELF-APPRaisal OF SYMPTOMS IN IRITABLE BOWEL SYNDROME (IBS). JE. Gomboroz, PA. Dewman, GW. Libby, MG Farthing. Dept. Gastroenterology, St Bartholomew's Hospital, London.

We have studied the determinants of consultation behaviour in IBS (Manning Criteria) using a more rigorous assessment of psychiatric morbidity than previous studies. Three non-consulters and four groups of IBS consultants (n=22) and non-consulters (n=18) were drawn from a community sample in terms of their response on the Bowel Disease Questionnaire (Talley et al, 1990). Beck Depression Inventory, Beck Anxiety Inventory and subjected them to a Structured Clinical Interview for DSM-III-R psychiatric disorders. 91% of consultants had seen a doctor for abdominal pain. We found, as have others, that they reported experiencing more severe, frequent, prolonged and disruptive bouts of pain than non-consulters. 68% had consulted about abnormalities of bowel habit. More consultants described their bowel habit as abnormal (73%) and disruptive (32%) than non-consulters (28% and 16%, respectively, P=0.02). An evaluation of their response to questions about the frequency and consistency of their stools confirmed that 86% of consultants rated this as having an abnormal bowel habit. However, 78% of non-consulters did also. Non-consulters therefore show a tendency to normalise their bowel dysfunction, which breaks down among the consultants. This finding suggests that there is an important difference between consultants and non-consulters in terms of their self-appraisal and perhaps in their ability to cope. We would regard our findings on the psychological factors as highly relevant in this respect. The consultants scored significantly higher than the non-consulters both on the BDI, mean (SD) 8.9(6.9) vs 4.8(3.5) (p=0.03) and the BAI 9.4(1.2) vs 5.7(1.2) (p<0.001). 14 (64%) consultants qualified for a DSM-III-R diagnosis of an affective disorder compared with 4 (22%) of non-consulters. There was no significant difference on psychological evaluation between the non-consulters and a symptom-free control group. We conclude that psychiatric morbidity is highly relevant to the clinical presentation of IBS through an influence on the patients' evaluation of their symptoms, which are necessarily subjective.

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INVESTIGATION OF GASTRIC MUCOSAL BLOOD FLOW, EPITHELIAL CELL PROLIFERATION AND NEUTROPHIL ACTIVATION IN GASTRIC ADAPTATION TO ASPIRIN-INDUCED MUCOSAL DAMAGE IN MAN. L. L. L. Bell and J. C. James, Dept. of Medicine, E. University of Münster, Münster, Germany.

The damaging effects of aspirin (ASA) on gastric mucosa and gastric adaptation to repeated exposure to ASA are well documented, but the mechanism of those effects are poorly understood. In this study, the effects of 14 days continuous oral ASA administration (1g b.i.d.) were examined in 8 healthy male volunteers. Mucosal damage was evaluated by gastroscopy at 3rd, 7th, 14th, 16th and 18th day, during which the mucosal blood flow was measured with laser-Doppler flowmeter and mucosal biopsies were taken for estimation of DNA synthesis [3H-thymidine incorporation into DNA]. Before each endoscopy, the microbleeding rate was measured in gastric washings. Blood samples were drawn for the assay of activation of neutrophils by measuring their association to platelets. - ASA induced acute gastric mucosal damage in gastric corpus; the endoscopy lanza score reached the maximum of 3.5±0.5 at 3rd day and then lesioned to become only minor (1±0±2) at the 14th day, thus confirming the occurrence of gastric mucosal injury. At the 14th day the mucosal blood flow significantly increased at 3rd day when compared to initial values (89±8 vs 52±5 ml/min/100g tissue) and remained elevated till the end of ASA administration. These results correlated well with increased DNA synthesis that at the 14th day reached about 78±19 vs 59±21 DNAIDNA. Initially and at the 16th day still remained significanly high (92±92 vs 59±21). Gastric mucosal microbleeding was highest at the 3rd day of ASA treatment and then decreased significantly to virtually normal values at the end of the study. The activation of neutrophils was increased during ASA administration and remained elevated till the 16th day. We conclude that; (1) initial mucosal damage to ASA is followed by an increased blood flow and mucosal cell proliferation and as a result activation of neutrophils; (2) gastric adaptation to ASA involves an increased mucosal blood flow and enhanced mucosal cell proliferation as well as the activation of neutrophils.
GASTROINTESTINAL SIDE EFFECTS OF NSAIDS: A COMMUNITY-BASED STUDY. R B Jones, C L Taiti Primary Health Care, University of Newcastle Upon Tyne.

Estimates of the frequency of gastrointestinal side effects of non-steroidal anti-inflammatory drugs (NSAIDs) vary widely and interpretation of most studies is difficult because there are no control groups for comparison. A community-based study reports on the prevalence and pattern of gastrointestinal symptoms in a large cohort of patients taking NSAIDs and in a matched control group.

Using computerised repeat prescribing systems in 8 general practices we identified 1141 patients taking long-term non-steroidal anti-inflammatory therapy and an equal number of age and sex-matched controls. A validated questionnaire was sent to each subject to obtain information about gastrointestinal symptoms. After a single reminder, the response rate for the patients was 89% and for the controls 86%.

The mean age of the subjects was 65.6 years: 45% were men and 55% women. The NSAIDs involved were aspirin (33%), ibuprofen (17%), naproxen (11%), piroxicam (9%), indomethacin (8%), diclofenac (7%) and other drugs (15%). Co-prescription with an H2 blocker was identified in 7% of subjects.

The twelve month prevalence of ulcer-like and reflux-like dyspepsia was almost identical in each group, at about 45%, with considerable overlap between symptoms; one in three patients and controls had consulted a general practitioner because of these symptoms. Constipation was significantly more frequent among the NSAID - taking patients and was the commonest reason for stopping medication.

Upper gastrointestinal symptoms in chronic NSAID takers are no more frequent than the background level in the community. Only a minority of patients report them to their general practitioners. Constipation is a common and under-reported problem in this group of patients.

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COCALABIN ABSORPTION DURING OMEPRAZOLE TREATMENT: SHORT AND LONG-TERM STUDIES. H Foster1, S Klinkenberg-Koop1, E Kruisinga1, C Lamers1, L Jansen1, I Biemond1, I Tertoolen1, S Meuwissen1, G Ziekengasthuis, 's-Hertogenbosch; 'Free University Amsterdam; 'University Leiden; 'University Nijmegen; The Netherlands.

INTRODUCTION: Cobalamin (COB) in food is protein bound. In the stomach COB is liberated by peptic digestion and hence absorbed. Omeprazole (OME) may impair COB absorption by potent inhibition of gastric acid secretion. We studied: 1) the absorption of protein-bound and unbound COB before and during OME treatment; 2) COB levels before and during long-term continuous treatment with OME.

METHODS: In 8 DU patients in remission the absorption of unbound and protein-bound COB were determined by measuring the 24 hr urinary excretion of unbound 57CO-cyanocobalamin or protein-bound 57CO-cyano-cobalamin on two consecutive days after oral administration of 1µg (1µC) after an overnight fast followed by long unlabeled COB i.m. 30 min later. Labeled COB was measured by a two-channel gamma spectrometer and expressed as % of the administered dose. Tests were performed before and during 9 OME treatment in two separate test periods with 20 or 40mg daily. 2) Serum COB levels were assessed by radio assay in 25 GERD patients before and during OME 20mg (n=9), 40mg (n=13) or 60mg (n=3) with a median treatment duration of 56 months (range: 36-81).

RESULTS: 1) Urinary excretion of unbound 57CO-cyanocobalamin was not different before and during OME 20mg (15.6±2.06 16.3±6.69, meansSEM); 40mg (13.49±2.89 17.5±1.93); Excretion of protein-bound 57CO-cyano-cobalamin was increased by 60±29% during OME 20mg (31.0±2.0 50.4±1.77; p<0.01) and 69±11% during OME 40mg (1.25±0.26 2.5±0.18; p<0.01).

2) Serum COB levels were not different before and during long-term OME treatment (298±27 261±16 mg/ml; meansSEM; N=180-900).

CONCLUSIONS: Absorption of protein-bound but not unbound COB is decreased during treatment with OME. However, serum COB levels do not change during long-term treatment with OME.

OMEPRAZOLE DOES NOT ALTER PLASMA GASTRIN IN PATIENTS WITH ACHLORHYDRIA S. Banjere1, JES Ardill, AD Beattie, RKL McColl2.

Departments of Medicine, and Therapeutics, Western Infirmary, Glasgow, **Depart of Medicine and Therapeutics, Western Infirmary, Glasgow, tDepart of Metabolic Medicine, Queen's University, Belfast.

The mechanism of hypergastrinaemia during omeprazole therapy is unclear, but is generally assumed to be entirely a consequence of acid suppression. However direct stimulation of G cells by the drug could also be a factor. In order to further investigate the mechanism of omeprazole induced hypergastrinaemia, we have studied the effects of the drug on plasma gastrin concentrations in patients with achlorhydria due to pernicious anaemia, in whom acid suppression cannot play a role.

We estimated fasting and peptone meal stimulated plasma gastrin in nine patients (7 male) with achlorhydria on two occasions 4 weeks apart to ensure reproducibility, and on a third occasion following 4 weeks of omeprazole 40 mg od.

Fasting plasma gastrins at the initial visit (median 1500, range 225-10675 ng/L) were similar to results pre omeprazole (1950, 240-16500 ng/L, p=0.90, p=0.001). Peak plasma gastrins were also similar at the initial visit (3750, 585-15600 ng/L) and pre omeprazole (2700, 585-16500 ng/L, p=0.91, p=0.0006). Despite the high fasting gastrin concentrations, the peptone meal produced a further elevation in plasma gastrin gastrin.

The median post prandial rise in plasma gastrin at the initial visit was 44% (1500-1700 ng/L). We defined this median time interval until the plasma gastrin returned to fasting levels was 120 minutes (range 10-150 minutes).

Fasting plasma gastrins were similar pre omeprazole (median 1500, range 225-10675 ng/L) and post omeprazole (1500, 315-7650 ng/L). Likewise, peak plasma gastrins were also similar pre omeprazole (2700, 585-16500 ng/L) and post omeprazole (2940-116250 ng/L).

Conclusions: 1) The hyperplastic G cell mass in pernicious anaemia can be further stimulated by a peptone meal, which causes a prolonged rise in plasma gastrin concentrations.

(2) Omeprazole has no effect on plasma gastrin in achlorhydric patients, which is consistent with its hypergastrinaemic effect being entirely secondary to acid inhibition.
ABNORMALITIES OF GASTRIC EMPTYING (GE) AND SMALL INTESTINAL MOTILITY IN PATIENTS WITH SPINAL CORD LESIONS S. Gupta, D. Evans, M. Benson, R.P. Gardner, D. Short, H. Frankel, P. Cochrane and D. Wingate*, Spinal Injuries and Gastroenterology Units, Stoke Mandeville Hospital, and *GI Research Unit, London Hospital Medical College, London.

Patients with high spinal cord lesions (SCL) suffer from many gastrointestinal (GI) problems due to denervation of the thoracic sympathetic and sacral parasympathetic nerves. Fealey et al. (Gastroenterology 1984; 87:69-75) reported delayed gastric emptying of liquids and semi-solids in a selected group of patients with high SCL. The aim of our study was to measure prolonged, ambulatory small intestinal motility and gastric emptying in a group of rehabilitated >2 yrs post injury, ambulant patients with SCL.

Fourteen patients (2-54 yr post-injury, 10M:4F, Age Range 25-70), with SCL (T11 above T1) were studied. Seven had liquid GE studies using impulse enterography. Data was expressed as T1/2 (time to 50% emptying). Seven patients underwent 24hr ambulatory manometry of the small intestine (3 microtransducers, 15cm apart, duodenal-jejunal, recording 0.1% mm Hg) and gastric emptying of a liquid mixed meal. Results will be presented.

This study has demonstrated that fasting and fed motility patterns are maintained in patients with spinal cord lesions with only minor abnormalities being detected. Liquid gastric emptying was significantly prolonged in high cord lesions. In the light of these findings, it is unlikely that the upper GI tract plays a significant role in abnormalities in GI function in these patients.

In the early postoperative period, there is a differential rate of return of phasic motor activity in the colon, and it is most delayed distally. Such imbalance in return of motility may occur across a left sided colonic anastomosis and may be a factor in its early disruption.

This hypothesis was tested in 14 patients (median age: 71yrs, range 48-78) undergoing recto-sigmoid anastomosis. Premedication, anaesthetic and postoperative regimens were standardised. A thin (od<2.5mm) manometric catheter was positioned trans-operatively across the anastomosis with a sensor 100mm proximal (P) and another 100mm distal (D). Pressure activity was recorded continuously from the end of surgery until the passage of flatus (m=31h, range 17-118) and data stored on a portable digital recorder. Semi-automated analysis, using a dedicated computer program, was performed. The trans-anastomotic pressure (TAP) was monitored by creating a 'subtraction' data set (P-D). Statistical analysis was performed using repeated measures ANOVA.

Monophasic pressure waves (>1cm H2O) were present early in the postoperative period at both sites (P: median 2.0hrs, inter-quartile range 0.3-120; D: 5.0hrs, IQR 1.7-60, p<0.1). Similarly, there was no significant difference in the timing of the return of motor complexes (P: 56hrs; 18-99; D: 27hrs, 15-33, p>0.1). The total number of pressure events (>50cm H2O) for each 2hr time epoch was similar at both recording sites, but there was an overall increase with time (Day 1: 3, 18: 3, 58: 5, p<0.001). The motility index (MI) was also decreased at both sites (P: D: p<0.005) but the overall MI increased with time (Day 1: 0.6, 18: 0.4, 58: 0.2, p<0.002). The maximum and minimum TAP were 152 and -68 cm H2O respectively. These pressure waves were uncommon and of short duration; the inter-quartile range for the gradients seldom exceeded 50cm H2O. There was no change in the pressure gradient with time after surgery.

Our data indicate that there is no difference in the return of phasic motor activity either side of the anastomosis. It is unlikely that intra-luminal pressure plays a significant role in causing the disruption of recto-sigmoid anastomoses in the early postoperative period.

Audit F232-F236

HEPATITIS B VACCINATION: FOR ALL HEALTH CARE WORKERS BUT NOT FOR DOCTORS? St J Conen, B Allinger*, G Scott, M Clark+. Dept of Microbiology, University College Hospital and Dept. Gastroenterology, St Bartholomew's Hospital*, London.

Hepatitis B vaccination is recommended for all health care workers. 90% of individuals vaccinated will develop an adequate antibody response. The exact duration of immunity is not known but is thought to be 3-5 years at which time a booster may be necessary. Previous studies have shown the poor uptake (49% overall) of vaccination by hospital doctors* and there have been considerable efforts by occupational health departments to improve this number. The aim of this study was a) to assess the current level of uptake of vaccination and b) to assess if doctors ensure continuing immunity. 157 physicians and surgeons were interviewed and data obtained regarding their hepatitis B vaccination status. Results. 63 (87.7%) of 71 house officers/senior house officers (HO/SHO) had been vaccinated against hepatitis B almost all while they were at medical school. 43 (68.3%) of these had been tested for seroconversion. 10 had been vaccinated more than 5 years ago but none had inquired about their immune status since that time. 66 registrars and senior registrars were interviewed. 47 (71.2%) had been vaccinated and 34 (72.3%) of these had been tested for seroconversion. In the group vaccinated more than 5 years ago 50% had been retested. 20 consultants were interviewed of which only 8 (40%) had completed a course of vaccination and 2 only had been tested for seroconversion. There were 19 gastroenterologists (in-training or consultants), all of whom regularly endoscoped, of which 31.6% were not immunised. In conclusion. More junior doctors are now immunised against hepatitis B and amongst HO/SHO's this reflects the success of student health vaccination programmes. However, there is inadequate follow up to ensure continuing immunity. Uptake of vaccine remains poor amongst consultants and most are at continuing risk of infection.

Open access endoscopy for acute dyspepsia presenting to an Accident and Emergency department.

R HARVEY, M GALVAGAS, J MYERS, C C AINLEY, M J GLYNN.
( Newham General Hospital, London. )

Open access endoscopy for G.P. referrals is now widely practised in the U.K. Particularly in inner city areas. In adduct by tumour patients used Accident and Emergency departments (A&E) as a source of primary care. We have studied the outcome of offering direct access upper gastrointestinal endoscopy to patients presenting to A&E with acute dyspepsia, who do not require admission.

Casualty Officers were circulated with instructions as to which patients to refer to the open access service. Patients were given a one hour appointment. Antacids were prescribed for interin symptomatic relief.

Over a 13 month period 173 patients were referred (mean age 42, range 18-86). 72% had epigastric pain. The duration of symptoms was evenly distributed from a few days to more than a year. 35% had not seen their General Practitioner (G.P.) with these symptoms. 36 patients did not attend. 137 endoscopies were performed. Diagnosis: Normal 68 (50%), Haustus hernia 15 (11%), Oesophagitis 17 (12%), Gastritis 19 (14%), Duodenitis 10 (7%). Peptic ulcer 14 (10%). Gastric carcinoma 0 (0%). During the study a consecutive series of 57 direct G.P. referrals for dyspepsia had 16 (29%) normal endoscopies (0.01)p.0.001 compared to the study group. 38 of the A&E patients were asymptomatic by the time of the procedure of whom 30 had normal endoscopies. 16 out of 29 symptomatic patients with normal endoscopies were reviewed in outpatients. The service was popular with A&E staff the increase in workload for the endoscopy unit was modest (<5%).

Following a cost audit of the scheme we predict that protocol modification and consequent improved case selection will optimise this service to compare favourably with G.P. direct referrals.

The Impact of a Specialised Bleeding Unit Serving Grampian Region: the May Forward.

F. BRADLEY, J. HASSON, D. WALMSLEY, R. KOUTER. X PARK. D. ANDERSON, P. FIELD. J. MCKINLEY. A. VINCENT. P. KREITLINGER.

A purpose designed GI Bleeding Unit to cover the population of Grampian Region was opened in Aberdeen in October 1991. An open access policy from the community and hospital services allows rapid admission to a unit six bedded unit with dedicated nursing and medical staff under the direction of a consultant gastroenterologist. A management policy is strictly observed with emphasis on vigorous resuscitation, rapid diagnosis and early surgery if appropriate. This report presents audit data collected prospectively during the first six months of operation.

A total of 386 patients were admitted with suspected GI blood loss. 270 were diagnosed as upper GI (70%), 56 as colonic (15%), and 58 had no evidence of bleed (15%). The 165 males with upper GI bleed had a mean age of 63 years (range 16-91), the 105 females age was 71 years (22-96), the age range and sex ratio for the colonic bleed were similar, 43% upper GI and 57% colonic bleeds were considered significant, with low haemoglobin or shock on arrival. The commonest sources in upper GI were duodenal ulcers (24%), oesophagitis (17%) and gastritis/erosions (13%) in colonic were diverticular disease (36%), haemorrhoids (12%) and polyae (10%), no bleeding point was identified in 12% of both upper GI and colonic bleed. The mortality for those with upper GI bleeds was 7% (7/249), for those requiring surgery was 14.2% (3/21), giving an overall mortality in the unit was 2.8% (1/144), surgical 14.2% (2/14) and overall was 5.1%. The average stay in the unit was 41 hours, with 45% being discharged directly home. The average stay in hospital was 6.9 days.

In summary, during the first 6 months the mortality rate from GI bleeding fell substantially, and the time spent in hospital significantly reduced. This has important treatment and resource implications.
SCLEORODERMA (SYSTEMIC SCLEROSIS): AN UNRECOGNISED CAUSE OF FAECAL INCONTINENCE.

AF Engel, MA Karmazin
St Mark’s Hospital, City Road, London UK.

Fibrosis of gastrointestinal smooth muscle is well recognised in scleroderma, causing upper gut dysmotility and constipation or chronic intestinal pseudo obstruction. An effect on continence has not been described.

Methods: Two patients with scleroderma, complaining of faecal incontinence, were studied by ano-rectal physiology studies, anal ultrasound, and histology in one. Patient A was a 62 years old female with a 9 year history of scleroderma and rheumatoid arthritis, 5 years of dysphagia, and 3 years of passive incontinence of liquid stools. Patient B was a 44 year old female with a 7 year history of CREST syndrome, dysphagia, 20 years of constipation, previous anterior resection for rectal prolapse, and 5 years of passive incontinence for solid stools. Both patients had typical skin changes of scleroderma.

Results: Both patients had a markedly reduced resting anal pressure (15, 20 cm H2O; normal > 50) but a normal squeeze pressure (80, 200 cm H2O; normal >80). Pudendal nerve function and ano-rectal sensation were normal. Anal ultrasound showed a very thin and hyperechoic internal anal sphincter, but normal external anal sphincter. Histology of the sigmoid colon (patient B) showed definite scleroderma fibrous replacement of smooth muscle.

Conclusion: Faecal incontinence can occur in scleroderma, and is characterised by passive incontinence due to fibrous replacement of the smooth muscle and impaired function of the internal anal sphincter. The external anal sphincter is unaffected. This symptom should be sought in patients with connective tissue disorders.

IS URGENT RESTORATIVE PROCTOCOLECTOMY A SAFE PROCEDURE IN UCERATIVE COLITIS?

J.S. McCourtney, J.O. Finlay
Department of Surgery, Royal Infirmary, Castle Street, Glasgow G6 9BF

Restorative proctocolectomy (R.P.) has become the standard elective procedure for ulcerative colitis (U.C.). The role of pouch surgery however, in the management of urgent cases of U.C. has not been established.

We performed a prospective study of 30 consecutive patients presenting with U.C. and treated by R.P. of these 12 (2 female, median age 25 years, range 14-42 years) underwent surgery within 48 hours of admission; the remaining 18 (9 female, median age 29 years, range 18-57 years) underwent elective surgery. 27 patients (90%) had covering ileostomies. There were no deaths in either group. Anastomotic/pouch leakage occurred in 1 patient in the urgent group and in 2 patients in the elective group. All 3 leaks occurred in patients without covering ileostomies. The groups were comparable for duration of surgery, blood loss, transfusion requirements and hospital stay. (see table: results expressed as medians and ranges, Mann-Whitney tests used throughout).

J-POUCH DURATION OF BLOOD LOSS BLOOD TX HOSPITAL SURGERY (mins)(al) (units) (stay) (days)

URGENT (n=12) 210(175-335) 290(150-1300) 0(0-3) 12(7-74)

ELECTIVE (n=18) 215(165-270) 349(50-1300) 0(0-3) 11(8-30)

p N.S. N.S. N.S.

At a median follow-up of 8 months (range 3-35 months) the 26 hour stool frequency was similar in each group (urgent: x5 (x3-13); elective: x7 (x3-18); p: N.S.).

These data suggest that R.P. with covering ileostomy may be safely performed as an urgent procedure in U.C.

CAN PERMEABILITY TO SUGARS PREDICT RELAPSES IN CROHN'S DISEASE?

R D'Inca, V Di Leo, D Martines, M Minotto, C Venturi, GC Sturniolo, R Naccarato. Division of Gastroenterology, University of Padua, Italy.

The efficacy of intestinal permeability, which is altered in active Crohn's disease (CD), in predicting relapses was ascertained by measuring lactulose/mannitol (L/M) excretion in 37 CD patients. Urine was collected for 6 hrs after oral administration of the sugar mixture at the beginning of the study and at 3-monthly intervals for one year thereafter. On each occasion, clinical (CDAI) and biochemical (ESR, alafglycoprotein, C reactive protein) activities were assessed in order to identify relapses. Twenty-six patients were initially in remission. Twenty patients had normal L/M test results while six presented altered permeability. Three of the latter had persistent arthritis. Five patients relapsed during the study period; in each case the relapse was anticipated by abnormal test results in the preceding 3 months. Fifteen patients remained in remission throughout the whole year and L/M tests were normal. In patients in remission the L/M test therefore had a 100% sensitivity and a 71% specificity for relapses. Eleven patients had active disease on entering the study: eight had abnormal L/M tests which reverted to normal only in the five patients who had remission. Three patients had normal L/M tests throughout the study period despite persistent active disease: in all of these patients, CD was confined to the colon.

In conclusion, L/M test is useful in predicting relapses in CD. It is sensitive to disease activity while its specitivity can be affected by the presence of extraintestinal complications or by the colonic extent of the disease.

SURVEILLANCE OF THOSE AT HIGH RISK OF COLORECTAL CANCER USING AN IMMUNOLOGICAL FAECAL OCCULT BLOOD TEST

MHE ROBINSON, CB WILLIAMS*, JD HARDCASTLE

Department of Surgery, University Hospital, Nottingham; * Endoscopy Department, St Marks Hospital, London

Haemocult (H/O) is insufficiently sensitive to screen subjects at high risk of colorectal cancer (CRC) while endoscopic surveillance remains controversial because of the costs and potential morbidity. Hemeselect (H/S)(SmithKline Diagnostics), an immunological faecal occult blood test, is more sensitive for CRC and adenomas than H/O. Our aim was to measure the sensitivity and specificity of H/S and H/O in subjects at high risk of CRC.

335 patients have undergone complete colonic investigation (adenoma followup, n=170; positive family history, n=108; cancer followup, n=49; longstanding colitis, n=12). All completed the H/S tests but 40 failed to satisfactorily do the H/O tests. 58 subjects had positive H/S tests (17.3%) and 11 had positive H/O (3.3%). Two people were found to have rectal cancers; both tests were positive in one and negative in the other. 15 patients had at least one adenoma ≥ 1 cm, 5 (33%) returning positive H/S tests and 3 (20%) with positive H/O. Forty-three of the 244 not found to have neoplasia had positive H/S tests (specificity= 82.4%). Specificity for neoplasia for the H/O test is 96.8%.

Surveillance programmes aim to detect large adenomas and early cancers. This immunological FOB test failed to detect two-thirds of such lesions and, on the basis of these small numbers, is unsuitable for high-risk group screening.
ACCUERATE ASSESSMENT OF COLORECTAL INFLAMMATORY BOWEL DISEASE (IBD) USING EARLY (1 HOUR) TECHNETIUM (Tc-99m) HMPAO WHITE CELL SCANNING.

(St. George's Hospital Medical School, London.)

The extent of colonic involvement in IBD has important implications for both treatment and prognosis. The current gold standard for such assessment is colonoscopy with biopsies. However, this can be uncomfortable, involves some risk and may not always be possible due to severely active disease or stricturing. Tc-99m HMPAO white cell scanning (Tc99m) is a non-invasive method which can detect sites of acute inflammation. There has however been uncertainty regarding the optimal timing of scanning, and some concern about false positives due to excretion of isotope into bowel.

To assess the accuracy of disease extent determination by this method, 49 patients with suspected colonic IBD underwent colonoscopy and Tc-99m scans within 10 days. Biopsies were taken from 8 sites extending from caecum to rectum. Extent of active colonic disease was assessed histologically using specific criteria and was given a score of 0-8. Tc-99m scans taken 1 hr and 3hrs post injection were assessed for involvement in each of the 8 colonic segments. Histology showed no active disease in 13 patients. All 13 had absent colonic activity on hr scans (specificity 100%), but 5 had colonic activity on 3hr scans (specificity 61%). Histology showed active disease in 36 patients, 33 of whom had colonic activity on both 1hr and 3hr scans (sensitivity 92%). The correlation between histological extent and 1hr scan extent was r = 0.9, (p<0.01). 3hr scans were also useful by demonstrating colonic transit of activity.

In conclusion, Tc-99m HMPAO white cell scanning 1hr post injection is a sensitive and highly specific investigation for suspected active colonic IBD and provides an accurate extent of disease assessment.

EFFECTS OF ADJUVANT 5-FUOROURACIL AND LEVAMISOLE ON T-CELL PROLIFERATION.

Centre for Digestive Diseases, The General Infirmary, Leeds.

It is unclear whether the beneficial effects of adjuvant therapy with 5-fluorouracil (5-FU) and levamisole are due to the immunomodulatory effects of levamisole. To determine this, T-cell proliferation was assessed using in vitro incubation of lymphocytes from patients with colorectal cancer. The study included 13 patients without obstruction and undergoing surgery. Control lymphocytes were assessed for 48 hours using a radiotelemetry capsule (RTC) and digital portable recorder.

Conclusions: Anal manometry, pouch distension volumes, and pouch inflammatory changes prior to ileostomy closure do not predict subsequent stool frequency or pouch sensory volumes. Preclosure measurements should therefore not influence management.

CANCER IN RELATION TO DIET.
**Small bowel/nutrition F249–F262**

**Tensor microsatellite polymorphisms in coeliac disease**

R. McManus, M. Moloney, Y.T. Chan, D.G. Hear, G. Whelton

Department of Clinical Medicine, Trinity Collegel Dublin, Dublin 2, Ireland.

Coeliac disease is tightly linked to a gene(s) located in the HLA region on chromosome 6. The tumour necrosis factor (TNF) locus is located in the MHC class III region which is in close physical proximity to the HLA genes. We have analysed genomic DNA samples taken from coeliac patients for evidence of a linkage of the disease phenotype with specific microsatellite alleles. Three variable number tandem repeats (VNTRs or microsatellites) are present in the vicinity of the TNF locus and are termed TNFα, TNFβ, TNFγ. The TNFα allele demonstrated only two alleles and was not useful for linkage analysis. TNFα is much more heterozygous with 10 different alleles present in our population. The most predominant allele (allele A1) was present at an apparent frequency (excluding the possibility of null alleles) of 0.596 in the coeliac population (n=25) as against 0.333 in the control population (n=30). 86.5% of affected individuals were either heterozygous or homozygous for this allele as opposed to 53.3% of the control population; the observed values are significantly different (p=0.002).

The TNFβ locus also has a high polymorphic information content. One allele (allele B1) is highly prevalent in the coeliac population (n=25), at an apparent frequency of 0.660, as opposed to a frequency of 0.133 in the control group (n=15). Of the coeliac tested (25), 88.0% were either heterozygous or homozygous for allele B1, as compared to 26.7% of controls which is a statistically significant difference (p=0.0003). Therefore both loci possess alleles which appear to be in strong linkage disequilibrium with the causative genetic lesion(s) for coeliac disease. This is especially true of allele B1, which may be of prognostic value. Since the association of the microsatellite locus with the disease gene or genes is unlikely to be as a result of a functional interaction (except perhaps through physical linkage to a secondary locus), these data, in conjunction with data from the HLA loci, may be a useful aid to mapping the disease locus.

**T cell receptor Vβ usage in peripheral blood and small intestinal biopsies of treated and untreated coeliac disease patients**

M. Hall, B. Sturgess, J. Lanchbury & P.J. Culliford

Molecular Immunology Laboratory and Rayne Institute, UMDNS, St Thomas' Hospital, London, UK.

Coeliac disease (CD) is characterised by gluten sensitive enteropathy, increased numbers of small intestinal intraepithelial lymphocytes (IEL) bearing αβ or γδ T cell receptors (TCR) and exhibits a strong HLA class II association. Dietary restriction of gluten reduces αβ TCR+ IEL numbers towards normal, but the γδTCR+ IEL numbers appear to be less affected. It has been hypothesised that an oligoclonal expansion of γδTCR+ IEL might contribute to the pathogenesis of CD.

In order to investigate this hypothesis, we have studied TCR Vβ usage in both peripheral blood and small intestinal biopsy specimens from untreated (n=7) and treated (n=6) CD patients and controls (n=2). Peripheral blood lymphocytes, IEL and lymphocytes from the underlying lamina propria of the biopsies were separated and analysed to determine whether there was any compartmentalisation of specific TCR Vβ usage, that might be involved in disease pathogenesis. Linear PCR amplification of TCR β-chains from the constant region through to the variable region was carried out on standardised TCR specific cDNA using amplification primer pairs designed to amplify members of 20 TCR β families. Direct comparisons were made between the peripheral blood and the different tissue compartments for each amplification primer pair to try and establish if any specific bias in Vβ usage existed.

We did not find TCR Vβ usage to be restricted in any cellular compartment in either the coeliac patients or controls. This study does not support the hypothesis of restricted TCR usage in coeliac disease.

**CT-Planimetry: An accurate and useful assessment of percentage hepatic replacement (PHR) of colorectal liver metastases**

S.F. Purslow, J. Rogers, N.S. Williams

Academic Surgical Unit, Royal London Hospital, London E1.

The percentage hepatic replacement (PHR) of colorectal liver metastases may be an important factor in assessing prognosis, and in clinical trial evaluation. Most imaging techniques used to assess PHR rely on subjective interpretation by radiologists. We have devised an accurate quantitative microcomputer based method using planimetry to measure the PHR from CT scans. For each sequential CT image the cross-sectional areas of liver and metastases are measured. PHR is calculated as the sum of cross-sectional areas of metastases divided by the sum of cross-sectional areas of liver. The method was extensively evaluated: Phantom studies: The PHR of 6 cadaveric livers were measured by CT-planimetry and by water displacement following dissection. Agreement between CT-planimetry and water displacement was good with a bias of 1.0% (0.0 to 2.1, 95% CIs) over a PHR range of 2.7 to 52.1%. Subjective assessment of PHR was assessed on 9 CT scans of patients with colorectal hepatic metastases by 5 radiologists and 9 surgeons. Coefficients of variation for subjective assessment ranged from 21.0 to 80.0 compared to 0.96 to 3.36 for objective CT-planimetry. Interobserver repeatability of CT-planimetry was assessed by repeated measurements on 10 CT scans by two independent observers. The agreement between observers was excellent with a bias of 0.04% (-0.21 to 0.31, 95% CIs). Relationship between CT-planimetry PHR and survival was assessed by a retrospective study of 20 patients with colorectal metastases. Significant correlation (p < 0.05, r = 0.72) was found between PHR and survival when a semi-log plot was used and patients with extrahepatic disease were excluded. In conclusion, CT-planimetry allows straightforward, accurate and repeatable measurement of PHR and avoids the inaccuracies of subjective interpretation. In addition, accurate measurement of PHR may have prognostic significance in patients with colorectal cancer metastases confined to the liver.

**THE LONG TERM RESULTS OF RESTORATIVE PROCTOCOLECTOMY FOR ULCERATIVE COLITIS: A HISTORICAL SERIES.**

F. Setti-Carrasso, RH Wilkinson, J. Ritchie, BJ Nicholls

St. Mark's Hospital, City Road, London, U.K.

Between November 1976 and December 1985, 110 patients (59 males, 51 females, mean age 31.6 years (range 14 to 60)) underwent restorative proctocolectomy or proctocolectomy for ulcerative colitis. There was one (1%) operative death. Patients were followed-up until death or February 1992 for a minimum of 74 to a maximum of 173 months from ileostomy closure. During the follow-up 20 (20%) patients were operated on for small bowel obstruction. There were 8 late deaths (4 disseminated disease, 1 late sepsis and 3 unrelated). Seven patients were lost to follow-up. Sixteen (16%) reservoirs were removed, defunctioned by an ileostomy not closed at the time of assessment or converted to a Kock reservoir. Reasons for failure included perianal and pelvic sepsis (n=8) and dysfunction (n=5). Two (3.8%) patients had a pouch-vaginal fistula. Eight (30%) failures occurred within the first year. Function was assessed at a mean of 99.3 months (range 63-173 months) in eighty patients with an intact reservoir. Their average number of bowel movements was 4.2/24 h (range 1-12). Night evacuation occurred regularly in 26 (32%) and 16 (20%) wore a pad. Continence was normal in 45 (56%), while 35 (44%) had minor mucous leakage. Twenty seven (35%) required antidiarrhoeal medication. General health: five patients in child bearing age gave birth to nine babies, all but two by caesarean section; seven (6.8%) patients had pre or postoperative thyroid dysfunction, three had kidney stones, two (1.8%) had haemorrhage, one chest and renal sarcoidosis and two had recurrent postoperative anemia requiring surgical intervention (i.e. iron. Ten (10%) patients postoperatively developed arthropathy and five (5%) erythema nodosum.
COELIAC DISEASE: ASSESSMENT OF THE SUITABILITY OF FOODS
The Rayne Institute, St. Thomas' Hospital, Lambeth Palace Road, London, SE1 7EH and *German Research Institute of Food Chemistry.

A sensitive and specific assay is required to detect trace quantities of gluten present in "gluten-free" foods. Detection of enzymatically altered gluten is not possible using most of the available assays. A peptide B3144, derived after peptic-trypsin digestion of α-gliadin, and corresponding synthetic peptides 3-56, was used to produce monoclonal antibodies.

Ascites derived from one of these antibodies, WBS was used to develop semi-quantitative immunoassay. Solutions of 1-500 μg/ml of coeliac-toxic prolamins were dotted onto nitrocellulose sheets. Additionally ethanolic extracts of 50 and 500mg/ml of rice, maize, millet and sorghum flours were dotted, as was an ethanolic extract of malt at the same concentrations.

The sensitivity of the assay was 1ug/ml for unfractionated wheat gliadin and rye prolamin, and 5ug/ml for barley and cut prolamin. Extracts of flours from coeliac non-toxic cereals did not cross-react in the assay. Enzymatically altered gluten, Frazers Fraction III (FFIII) was detectable at 50μg/ml. Malt, which represents a partial hydrolysate of barley prolamin, was easily detectable and appeared to contain the equivalent of 100μg of barley prolamin per 100g of malt.

A sequenced peptide of gliadin has been used to raise a monoclonal antibody which is specific for those prolamins which exacerbate CD. We have developed a sensitive and specific iodinated peptic assay for the measurement of gluten in foods which can be used to detect enzymically altered gluten.

THE EFFECT OF ENTERAL FEEDING ON COLONIC MOTILITY IN MAN

The pathogenesis of enteral feeding related diarrhoea remains unclear. In previous studies of normal subjects we have shown that it occurs more commonly during intragastric than intraduodenal feeding, and is more likely to result from disturbed colonic than small intestinal function. We have also shown that when infusing a polymeric enteral diet, either intragastrically or intraduodenally, at 1.39 ml/min (1.39 kcal/ml, 8.75 mg/min), the colonic contractile activity was significantly lower than that seen in the fasting state. However, during that study, diarrhoea was only induced in 1 of 14 subjects. The aim of the present study was to determine whether a higher infusion rate of an enteral diet could evoke an abnormal colonic motility response.

Intraluminal pressure recordings in the unprepared descending and sigmoid colon were undertaken in 6 normal subjects on 2 separate occasions in random order. Continuous recordings were made for a duration of 9 hours: 3 hours before and 6 hours during infusion of a polymeric enteral diet at 2.78ml/min (4.2 kcal/min, 26.1 mg/min). On one occasion the subjects received intragastrically (group I) and on the other intraduodenally (group II). The pressure records were analysed in 10 minute epochs for the study segment (sum of four channels) activity index (AI = area under the curve: mmHg.min) by fully automated computer analysis.

Of the 14 subjects in group I, 1 developed diarrhoea, compared to only one in group II. There were no significant differences in the AI between the two groups prior to feeding: Mean(SE), 521(24) vs 543(36) mmHg.min. In the first 3 hr of feeding the AI in group I fell to 301 (22), p < 0.001, whereas in group II it remained similar to fasting at 465(35). In the second 3 hr the AI in group II had fallen to 229(30), p < 0.001, a level similar to that seen in group I - 254(20).

These data demonstrate that following the infusion of a polymeric enteral diet there is a suppression of colonic motor activity, and that this suppression occurs at an earlier stage during intragastric feeding, despite the frequent occurrence of diarrhoea.
F255

INTESTINAL FUNCTION AND POSTOPERATIVE ENTERAL NUTRITION FOLLOWING LIVER TRANSPLANTATION
C. Wicks, *S. Somanandam, **J.S. Menzies, *L. Bjarnason and Roger Williams. Institute of Liver Studies and **Department of Clinical Biochemistry, King’s College Hospital, and **Department of Chemical Pathology, St Thomas’ Hospital, London.

Conventional postoperative management of liver transplant patients often includes total parenteral nutrition which is associated with significant complications and is expensive. We report on nine consecutive patients who underwent orthotopic liver transplant with no intestinal surgery and were managed by early enteral nutrition.

Methods: Patients were assessed by a combined absorption-permeability test, using 3-OM-D-glucose, D-xylene, L-ramhose and melibiose, which assesses active and passive carrier mediated transport and trans and paracellular permeability, respectively. Patients underwent a pre-transplant assessment followed by sequential studies 14 hours, 3 and 5 days after transplantation to assess whether small intestinal absorption was affected by the surgery and how long it took to recover. All nine were given a whole protein nasogastric feed (Osmonil, Abbott Laboratories) within 24 hours of surgery (venous-venous bypass was performed prior to hypothermy to minimize intestinal damage), via a fine bore nasogastric feeding tube.

Results: Mean 5 hour urine excretion of 3-OM-glucose and D-xylene fell significantly (p<0.001) immediately postoperatively from 34.1±4.4% to 9.3±3.5% and 27.5±3.3% to 6.0±2.5%, respectively. Intestinal permeability (melibiose/L-ramhose urine excretion ratio) increased significantly (p<0.01) from 0.040±0.011 to 0.105±0.021. All values had returned to preoperative levels by the 3rd day. All nine tolerated the feed well without any complications and were started on a normal diet within 10 days.

Conclusions: Functional abnormality of the small intestinal mucosa is evident immediately following liver transplantation but is mild and rapidly reversible. Enteral nutrition can therefore potentially be used at an early stage following liver transplantation. Substituting enteral for parenteral nutrition in these patients may reduce sepsis and other TPN related complications and has major financial implications.

F256

IS INSULIN LIKE GROWTH FACTOR (IGF-1) AFFECTED BY CHRONIC GASTROINTESTINAL DISEASE OR THE ACUTE PHASE RESPONSE?
Morrice AJ, Bakhshandeh T, Park RMB, Qoin JDA, Davidson PJ, Cruickshank AJ, Beastall GE, Russell RI. Gastroenterology Unit and Department of Biochemistry, Glasgow Royal Infirmary.

It has been suggested that insulin like growth factor (IGF-1) may be useful as a marker of nutritional status. IGF-1 levels in acutely ill patients have been shown to correlate with nitrogen balance and energy intake. Before assessing if IGF-1 could be a marker of nutritional status in patients with chronic gastrointestinal disease we attempted to ascertain the effect of the pre-existing gastrointestinal illness on IGF-1 and whether IGF-1 is affected by the acute phase response in such patients. We have measured IGF-1, Interleukin-6 (IL-6) and C-reactive protein (CRP) levels in 23 samples from 7 patients with Crohn’s disease attending a Nutrition Clinic, 16 patients with Ulcerative colitis and 9 patients with Coeliac disease. All patients were thought to be in remission or be on a gluten free diet. These have been compared with 181 healthy controls with no gastrointestinal disease.

Results: [Median (range)]
- Crohn’s: IGF-1 22ng/ml (13-72), IL-6 89.5ng/ml (36-737), CRP 7.5ng/ml (1-135), Ulcerative colitis: IGF-1 28ng/ml (12-135), IL-6 31ng/ml (19-72) CRP 5.5ng/ml (5-40) and Coeliac disease IGF-1 25ng/ml (11-72), IL-6 23ng/ml (15-64), CRP 5 controls IGF-1 18ng/ml (20-579). Serum IGF-1 levels significantly reduced in all patient groups (p<0.01) compared to controls but there was no significant difference in IGF-1 levels between patient groups.

Crohn’s disease patients had a higher IL-6 compared to U.C. and coeliac disease (p<0.01). CRP levels in Crohn’s were higher than U.C. patients (p<0.05) and the coeliac disease patients. There was no correlation between IGF-1 and CRP in any patient group.

Conclusion:
1) IGF-1 levels are significantly reduced in chronic gastrointestinal disease.
2) The reduction of IGF-1 appears independent of acute phase response in chronic gastrointestinal disease.

F257

CLINICAL EVALUATION OF THE PUSH-ENTEROSCOPE (OLYMPUS SIF 10) IN THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL DISEASE.
H.H. Tsai, J.Y. Yiannakou, I.T. Gilmore, A.I. Morris. Department of Gastroenterology, Royal Liverpool University Hospital, Liverpool.

Previous experience in push-enteroscopy had been carried out using a standard or pediatric colonoscope. The specially designed push-enteroscope (Olympus SIF 10) have recently been available and we have assessed its clinical usefulness in 16 patients (mean age 49.9 yrs, range 20-73 yrs; 6 male, 8 female).

The main clinical indication was for obscure gastrointestinal bleeding (13 patients). Of these, all had significant blood loss with a mean pre-enteroscopy transfusion requirement of 12.8 units (range 0-50) and all had prior gastroscopy, colonoscopy, large and small bowel contrast radiology. 4 patients had technetium and red cell scans.

In the remaining 3 patients, enteroscopy was carried out for suspected small bowel polyps. Enteroscopy was carried out under sedation. The enteroscope was passed into the mid-jejunum, 60 cm beyond the ligament of Treitz in all cases except one, who had a stenosing carcinoma in the lower duodenum.

Of the 13 bleeding cases, angiodysplastic lesions were detected in 4 patients and a lower duodenal carcinoma in 1 patient. No pathology was detected in the remaining giving a detection rate of 38%. The sites of the angiodysplastic lesions in the 3 patients were: 1 solitary; mid-jejunum 2, multiple; in stomach, mid-jejunum 3, multiple; duodenum and mid-jejunum 4, multiple; mid-jejunum. All 4 received laser photocoagulation and 3 required no further blood transfusions. There were no adverse effects of the procedure.

Push enteroscopy with the specially designed enteroscope appeared safe and clinically useful in the diagnosis and treatment of obscure gastrointestinal bleeding.

F258

SUPERIOR MESENTERIC ARTERY BLOOD FLOW CHANGES AFTER FEEDING: RELATIONSHIP TO CALORIFIC CONTENT OF FOOD.
*Parker D, +Carlisle E.M, *Read A.E, +Weills P.N.T.
*University of Liverpool, *Department of Medicine, *Bristol Royal Infirmary. +Department of Medical Physics, Bristol Royal General Hospital.

The post-prandial increase in superior mesenteric artery blood flow (SMABF) is well recognised and is dependent upon the calorific content and chemical composition of food in the duodenum. The mechanism behind this increase is unknown. We studied the relationship between SMABF and calorific content of food and its relationship with post-prandial endogenous hormone levels.

Six healthy non-smokers (3 male, 3 female, aged 20-26 years) were observed supine and fasting. A randomised, double-blind study was undertaken; an isovolumetric liquid meal consisting of corn oil, skimmed milk powder and glucose powder in varying dilutions was given on four separate visits to each volunteer. The calorific loads given were 800, 1600, 2400 and 4800kJ. Pre- and post-prandial SMABF was measured using a duplex ultrasonic scanner. Plasma samples were taken before and at 15, 30, 60 and 120 minutes after feeding: levels of insulin, glucagon, gastrin, vasoactive intestinal polypeptide, neurotensin, adrenaline and nor-adrenaline were measured. The mean peak % SMABF increase following feeding rose from 128 (SEM=30.4) with the 800kJ meal to 322 (SEM=67.1) with 4800kJ meal and appeared to be directly proportional to calorific content (r=0.98; p=0.017; df=2). These changes occurred between 15 and 30 minutes after feeding in all subjects. The mean peak % increase in insulin concentration rose from 30 (SEM=8.3) with 800kJ meal to 91 (SEM=19.1) with the 4800kJ meal and exhibited a curvilinear relationship (r=0.92; p=0.086; df=2).

These results suggest that calorific content of food may influence the magnitude of post-prandial SMA vasodilatation. A role for hormones in inducing post-prandial vasodilatation is not proven.
L-ARGININE, UNLIKE D-ARGININE, IS A SMALL INTESTINAL SECRETORY STIMULUS: STUDIES IN AN ANIMAL MODEL IN VIVO. FH Mourad, LID O'Donnell, ML Clark, MGD Farthing, Dept. of Gastroenterology, St Bartholomew's Hospital, London ECIA 7BE.

Intestinal water and electrolyte absorption can be significantly enhanced by L-arginine. However, studies in human jejunum have shown that the basic amino acid L-arginine (L-Arg) induces water secretion rather than absorption, a phenomenon that is not fully understood. To study the mechanism of L-Arg-induced secretion, we have used an animal model to investigate the effect of L-Arg on water movement in rat jejunum in vivo.

Under phenylephrine alone anesthesia, a 25 cm jejunal segment of adult male Wistar rats (180-220g) was isolated between two cannulae and perfused in situ with a solution containing 20mM L-Arg and [14C]-PEG 4000 as a non-absorbable volume marker. After 30min equilibration period, 3x10^6 collections of the effluent were obtained. Parallel groups of animals were similarly perfused with either a saline solution or a solution containing 20mM D-Arg. All solutions used were rendered iso-osmotic (300mOsm/kg) by the addition of sodium chloride. Arginine concentration in the effluent was measured by the colorimetric method of Sakaguchi and arginine absorption calculated accordingly.

Jejunal segments perfused with saline had net water absorption (median 17µl/min/g dry intestinal weight [interquartile range 2 to 35], n=15), whereas L-Arg induced net water secretion (-10 [-14 to -4.7], n=13; p<0.05). This secretory property was not shared by D-Arg which produced net water absorption similar to saline (21 [17 to 33], n=5). L-Arg was more readily absorbed than its D-isomer (9.8±0.8µmol/min/g [6.9 to 12.2] vs 2.2 [1.4 to 3.4]; p<0.01).

Thus, 20mM L-Arg induces water secretion in rat jejunum; this is not osmotically driven since D-Arg caused net water absorption despite being less absorbed. L-Arg appears to be a small intestinal secretagogue; whether this effect is related to its physiologic role as a substrate for generation of nitric oxide needs further investigation.

METHODS: 34 Ashkenazi Jews with coeliac disease and 37 ethnically matched controls from Rehovot, Israel, were studied using sequence-specific oligonucleotide probes, in conjunction with gene amplification by the polymerase chain reaction, to determine alleles at the DRB, DQA1, DQB1 and DPB loci with additional specific DR sub-typing. Coeliac disease was diagnosed in all cases using the classic ESPGAN criteria. Results: Significant associations with coeliac disease were found at the DRB1 locus with alleles DQB1*0301 (45% vs 15%), DQA1*0501 DQB1*0201 (70% vs 6%); p<0.001. The majority of individuals with coeliac disease but lacking these alleles possessed the alleles DRBI*0402 DQA1*0301 DQB1*0302 and accounted for 20% of the coeliac population. A further 6% were homozygous for DRBI*0701. No associations were seen at the DPB locus either in the overall coeliac group or among the DQ2 negative individuals. No additional associations with coeliac disease were seen with individual DR3 haplotypes as defined at the DRB3 locus.

Conclusion: This study confirms the association between coeliac disease and the DQA1*0501 DQB1*0201 alleles, but notes that this 'unifying' hypothesis does not cover 30% of coeliac disease among Ashkenazi Jews.

THE LONGITUDINAL DISTRIBUTION OF INFLAMMATORY CHANGES IN THE ILEAL RESERVOIR AFTER RESTORATIVE PROCTOCOELECTOMY FOR ULCERATIVE COLITIS.

P Setti-Carraro, IC Talbot, RJ Michelle.

St. Mark's Hospital, City Road, London, U.K.

Little is known of the longitudinal distribution of inflammatory changes in the ileal reservoir. Fifty nine patients who had undergone restorative proctocolectomy for ulcerative colitis were examined personally 5.3 to 14.5 years (mean 8.7 years) postoperatively. There were 37 males and 22 females, of mean age at presentation of 33.4 years. A rigid sigmoidoscopy of the reservoir was performed. Four zones in the posterior midline starting at 5 cm from the anal verge and extending proximal at 5 cm intervals were inspected. A macroscopic score (1) was given to a biopsy taken at each level. The degree of acute and chronic inflammation was assessed using a histopathological scoring system (2). All reservoirs showed endoscopic abnormalities, more marked distally in 14 (24%). However, when macroscopic score was >3 changes were diffuse. In 25.4% an increased gradient from proximal to distal of both chronic and acute inflammatory changes in 17 (29%) of these the mucosa of the upper part of the reservoir was histologically normal.


CROHN’S DISEASE: DIFFUSE JEJUNOLEITIS MANAGEMENT, PROGNOSIS AND OUTCOME.

W C Tan, H A Andrews, R N Allan.

Gastroenterology Unit, General Hospital, Steelhouse Lane, Birmingham B4 6NH.

There is microscopic evidence of diffuse disease in patients with focal Crohn's disease. Macroscopic diffuse jejunileitis is uncommon, but important because of associated high morbidity and mortality. The reported excess mortality has no analysis of the outcome among such patients for more than 20 years. This analysis includes 34 patients with diffuse jejunileitis diagnosed between 1960 and 1991 to determine clinical features, optimal medical and surgical management, and the long term survival.

At diagnosis diffuse jejunileitis affects younger patients (mean age 26.4 years) than those with distal ileal disease (mean age 33.3 years). The mean follow up was 16 years. The principal presenting symptoms, either alone or in combination, were colicky abdominal pain (91%), weight loss (62%) and diarrhoea (53%). During follow up most patients (77%) received corticosteroids for periods of more than 6 months. The annual operative rate was highest in the first year after diagnosis (35%) and then remained constant at 15% for the next 10 years before falling to 7% per year. Surgical intervention rates were higher in younger patients (P<0.001).

Only 2 patients have died, one of unrelated problems. Despite the high morbidity the overall outcome was good. 75% of the patients currently under review are asymptomatic and only 4 are still receiving corticosteroid therapy. The observation that operative intervention rate falls with time suggests that the disease does "burn itself out" and the excess mortality reported previously has now been eliminated.
MEDIUM-CHAIN TRIGLYCERIDES IN Pancreatic Insufficiency
Caleari S, Benini L, Bronteugnani MT, Fioretta A, Sembenini C, Bardelli E, Castellani G, Vantini I. Dept Gastroenterology, University of Verona at Valeggo Mt, Italy.

Medium-chain triglycerides (MCT) are used in pancreatic insufficiency because they are easily hydrolyzed, whereas long-chain triglycerides (LCT) can be absorbed also as triglycerides. This assumption is based on few hard data, and the decrease of steatorrhoea using MCT could be considered an analytical error, since the Van De Kamer method does not extract completely MCT from feces. We have therefore evaluated the absorption of MCT and LCT and the effect of pancreatic supplements in patients with pancreatic insufficiency (fasicel fat >20 g/day, Pancreolauril TE <10%). Fecal fat was assayed with a method (Jesewich et al. Clin Biochem 1970; 31:157) which accurately measures both MCT and LCT. We studied 4 patients (1 protein-calorie malnutrition, 3 chronic pancreatitis). The patients were kept on a standard low fat diet (15 g fat/day) with the addition of 60 g of butter without or with pancreatin (LCT or LCT+P respectively) or of 55 g of MCT without or with pancreatin (MCT or MCT+P) for periods of 5 days. In the last 3 days of each period feces were collected, weighed and assayed for fat content. Fecal weight and fat concentration and output (g/day) are shown in the table.

<table>
<thead>
<tr>
<th>Weight (g/day)</th>
<th>Fecal weight</th>
<th>Fat losses</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCT</td>
<td>36.7 ± 16.8</td>
<td>363 ± 88.9</td>
</tr>
<tr>
<td>LCT+P</td>
<td>36.7 ± 16.8</td>
<td>363 ± 88.9</td>
</tr>
<tr>
<td>MCT</td>
<td>36.7 ± 16.8</td>
<td>363 ± 88.9</td>
</tr>
<tr>
<td>MCT+P</td>
<td>36.7 ± 16.8</td>
<td>363 ± 88.9</td>
</tr>
</tbody>
</table>

In conclusion, these preliminary data confirm that MCT are absorbed better than alimentary fats and may be useful in patients with pancreatic insufficiency. Pancreatic supplements are necessary for their optimal absorption in the presence of pancreatic insufficiency.

ENDOSCOPIC BILE DUCT STONE REMOVAL [ES] IN RELATIONSHIP TO LAPAROSCOPIC CHOLECYSTECTOMY

At the outset of minimally invasive gallbladder surgery, a policy decision was made to manage bile duct stones endoscopically on account of the difficulty in negotiating the cystic duct cholechocholithically, and the impossibility of removing stones from the intraduodenal ducts via the cystic duct route.

With the advent of laparoscopic cholecystectomy in May 1990, a decision was made to continue this policy and not to undertake operative cholangiography. Patients were submitted to ES pre-operatively if the bile duct on ultrasound was greater than 6 mm diameter, if there was gallstone pancreatitis or a history of jaundice. Postoperative ES was performed if clinically indicated.

Laparoscopic cholecystectomy has been performed in 434 patients (16 conversions to open). 52 had a pre-operative ES (12%), 29 were planned with cholecystectomy in mind (gallstone pancreatitis 11, suspected stones 18). Only 5 patients had duct stones. 23 patients had an ES to diagnose gallstones, and of these, 10 had duct stones. Postoperatively, 16 had an ES for symptoms suggestive of stones and only 6 had stones. There was an overall stone incidence of 5%.

The policy of selective ES is appropriate and no complications occurred as a result of eliminating peri-operative cholangiography and peri-operative duct exploration. It is suggested that the criteria for both pre-operative and postoperative ES could be further refined.

WHERE HAVE ALL THE BILE DUCT STONES GONE?
D. S. Watkin, D.J. Warwick, M.H. Thompson.
Department of Surgery, Southmead Hospital, Bristol. BS10 5NB

Details of patients treated for gallstones on one firm have been kept since 1991. Until 1990 it, young patients with a gall bladder in situ and symptomatic stone disease, complicated or not, were treated by cholecystectomy. Some were not fit by pre-operative ultrasonography and liver function tests (indirect cholangiography). Elderly or unfit patients with duct stones were treated endoscopically; a policy not changed since 1981.

Since adopting the new protocol there appeared to be fewer duct stones in patients undergoing cholecystectomy.

In the eight years up to 1989 78 of 469 (17%) of patients undergoing open cholecystectomy were found to have common duct stones. Since September 1990 204 cholecyctoptyes have been performed, 201 laparoscopic and 3 planned operations. Five of the patients undergoing laparoscopic cholecystectomy had duct stones removed as did all the patients having planned operations. A further 2 patients have presented with duct stones in the year following laparoscopic cholecystectomy, giving a frequency of 10 in 204 (5%), a highly significant reduction (p < 0.0001).

We conclude that indirect cholangiography results in a low rate of detection of duct stones but this may be unimportant.
RECONSTITUTION OF SINGLE POTASSIUM CHANNELS FROM BOVINE
GALLBLADDER EPITHELIUM

S. Kriscionite, A. D. Bouchier, B. H. Ashley
Departments of Medicine and Biochemistry, University of
Edinburgh, Scotland, UK.

Apical and basolateral plasma membrane vesicles (APMV
and BLMV respectively) were prepared from the mucosal
epithelium of healthy bovine gallbladders which had been
obtained from an abattoir within 1 hr of death. We adapted
standard subfractionation techniques used in other studies,
including the use of self-forming Percoll density gradients, to
form closed membrane vesicles containing 0.4 M sucrose.
Vesicular ion channels were subsequently incorporated into
double-layer planar lipid bilayers. These were formed
across a small aperture separating two solution-filled
chambers designated cis and trans, containing 450 mM
and 50 mM KCl respectively (each buffered to a pH of 7.4).
Vigorous stirring of vesicles (final concentration -5 mg
protein/ml) into the cis chamber, especially in the
presence of 1-2 mM Ca2+, usually resulted in the
incorporation of 1 or more channels within 40 min
(presumably following vesicle-bilayer fusion). Most of the
channels were selective for K+ and measured reversal
potentials close to the Nernstian K+ equilibrium potential
of -56mV under these ionic conditions (potentials are
quoted as cis-trans, following the standard convention).
In addition to low-conductance voltage-insensitive APMV K+
channels (1 ± 3 pS, mean ± SD, n=5, calculated as the
equipotence conductance from plots of single-channel current vs
voltage), we observed evidence for several distinct types of
K+ channel in BLMV preparations. Conductances ranged
from 10-450 pS, and included a species of high-conductance
K+ channel (Kactivated channel). This was voltage- and
Ca2+ dependent (increasingly activated at
more positive potentials, and by increasing cis Ca2+ to
10mM, and blocked by 1-10 mM tetraethylammonium (added to the
trans compartment).
Plasma membrane ion channels are of importance to
gallbladder function. Planar bilayer reconstitution is a
useful adjunct to patch-clamp studies, especially for
small amounts of human tissue and for relatively inaccessible channels located in basolateral membranes.

COMPARISON OF THE COST OF LAPAROSCOPIC AND MINI-
CHOLECYSTECTOMY: A RANDOMISED TRIAL

A. J. McMahon, T. J. Russell, J. N. Barter, P. J. O'Dwyer
Depts of Surgery, Western and Royal Infirmary, Glasgow UK
and Health Services Research Unit, University of Aberdeen, UK

Laparoscopic cholecystectomy is claimed to cost less than
open cholecystectomy. The aim of the present study was to assess
the in-hospital cost of laparoscopic (LC n=73) and
minilaparotomy cholecystectomy (MC n=71) as part of a
prospective randomised controlled trial.

A detailed breakdown of theatre, ward, and staffing costs
was obtained from the resource management unit of the
hospitals. The median operation time in the LC group
was 65 minutes compared to 30 minutes in the MC group
(Mann-Whitney U test p<0.001), and hence the median
theatre costs of LC were higher (LC £700 versus MC £573,
p<0.001). There was an additional theatre cost of £60
(Video-laparoscopic equipment) and £203 (disposable LC
instruments kit) per patient in the LC group. Average post-
operative hospital stay in the laparoscopic group was 3 days
compared to 4 in the minilaparotomy group (p<0.001),
hence total ward costs were greater in the minilap group
(LC £295 versus MC £199, p<0.001). The median total
hospital costs for LC (£1443) was substantially higher than
that of MC (£1021) - p<0.001. If non-disposable
instruments had been used, LC would still have been
significantly more expensive than MC (95% C.I. of the
difference £58 to £198, P<0.001).

In conclusion, LC is significantly more expensive than MC.
However, this additional cost of LC can be substantially
reduced by the use of re-usable instruments.

RETURN TO NORMAL ACTIVITY AFTER LAPAROSCOPIC AND
MINI-CHOLECYSTECTOMY: A RANDOMISED TRIAL

C. Morrison, G. Ramsay, D. Galloway, G. Sunderland, P. J. O'Dwyer
Depts of Surgery, Western and Royal Infirmary, Glasgow UK
and Health Services Research Unit, University of Aberdeen, UK

Laparoscopic cholecystectomy (LC) is said to be followed by
a more rapid return to normal activity than open
cholecystectomy, but there is a paucity of objective data to
support this claim. The aim of the present study was to assess
return to normal activity after LC and minilaparotomy
cholecystectomy (MC) as part of a randomised trial.

A questionnaire asking about return to normal activity, and
containing an adapted SF-36 health survey
questionnaire, and the hospital anxiety and depression scale
(HADS) was sent to patients at 1, 4 and 12 weeks post-
operatively. In this interim analysis, a reply to at least one
questionnaire was obtained from 131 out of 137 (96%) patients
(MC n=62, LC n=69). There was a more rapid return to work
in the LC (median 12 days versus MC 20 days, p<0.001),
social activity (LC 14 versus MC 21 days, p<0.001), and
hobbies (LC 9 versus MC 11 days, p<0.001). Only 24% of patients were in
paid employment, and in these, the median time to return to work
was 7 weeks in both groups. At one week, the LC group had
better physical mobility (p=0.03) role functioning scores
(p=0.04) and lower pain scores (p=0.001) than the MC group,
but by 4 weeks only the physical mobility score was better in
the LC group (p=0.043). There were no significant differences in
SF-36 mental and social functioning domain and HADS scores
between the groups.

In conclusion, this study provides objective evidence of a more
rapid return to normal activity after laparoscopic
cholecystectomy compared to minilaparotomy cholecystectomy.

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL) FOR
BILE DUCT CALCULUS USING A PIEZOELECTRIC
LITHOTRIPTER: S. Ghosh, S. Mousa, K.R. Palmer,
Gastrointestinal Unit, Western General Hospital, Edinburgh.

There is considerable experience of biliary ESWL using the Dornier electrichydraulic
lithotripter. Although often successful, the procedure is painful and general anaesthesia or
intravenous sedation may be necessary. Piezoelectric lithotripsy is better tolerated but
experience is much more limited. 18 patients (49-84 years) underwent ESWL for bile
duct calculi using the Wolf 2300 piezoelectric
lithotripter. All had unsuccessful attempts at
endoscopic or t-tube extraction. 12 patients
had solitary calculi, 6 patients had 2-3 stones;
median stone size was 20mm (range 15-40mm).
Shock waves were focused ultrasonically,
masobiliary (19) or t-tube (3) cholangiography
was used to define stone position and
fragmentation. 1-3 (median 2) sessions per
patient of 1500 - 1900 (median 1650) shocks
each lasting 20-25 minutes over a 1-15 (median
3) day period were used. MTBE infusion (5
patients) and sphincterotomy enlargement (7
patients) were also employed.

Stone fragmentation was achieved in 17
patients (94%) and patients (678) had confirmed bile duct clearance. The failures
underwent surgical cholecdocholithotomy (5),
biliary stenting (2), extracorporeal lithotripsy (1)
or no treatment (1). ESWL failure was due to
obstructive obesity, stone calcification or
difficulty of focusing. No complications
developed and the procedures were well tolerated
without the need for sedation or analgesia.
Piezoelectric ESWL is an acceptable, safe and
moderately effective treatment for bile duct
calculi.
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OBSTRUCTIVE JAUNDICE PROMOTES BACTERIAL TRANSLATION
R. Clements, C.M. Sevitt, J. Hill, M. D. Parry and R.H. Halliday
(introduced by Dr. P.J. Hoofnagle).
Dept. of Surgery, Queen's University, Belfast, N. Ireland.

Infection and endotoxaemia continue to be the major source of morbidity and mortality in patients with obstructive jaundice. Bile salts emulsify endotoxins and their release from the gastrointestinal tract (GIT) may result in bacterial overgrowth and consequently translocation into the portal circulation. The aim of this study was to investigate the effects of experimental obstructive jaundice on GIT structure and bacterial flora in relation to translocation of bacteria to mesenteric lymph nodes (MLN), portal blood and systemic organs.

Method: Three groups of Wistar rats were studied (No operation (N=6), Stent insertion (N=6), Bile duct ligation (BDL) (N=16)). After 3 weeks, portal blood was cultured aerobically and anaerobically. The MLN, liver, spleen, lungs and a 1 cm segment of colon was removed and homogenised in an anaerobic cabinet. Aliquots of each of the homogenates were quantitatively cultured for aerobic and anaerobic bacteria. Segments of terminal ileum and colon were excised and prepared for histological examination. Plasma was assayed for bilirubin, endotoxin and antigyclophil antibody (AOGA) concentrations. Results: Compared to control and sham operated animals, jaundiced rats had significantly increased bacterial translocation (P<0.02, Fisher's exact test) which correlated with increased plasma endotoxin and AOGA concentrations (P<0.05, Spearman Rank). There was no qualitative or quantitative difference in colonic bacterial flora or intestinal structure between groups:

<table>
<thead>
<tr>
<th>No op.</th>
<th>Bile duct</th>
<th>Sham op.</th>
<th>Bile duct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (umol/l)</td>
<td>0.9 ±0.2</td>
<td>0.8 ±0.3</td>
<td>0.9 ±0.2</td>
</tr>
<tr>
<td>Endotoxin (pg/ml)</td>
<td>59.2 ±24.6</td>
<td>59.2 ±24.6</td>
<td>59.2 ±24.6</td>
</tr>
<tr>
<td>AOGA (82.6)</td>
<td>82.6</td>
<td>82.6</td>
<td>82.6</td>
</tr>
<tr>
<td>Ratio (%)</td>
<td>28</td>
<td>28</td>
<td>28</td>
</tr>
</tbody>
</table>

Conclusion: Experimental jaundice promotes translocation of enteric bacteria, despite there being no demonstrable change in intraluminal colonic flora or intestinal structure. Circulating endotoxin may induce this phenomenon and perpetuate a cycle of bacterial translocation.

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THE EFFECT OF URSODEOXYCHOLIC ACID TREATMENT IN PRIMARY SCLEROSING CHOLANGITIS (PSC) S. O’Brien, R. L. Greis, A. W. Haffield, The Middlesex Hospital, Mortimer St, London WIN 8AA.

The observation that treatment with UDCA is associated with improvements in symptoms and liver biochemistry in patients with primary biliary cirrhosis has prompted the investigation of the efficacy of UDCA treatment in patients with PSC.

Between 1988 and 1992, 14 patients (7 male, mean age 52 years; range 27-71 years) with PSC have been treated with UDCA (10mg/kg body weight). Symptoms of jaundice or cholestasis were present in 11 patients. All patients had classical cholangiographic and/or histologic features of intractable PSC while 13 patients had one or more strictures of the extrahepatic biliary tree. Seven patients had a dominant bile duct stricture requiring intervention with dilation (N=7) and/or stenting (N=4) during the treatment period.

UDCA treatment was followed-up for a mean of 25.7 months (range 25-56 months) and short-term improvement in clinical symptoms and liver biochemistry was observed in 13 of 14 patients (92.8%). No adverse side effects were reported with UDCA treatment and significant improvements in clinical symptoms and liver biochemistry were observed in 10 of 11 patients (90.9%) who have been followed for 16 months longer and patients remain stable.

Following 12 months treatment with UDCA alkaline phosphatase decreased from (mean ± SEM) 126.8 ± 233.9 to 71.5 ± 7.7 (P<0.01; Student’s T test), bilirubin decreased from 82.6 ± 22.2 to 25.7 ± 7.5 (P<0.01) and aspartate aminotransferase decreased from 232.6 ± 76.6 to 97.1 ± 14.6 (P=0.06).

Follow-up after 1 year has demonstrated that the improvements in clinical symptoms and liver biochemistry have been sustained for up to 45 months in 8 patients. Two other patients remain clinically well after 32 and 42 months respectively on treatment although liver biochemistry has recently deteriorated and 1 patient died after 18 months from progressive hepatic failure.

UDCA treatment is associated with long-term improvements in clinical symptoms and biochemical cholestasis in the majority of patients with PSC. However appropriate endoscopic therapy should also be performed in those patients with dominant bile duct strictures.

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PROPHYLAXIS OF BILIARY STENT BLOCKAGE USING CYCLICAL ANTIBIOTICS AND URSEDOXYCHOLIC ACID. S. Ghosh, K.R. Palmer, Gastrointestinal Unit, Western General Hospital, Edinburgh.

Biliary stent blockage is due to a combination of bacterial colonisation and restricted turbulent bile flow through the endoprosthesis. We reasoned that a combination of cyclical antibiotics and a choleretic agent might reduce the rate of stent occlusion.

87 consecutive patients aged 62-85 (median 70) years underwent endoscopic biliary stenting for unresectable malignant biliary obstruction using 10 or 11.5 F straight prosthesis. 70 patients were treated with a regime comprising monthly cycles of Ampicillin 500mg qid, Metronidazole 400mg bid and Ciprofloxacin 500mg bid, substituting (46 teaching, 13 district general) percutaneous catheter submitted prospective data from September 1990-1992. A total of 2236 cholecystectomy were audited over the study period which represented a consecutive data of cholecystectomies performed. LC was attempted in 1655 (74%) patients and completed in 1427 patients (conversion rate to open procedure - 14%). For each patient the proportion of cholecystectomy patients having LC was 74% (median) (range 30-99) over the study period. The mean operation time in the completed laparoscopic cholecystectomy patients was 100 minutes (range 30-330) and overall hospital stay 4 days (1-33). There were eight deaths (0.5%) after LC although only 2 were directly attributable to the laparoscopic procedure. In the LC group there were 96 complications (5.8%), 45 (2.7%) of which were major requiring further invasive intervention. Thirty five patients (2%) required early or delayed laparotomy for major complications such as bleeding or bile duct injury. The additional bile duct injuries in the LC series, 5 were noted during the initial procedure and 6 were recognised later due to jaundice or bile leaks. Ductal injuries occurred after a median of 20 laparoscopic cholecystectomies.

In conclusion LC has rapidly replaced OC in the treatment of gallbladder disease. Although the overall mortality and complication rate associated with LC is similar to OC, the bile duct injury rate is higher.

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A PROSPECTIVE AUDIT OF THE INTRODUCTION OF LAPAROSCOPIC CHOLECYSTECTOMY IN THE WEST OF SCOTLAND G. M. Fullarton, G. Bell and The West Of Scotland Laparoscopic Cholecystectomy Study Group Pancreatitis-Biliary Unit, Royal Infirmary, Glasgow G059

Although laparoscopic cholecystectomy (LC) has rapidly developed in the treatment of cholelithiasis in the UK in the absence of controlled clinical trial data it's outcome parameters compared to open cholecystectomy (OC) remain unclear. We have prospectively audited the introduction of LC in the West of Scotland over a 2 year period to attempt to assess this new procedure. A total of 45 surgeons in 17 hospitals (46 teaching, 13 district general) performing LC submitted prospective data from September 1990-1992. A total of 2236 cholecystectomies were audited over the study period which represented a consecutive data of cholecystectomies performed. LC was attempted in 1655 (74%) patients and completed in 1427 patients (conversion rate to open procedure - 14%). For each patient the proportion of cholecystectomy patients having LC was 74% (median) (range 30-99) over the study period. The mean operation time in the completed laparoscopic cholecystectomy patients was 100 minutes (range 30-330) and overall hospital stay 4 days (1-33). There were eight deaths (0.5%) after LC although only 2 were directly attributable to the laparoscopic procedure. In the LC group there were 96 complications (5.8%), 45 (2.7%) of which were major requiring further invasive intervention. Thirty five patients (2%) required early or delayed laparotomy for major complications such as bleeding or bile duct injury. The additional bile duct injuries in the LC series, 5 were noted during the initial procedure and 6 were recognised later due to jaundice or bile leaks. Ductal injuries occurred after a median of 20 laparoscopic cholecystectomies.

In conclusion LC has rapidly replaced OC in the treatment of gallbladder disease. Although the overall mortality and complication rate associated with LC is similar to OC, the bile duct injury rate is higher.
We compared cost-effectiveness of ESWL with adjunct bile acid treatment (55 pts), elective conventional (45 pts) and laparoscopic (47 pts) cholecystectomy. Selection for ESWL was performed according to the Munich criteria. 

Cost-effectiveness outcomes in the ESWL group, 60% of pts had 1 stone, and 40% 2 or 3 stones. Actuarial analysis showed complete stone dissolution after one procedure in 83% and 85% of pts with solitary and 35% of pts with multiple stones. None of the 9 pts with a calcified rim stone was stone free. Major complications were pancreaticitis and obstructive jaundice (each 1 pt: successful endoscopic treatment). One pt in the conventional cholecystectomy group was operated for incidental hernia. In the laparoscopic cholecystectomy group, 3 pts had laparotomy because of adhesions, hemorrhage or bile leakage (each 1 pt: uneventful recovery). Subjective health outcomes: persistent complaints after ESWL, conventional and laparoscopic cholecystectomy occurred in 59%, 11% and 14% resp. (p<0.05) and new complaints in 12%, 11% and 5% resp. Patient appreciation score (mean ± SD) (very bad; 10=excellent) was 6.2±2.4, 8±3.2 and 9.3±1.3 resp. (p<0.05). In the ESWL group, patient appreciation score, and absence of symptoms were significantly related to absence of stones. In case of complete stone dissolution, patient appreciation and absence of persistent symptoms was not different from cholecystectomy groups. ESWL efficacy: after ESWL, conventional and laparoscopic cholecystectomy, mean hospital stay was 2.4, 10 and 3.5 days resp (p<0.05). Hospital costs were highest after conventional and lowest after laparoscopic cholecystectomy. Job or household activities were resumed after 7, 43 and 11 days resp. (p<0.05). Conclusion: After ESWL, patient appreciation and absence of symptoms is only high in the case of complete stone dissolution. Laparoscopic cholecystectomy is cheaper, with excellent objective and subjective health outcomes.

LONG TERM FOLLOW UP OF BILIARY ENDOPROSTHESIS INSERTION FOR COMMON BILE DUCT STONES

A Lari, B Davidson, R Horton, A Burroughs, J S Dooley

Royal Free Hospital and School of Medicine, London

Common bile duct (CBD) stones in elderly patients are best treated by endoscopic sphincterotomy (ES). CBD clearance cannot be achieved a biliary stent may be inserted. However few reports on their long term outcome are available.

Over a three year period Jan 1987-Dec 1989 100 patients with CBD stones were referred for endoscopic stone removal. In 14 of these patients (3M, 11F, median age 83 years, range 79-97 years) the CBD could not be cleared endoscopically and a stent was inserted. Twelve of the 14 patients were jaundiced and 5 had acute cholangitis (AC).

The maximum diameter of the impacted stones ranged from 10-42mm with a median of 17mm. Stent insertion resolved jaundice and sepsis in all cases and all patients were discharged from hospital. In-patient stay ranged from 1-82 days (median 12 days) and was significantly increased by the presence of acute cholangitis (p=0.03, Mann U).

Long term follow up was obtained in 12 of the 14 patients (86%) by referral to GP's and out patient notes. Six patients are alive (median follow up 4 years, range 36-60 months). One of the 6 developed further jaundice due to stent migration and had further ES and stone removal. Six patients died at 1,3,12,32,36 and 42 months following stent insertion from unrelated causes. One developed further AC requiring antibiotic treatment and another required stent replacement.

Stenting of CBD stones in elderly patients is safe and effective but associated with further biliary problems in 25% of cases on long term follow up.
**F279**

**PROMOTION OF GALLBLADDER EMPTING BY RAPID INTRAVENOUS ADMINISTRATION OF AMINO ACIDS: A DOSE FINDING STUDY.**

G. Zoli, A. Ballerini, I. Hasty, LID O'Donnell, M. Clark, MIG Paring. Dept. Gastroenterology & Radiology, St Bartholomew's Hospital, London, UK & I Medical Pathology, University of Bologna, Italy.

Patients receiving total intravenous nutrition have inert gallbladders and as a consequence develop gallbladder sludge and gallstones; these can be prevented by enhancing gallbladder emptying. We have explored the efficacy of rapid infusions of intravenous amino acids (IVAA) in stimulating cholecystokinin (CCK) release and gallbladder contraction, and determined the minimum infusion regimen capable of producing gallbladder emptying.

Eight healthy fasted subjects on separate mornings received in random order four different infusion regimens of an IVAA mixture (Synthetic 14, 85 g/l amino acids). Gallbladder volumes were determined by ultrasonography before and at 5 min intervals for 60 min after commencing the infusion. Blood was obtained by an indwelling i.v. cannula before and at 10, 20, 30, 45 and 60 min after the start of the infusion. Plasma CCK was measured by bioassay.

The mean (SEM) emptying fraction with the various IVAA regimens were: 61.0±12.5% with 250ml in 30 min, 76.4±4.5 with 250ml in 10 min, 63.6±4.8 with 125ml in 5 min, and 24.4±8.0 with 50ml in 5 min. The latter regimen produced significantly less emptying than the other three (p<0.005). All IVAA regimens produced significant (p<0.001) rise in plasma CCK concentrations. Peak and integrated plasma CCK concentrations were not different with infusions of 250ml in 30 min (mean 5.9±1.1 pmol/l, 211.3±32.2pmol/l/60min, respectively), 250ml in 10 min (8.2±0.5, 225.6±16.3), 125ml in 5 min (7.6±0.7, 192.9±20.6), but were significantly lower with the infusion of 50ml in 5 min (2.1±0.2, 82.4±6.3; p<0.001).

Interval rapid infusion of IVAA in a load as low as 125ml in 5 min promotes CCK release and gallbladder emptying and should prove useful therapeutically, not only during intravenous nutrition, but also in other situations associated with gallbladder inertia, such as critically ill patients in intensive care units and during the post-operative period.

**F280**

**ACTIVATION OF MUCOSAL EOSINOPHILS IS AN EARLY STEP IN INDOMETHACIN/(INDO)-INDUCED SMALL INTESTINAL ENTEROPATHY.**

A. Anthony, A.P.Dilllon, G. Nygaard, C. Piascik, M. Hudson, R.E. Founder, A.J. Wakefield. Inflammatory Bowel Disease Study Group, Royal Free Hospital School of Medicine, London, UK.

In the rat, oral indo causes early jejunal villous shortening and infiltration of the epithelium by eosinophils, prior to neutrophil infiltration (NI) (Anthony et al. Pathol Int 1992; 42:164-A). This study quantified, both early eosinophil infiltration of the surface epithelium and their subsequent depletion from the jejunal mucosa at later times. Methods: Groups of 5 male Sprague-Dawley rats received a single oral dose of indo (15mg/kg) or vehicle. The animals were anaesthetised at 0.5 (pre NI) or 6 hours (post NI) after dosing and the small bowel was perfusion-fixed. Up to 20 sections from the jejunum were taken for histochemical staining (carbol-chromotropic method) of both eosinophils and free eosinophil granules. The results are expressed as combined total eosinophils and free eosinophil granule clusters that (a) infiltrate the epithelium per cross-section at 0.5 hours and (b) are present (per villus) within inflamed villi at 6 hours (means ±SEM). Other animals (total = 10) had blood taken for estimation of plasma indo by hplc. Results: There was extensive infiltration of an intact surface epithelium by mucosal eosinophils as well as by free eosinophil granules, in otherwise normal villi, at 0.5 hours (indo: 19.9±2.3, vs controls: 2.5±0.7, P<0.05). There was a positive correlation between eosinophil and eosinophil granule infiltration of the epithelium (r=0.978). By 6 hours, shortened and inflamed but intact villi showed marked depletion of eosinophils from the lamina propria (indo: 0.85±0.16 vs controls: 18.0±0.86, P<0.01). Mean plasma indo levels at 0.5 and 6 hours were 26 and 36ug/ml respectively. Summary: Jejunal mucosal eosinophils undergo mobilisation towards and degradation within the epithelium as early as 0.5 hours after oral indo and are virtually absent 5.5 hours later. Conclusion: Eosinophil activation is an early histological change in this model and merits further detailed investigation. (This study was funded by Glaxo Group Research Ltd, Ware, UK).

**F281**

**DETECTION OF ANTI - HEPATITIS A IgM AND IgA IN SALIVA.**


* Dept. of Medical Microbiology, Virus Reference Laboratory, University College Dublin, Belfield, Dublin 4.
**Dept. of Medicine and Gastroenterology, Royal College of Surgeons in Ireland, and Beaumont Hospital, Dublin.

An evaluation has been made of the usefulness of salivary immunoglobulins in the detection of Hepatitis A (HAV) infection. Currently, determination of infection involves assaying for anti-HAV IgM (for recent infection) or IgG (for past infection) in serum. Saliva would be superior to serum for use in diagnosis, in that collection is quick, simple and non-invasive, and involves less risk of exposure to serious disease for those handling the sample.

Two capture Erythrocyte Linked Immunosorbent Assays (ELISA's) for anti-HAV IgM and IgA were developed, and used to detect specific antibody levels in the saliva of 26 acute HAV patients. Paired sera from these patients were also assayed for anti-HAV IgM (by the Welcozyme anti-HAV IgM assay) and for anti-HAV IgA (by an in-house assay), and the results compared to those of the salivary assays. It was found that 96.2% (25/26) of the patients positive for anti-HAV IgM in the serum assay were positive in the salivary assay. The salivary anti-HAV IgM assay detected 88.5% (23/26) of the positives detected by the serum assay. The three negative samples in the salivary anti-HAV IgA assay were positive in the salivary anti-IgA assay. More importantly, the negative sample in the salivary anti-HAV IgM assay was found to be positive in the salivary anti-IgA assay.

We therefore conclude that, although the sample was small, saliva has the potential to be used diagnostically in place of serum in Hepatitis A infection. However, in order to detect all cases of recent infection using saliva, our data suggests that it may be necessary to combine the anti-IgM and anti-IgA tests into a single assay. Work is in progress in this direction, as well as on a salivary anti-HAV IgG assay.

**F282**

**GENETIC POLYMORPHISMS OF TUMOUR NECROSIS FACTOR a (TNFa) AND IL-10 (IL-1B) IN INFLAMMATORY BOWEL DISEASE.**

J.C. Mansfield, H. Helden, A.G. Wilson, E.S. di Giovin, C.D. Holdworth, G.W. Duff. Section of Molecular Medicine, Department of Medicine, University of Sheffield, and Department of Gastroenterology, Royal Hallamshire Hospital, Sheffield, S10 2JF.

Expression of TNFa and IL-1β is increased in the inflammatory lesions of inflammatory bowel disease. The promoter regions of the genes for these cytokines have single base pair polymorphisms at positions -308 of TNFa and -511 of IL-1B. In this study we have determined the allelic frequencies of these genes in Caucasian patients with ulcerative colitis, Crohn's disease and a healthy local control population.

Genomic DNA was used as template for amplification by the polymerase chain reaction (PCR), using primers specific to the polymorphic region and designed to create a restriction enzyme site in one allele. After digestion with restriction enzyme, the PCR product was run on a polyacrylamide electrophoresis gel to identify the alleles.

The allelic frequencies (%): are:

<table>
<thead>
<tr>
<th>Allele</th>
<th>Crohn's</th>
<th>U.C.</th>
<th>Control</th>
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<tbody>
<tr>
<td>n=78</td>
<td>n=113</td>
<td>n=156</td>
<td></td>
</tr>
<tr>
<td>TNFa-1</td>
<td>76</td>
<td>69</td>
<td>77</td>
</tr>
<tr>
<td>TNFa-2</td>
<td>24</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>IL-1β-1</td>
<td>69</td>
<td>63</td>
<td>60</td>
</tr>
<tr>
<td>IL-1β-2</td>
<td>31</td>
<td>37</td>
<td></td>
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</table>

X² tests show no significant differences between disease and control groups. Analysis of these cytokine polymorphisms does not provide new genetic markers for inflammatory bowel disease.
LONG TERM RISK OF PEPTIC ULCER DISEASE IN PEOPLE WITH HELICOBACTER PYLORI INFECTION - A COMMUNITY BASED STUDY
DIE Cullen, B. Collins, KJ Christianen, J Epis, JR Warren, KJ Cullen. Royal Perth Hospital and the Busselton Population Studies Group

The aim of this study was to determine the long term risk of peptic ulcer disease (PUD) in the community in subjects who are seropositive for Helicobacter pylori (Hp). We studied 407 randomly selected adults (293 men, mean age 54 (range 40-66 years) using an acid-glycine extract ELISA technique to detect anti-Hp antibody on stored sera sampled between 1966 and 1990. In addition we performed a postal questionnaire survey and a review of medical records for PUD (verified by endoscopy or barium meal reports). All 407 subjects had serum analysed from specimens taken in 1990, 357 (88%) subjects had at least one other serum analysed from blood sampled between 1966 and 1978, and 174 (43%) subjects had at least two old serum samples analysed. RESULTS: The mean follow-up period for those tested on more than one sera was 18 years (range 12-25 years). 362 (89%) subjects responded to the questionnaire and 376 (92%) had review of patient records. A positive test for anti-Hp antibody was present in one or more sera in 157 (39%) subjects. Of these 157 Hp seropositive people. 24 (15%) developed a definite and verified duodenal ulcer (DU) between 1966 and 1991, compared with only 7/250 (3%) Hp seronegative subjects. (RR=5.5, 95% CI 2.4-12.4) Over this same time period, 30/157 (19%) Hp seropositive subjects had a definite or possible peptic ulcer (DU and/or GU) compared with 11/250 (4%) Hp seronegative subjects (RR=4.3, 95% CI 2.2-8.4)

CONCLUSION: Adults in the community with serological evidence of Hp infection have a significantly increased risk of clinical PUD compared with Hp seronegative subjects with approximately 1 in 6 Hp seropositive subjects developing PUD over 25 years.
DETECTION OF H Pylori IN Fecal Samples FROM PATIENTS WITH DIARRHEA
S M Kelly, G R Gibson (Introduced by J H Cummings)
Departments of Gastroenterology, Addenbrooke’s Hospital, Cambridge and MMC Dunn Nutrition Centre, Cambridge.

The recent isolation of H pylori from faeces indicates that this microorganism can be transmitted via a faecal-oral route of spread. In this study, we determined the presence of H pylori in faeces from patients with dyspepsia. Patients underwent diagnostic gastroscopy at which biopsies for histology and a urea test were taken, or underwent a 14C urea breath test, to detect gastric colonisation with H pylori. These patients also donated a stool sample for bacteriological analysis. Fresh faecal samples were collected and immediately suspended in 0.1 M Sodium Phosphate buffer (pH 7.0) which had been prepared and stored under anaerobic conditions at 37°C, to give a final concentration of 20% (w/v). Slurries were then centrifuged at 15,000g for 30 mins. The resultant bacterial pellet was washed in buffer, centrifuged again and plated out on selective growth media (Bent supplement Columbia Agar Base and 5% (+ blood added – Oxoid). A further aliquot was used to test for urease activity.

To date, 23 patients have been studied. 14 had positive gastric biopsies or breath test for H pylori, 9 were negative. In the 14 positive patients, 15 gave a positive urease test in under 2 mins. By comparison, the 9 negative patients gave a very slow, or completely negative reaction. Pure cultures of H pylori were obtained from 9 of the 14 positive subjects. Bacterial identification was carried out on the basis of colonial characteristics, Gram reaction, microscopic examination, urease and methyl-red tests. Similar colonies were not isolated from any of the negative patients. This study confirms that H pylori can be found in faecal samples and therefore that faecal-oral transmission is feasible. A rapid faecal test on concentrated faecal samples may be a clinically useful marker for H pylori infection.

A DIRECT RELATIONSHIP BETWEEN INFECTIVE LOAD OF HELICOBACTER PYLORI AND OXYGEN FREE RADICAL (OFR) PRODUCTION IN ANTRAL MUCOSAL BIOSPES
G R Davies, G C Collins, N Banatyal, D S Rampton, GI Science Research Unit and Dept of Epidemiology & Medical Statistics, London Hospital Medical College, London E1, UK.

We have previously shown that H pylori (HP) infection is associated with excessive antral mucosal oxygen free radical (OFR) production, and that HP organisms and culture supernatant stimulate OFR production from neutrophils in vitro. If these phenomena were of relevance to pathogenesis, the numbers of HP present and the production of mucosal ROMs in gastric mucosal biopsies should be directly related. The study aimed to demonstrate such a relationship. Methods Gastric mucosal biopsies were taken, as close together as possible, from the juxtapyloric antrum. Mucosal OFR production was assessed using luminol (75μmol)-dependent chemiluminescence (CL). Following CL assay, biopsies could be formalin-preserved, and normal-quality H and E sections obtained. Histological assessment of density of HP infection and mucosal damage was made on these sections by an independent observer in 11 patients. 2 additional biopsies were taken for culture, with HP infective load expressed as colony forming units(CFU)/mg. Results Biopsies infected with greater numbers of HP by histological assessment produced more OFR: Grade 0 (no organisms seen), CL (expressed as median (quartile range) photon emission x 10^3/min/mg minus background) -1.18 (-2.8 to 4.3), n=25; Grade 1, 1.71 (-3.1 to 7.9), n = 24; Grade 2, 2.6 (-3.2 to 4.8), p = 0.004 (x70, bacteria per biopsy) 12.1 (3.6 to 26.4) n=14; (p=0.004 Kruskal Wallis). CL was positively related to histological assessment of mucosal damage (Gammon et al., Gastroenterology 1991). The regression of colony counts from adjacent mucosal biopsies was poor: CV of the differences between the 11 pairs of CFU scores was 279%. The average CFU/mg level of each patient did not correlate significantly with their the CL result. Conclusions The direct relationships found between OFR production and histology, and between infective load of H pylori, OFR production and histological damage, is further evidence for a pathogenic role of OFR in H pylori-related disease. Comparison of results from different biopsies of the same patient is made difficult by the marked variation in HP infective load over small areas of mucosa.


HIV infected patients with intestinal Cryptosporidiosis often have profuse diarrhoea. The pathogenesis is incompletely understood. We assessed ileal function in HIV infected patients with a dual radiostopic test and compared the results with that obtained in patients with ileal Crohn’s disease who’s diarrhoea may be in part due to incomplete absorption of bile acids. Methods: Twenty healthy controls, 13 patients with ileal Crohn’s disease and 7 HIV positive patients, 4 of whom had intestinal Cryptosporidiosis, underwent whole body retention measurements seven days following ingestion of a synthetic bile acid 75SeHCAT (1 μCi) and 56Co VitB12 (0.5 μCi) with intrinsic factor. Results: The mean (+SD) retention of the radioisotopes was:

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Crohn’s</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>75SeHCAT</td>
<td>38.4±10.9</td>
<td>10.3±13.4</td>
<td>27.6±22.7</td>
</tr>
<tr>
<td>56Co VitB12</td>
<td>60.8±16.1</td>
<td>41.3±27.7</td>
<td>25.6±22.8</td>
</tr>
</tbody>
</table>

All 4 patients with Cryptosporidiosis had malabsorption of 75SeHCAT and/or 56Co VitB12, to a greater extent than patients with Crohn’s ileitis. Conclusion: HIV infected patients with Cryptosporidiosis had impaired ileal function with severe malabsorption of Vit B12. This suggests that the frequency of VitB12 deficiency in these patients and the latter may explain the large volume diarrhoea seen in Cryptosporidiosis.

A SECOND SPECIES OF INTESTINAL MICROSPORIDIA CAUSES DIARRHOEA IN AIDS AND IS APPARENTLY ELIMINATED BY ALBENDAZOLE
Blanshard C, Ellis DS, Chauhan D, Gazzard BG, The HIV/GUM Unit, Westminster Hospital, London. The EM Department, London School of Hygiene and Tropical Medicine.

We have previously described a second intestinal microsporidian in an AIDS patient with diarrhoea but in that case were unable to study the ultrastructure of the organism or its response to therapy. We now describe a second case of infection with this organism. A homosexual man, known to have had the acquired immunodeficiency syndrome since December 1990, presented in April 1992 with a 6 month history of diarrhoea and 12kg weight loss. Glardia were initially present in the stools but he had failed to respond to metronidazole. Upper GI endoscopy showed atrophic duodenal mucosa. Glardia and microsporidia were present on biopsy, and microsporidia spores were seen in faecal smears stained with Giemsa. At electron microscopy the microsporidia were morphologically different from Enterocytozoon bieneusi: they were present in a septated vacuole, had no electron-lucent clefts and electron dense discs and in the spores the coils of the polar tube were arranged in a single row of 8 coils. They were similar to an organism recently seen in the stools of an AIDS patient named "Cheatella intestinalis". Despite eliminating the glardia the patient became severely ill with vomiting, copious diarrhoea and continuing weight loss, but after receiving oral albendazole in June his symptoms had resolved completely and he had gained 8kg. Repeat duodenal biopsies and stools were negative for microsporidia. He had a clinical and parasitological relapse one month after stopping albendazole but responded to a second course and remains well on maintenance therapy.

The response of this organism to albendazole emphasises the importance of looking for microsporidia in AIDS patients with diarrhoea.