LANSOPRAZOLE PROVIDES GREATER SYMPTOM RELIEF THAN OMEPRAZOLE IN REFUX OESOPHAGITIS. A S Mee, J L Rowley and the Lansoprazole Study Group, Royal Berkshire & Battle Hospitals NHS Trust, Reading, RG1 5AN, UK.

Lansoprazole, a second generation proton pump inhibitor, provides effective symptom relief and healing in reflux oesophagitis. Its greater bioavailability compared to omeprazole results in superior initial acid suppression. This study was designed to compare symptom relief and healing rates in patients with reflux oesophagitis.

Methods 604 patients with endoscopically proven reflux oesophagitis, were randomly assigned to receive lansoprazole 30mg or omeprazole 20mg daily for up to 8 weeks. Daily assessment of symptoms was made by the patient using a Visual Analogue Scale. Clinical symptoms were evaluated at weeks 1, 4 and 8. Endoscopic assessment of healing, defined by normalisation of the oesophageal mucosal appearance, was made at weeks 4 and 8.

Results 282 patients in the lansoprazole group and 283 patients in the omeprazole group were eligible for inclusion in the per-protocol analysis. At 3 days, there was a significant improvement in daytime symptoms of heartburn for patients in the lansoprazole group, compared to the omeprazole group (p<0.05). A similar but non significant trend was seen at 7 days. Clinical assessment at 7 days demonstrated significant improvement in daytime epigastric pain in the lansoprazole group, compared to the omeprazole group (p<0.03), with a similar but non significant trend in night-time epigastric pain. Oesophagitis was healed in 69% of patients in the lansoprazole group and 63% of patients in the omeprazole group at 4 weeks. This increased to 87% and 82% respectively at 8 weeks. Both treatments were well tolerated.

Conclusion Lansoprazole provides greater symptom relief compared to omeprazole during the first week of treatment, with a greater number of patients healed after both 4 and 8 weeks treatment.

COLORECTAL T91-T105


Aim: As faecal tumour necrosis factor-alpha (TNF-α) is elevated in most HIV-positive patients with microsporidiosis, we used thalidomide, an anti-TNF-α agent, as a novel treatment. Patients and methods: 12 HIV-positive subjects (mean CD4 count 28 cells/mm³) with chronic diarrhoea of twelve months duration (range 2-24, sd 9) due to microsporidiosis were recruited. All had received albendazole without effect on their symptoms. TNF-α testing was measured using a standard sandwich ELISA. Subjects were prescribed a four week course of thalidomide, 100mg nocte. At the end of the study period a repeat stool sample for microbiology and TNF-α was provided and weight, symptoms and antidiarrhoeal use prior to and during treatment were recorded.

Results: Mean bowel frequency fell from 6/day (range 2-10, sd 2.4) to 1.8/day (range 1-4, sd 0.8) [p<0.0001]. Mean weight increase was 1.4 kg (range 0-3, sd 2). Mean antidiarrhoeal use fell from 6 tablets a day (range 0-15, sd 5) to 2.8 a day (range 0-15, sd 5.1) [p<0.005]. TNF-α fell from 19.4 u/ml (range 7.8-72.9, sd 26) to 8.3 u/ml (range 7.8-11, sd 1.3) [p=0.3]. Microsporidial spores were still identified in the stools post therapy.

Three patients experienced a generalised rash and one was sedated. A further patient had a relapse of diarrhoea at one week.

Conclusion: Thalidomide is a novel and effective treatment for diarrhoea due to microsporidiosis.


WESSEX COLORECTAL CANCER AUDIT: COLOSTOMY RATES FOLLOWING COLON AND RECTAL SURGERY. B Foxard, N Thompson, B Mee, on behalf of the Wessex Colorectal Cancer Audit Working Group. Cancer Intelligence Unit, Institute of Public Health Medicine, Dunn House, Romsey Road, Winchester SO22 5OH

A population based audit on patients diagnosed with colorectal cancer is in progress. This analysis reports on 2957 patients diagnosed with primary colorectal cancer between September 1991 and August 1993. 74% of all rectal cancers underwent a potentially sphincter preserving operation. For elective rectal and colon procedures the colostomy rate was 28%, as compared to 41% for emergency procedures. In elective rectal anterior resections 39% had a temporary colostomy, which reduced to 9% at one year. The proportion of elective rectal anterior resections with a colostomy for surgeons performing more than 10 rectal procedures per year was 68% compared to 36% for those performing less (p<0.005).

The leaked rate in the elective rectal resections having a colostomy at the first operation was not significantly different at 4.5% as compared with 8.7% for cases with no colostomy. However, the re-operation rate as a result of leakage in elective rectal cancer patients with a defunctioning colostomy occurred in 18% of patients as compared to 3% when no initial colostomy was performed. A higher proportion of patients who died post operatively having experienced a leak did not have a colostomy (11.7%,16/137) than had a colostomy (4.3%, 4/93) (p=0.087).

Thus surgeons who operate most frequently on rectal cancers have a higher use of colostomies. These data suggest that use of colostomies result in a reduction in morbidity and mortality.
NON-STEROIDAL ANTI-INFLAMMATORY DRUGS, ASPIRIN AND COLO-RECTAL CANCER: A RECORD-LINKAGE CASE-CONTROL STUDY

T M Macdonald, J MM Evans, AD McMahon, MM McGlacken, G White, DG McDermot, FE Murray. Medicines Monitoring Unit, Dept of Clinical Pharmacology, Ninewells Hospital, Dundee, DD1 9SY

Recent evidence from both experimental and epidemiological studies has suggested that non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin may be associated with reduced incidence of colorectal cancer (CRCA). The aim of this study was to evaluate the relationship between CRCA and prior use of NSAIDs and aspirin.

Methods A case-control study was conducted using a purpose-built record-linkage database containing all dispensed drug and hospitalisation data for the population of Tayside. 455 cases among 319,465 people, resident since Jan 89, who were first hospitalised with histologically and surgically proven colorectal adenocarcinoma between Jan 90 and Dec 92 were used. Up to six age and sex-matched community controls (n = 2,725) and two hospital controls (n = 908) (hospitalised with any diagnosis at the same hospital within 3 months of the case) were randomly generated from the study population. Exposure to NSAIDs and aspirin at any time from Jan 89 was assessed and modelled using conditional logistic regression. This process was repeated using a Recent exposure (120 days) variable. Results are given as odds ratios (OR) with 95% confidence intervals.

Results The unadjusted ORs for ever exposure to NSAIDs were 0.9 (0.7, 1.1) with community controls and 0.6 (0.5, 0.8) with hospital controls. The ORs for aspirin were 1.2 (0.8, 1.9) and 0.5 (0.4, 0.8) respectively. There were no changes in these results in a conditional logistic regression analysis that adjusted for the confounding effects of aspirin and NSAIDs simultaneously. Use of NSAIDs during the 120 days prior to the index date was also significantly associated with a reduced risk of CRCA, with adjusted ORs of 0.6 (0.4, 0.8) using community controls and 0.4 (0.3, 0.6) using hospital controls.

Conclusion These data support the hypothesis that use of NSAIDs is associated with a reduced risk of CRCA. However, the association is less conclusive for prescribed aspirin.

LOCAL RECURRENCE AFTER STANDARD AND LAPAROSCOPICALLY ASSESSED ABDOMINAL RESECTION OF COLORECTAL CARCINOMAS: A. J. Waghorn, H Scott; Spencer, C Wood, M Pignatelli, W Kmiot. Royal Postgraduate Medical School, D Cane Road, LONDON W12.

The removal of colorectal cancers using a laparoscopic method is a relatively new technique, but there is controversy regarding its appropriateness oncologically. 35 consecutive patients who had undergone colorectal excision over an 18 month period (17 by a standard open method and 18 by a laparoscopically assisted method) were reviewed independently in a dedicated colorectal clinic 1 to 2.5 years following resection. The type of operative procedure performed was similar in both groups. The excised tumours were reviewed by a specialist colorectal histopathologist.

Local Recurrence

<table>
<thead>
<tr>
<th></th>
<th>n=18</th>
<th>n=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>67(50-83)</td>
<td>65(53-79)</td>
</tr>
<tr>
<td>Dukes Stage B+C (90%)</td>
<td>16(90%)</td>
<td>14(82%)</td>
</tr>
</tbody>
</table>

Overall

<table>
<thead>
<tr>
<th></th>
<th>n=18</th>
<th>n=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median number of lymph nodes</td>
<td>9(2-17)</td>
<td>10(5-18)</td>
</tr>
<tr>
<td>Average length of stay (days)</td>
<td>10.4</td>
<td>11.4</td>
</tr>
</tbody>
</table>

We are concerned that the high local recurrence rate may be due partly to inadequate tumour resection laparoscopically.
T97

CONTROLLED STUDY OF OUTCOME IN ILEAL CROHN'S DISEASE: A COMPARISON OF PERFORATING AND NON-PERFORATING INDICATIONS FOR THE INITIAL RESECTION

Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH.

Resection for ileal or ileo-colonic Crohn's disease is followed by further resection in a significant proportion of patients. It has been suggested (Greenstein et al. Gut 1993; 15: 288) that the presence of an abscess, fistula or frank perforation ("perforating" features) at the initial operation predicts a more aggressive form of the disease with increased recurrence and reoperation rates. We therefore undertook a controlled study to determine whether surgical outcome differed between perforating and non-perforating disease.

Methods: The medical records of 192 Crohn's disease patients under review after ileal resection in Southampton since 1970 were studied. Each of the 64 patients with perforating (P) indications for their initial surgery (20 abscesses, 20 fistulae, 18 abscesses with fistulae, 4 abscesses with perforation and 2 perforation alone) was matched for age at diagnosis, sex and family history with two patients with non-perforating indications (NP). Rates of second and third ileal resection were analysed by life-table analysis. Median follow-up was 125 months.

Results: Twenty two patients (34%) with perforating indications and 38 (30%) with non-perforating indications underwent second resections. Cumulative re-operation rates in the P and NP groups, respectively, were 25.1% and 20.9% at 5 years and 38.3% and 35.6% at 10 years (NS). Five year cumulative rates for third resection in 5 P and 12 NP patients were 18.5% and 19.7% respectively (NS).

Conclusion: Patients with evidence of perforating and non-perforating features at initial operation had similar re-operation rates for the second and third resections. This first controlled study refutes the hypothesis that a more aggressive course of Crohn's disease can be predicted by the presenting features.

T98

GENETICS VS. ENVIRONMENT IN INFLAMMATORY BOWEL DISEASE: CONCORDANCE RATES IN 130 TWIN PAIRS

NP Thompson, R Driscoll, RE Pounder, A J Wakefield.
Inflammatory Bowel Disease Study Group, Royal Free Hospital School of Medicine, Nat Assoc for Colitis and Crohn's Disease, London NW3.

Aim: To determine the level of concordance for Crohn's disease and ulcerative colitis in identical and non-identical twin pairs.

Introduction: There has been only one previous inflammatory bowel disease (IBD) study using twins. In Crohn's disease concordance was greater in monozygotic than dizygotic twins, in ulcerative colitis concordance was low in both groups. Linkage analysis studies have not shown an HLA association with either Crohn's or ulcerative colitis. There is a 10-20% incidence of IBD in family members of those with these diseases.

Methods: The National Association for Colitis and Crohn's Disease (NACC) is a UK patient support organisation, with about 6,000 members of whom about half have Crohn's disease. All were sent an invitation to be involved in a study of twins. Those who replied were sent a follow-up questionnaire, and if necessary a reminder. This determined the nature of the disease and zyosity, using a validated questionnaire. Concordance rates were compared using Maenet-Haaszel Chi-squared tests. Results: 216 NACC members replied to the initial invitation, of whom 184 (85%) replied to the questionnaire. 130 twin pairs were identified in whom at least one had IBD and twin concordance was known (68 with Crohn's disease and 62 with ulcerative colitis). The mean age at diagnosis was 30 years in those with Crohn's disease and 35 years in those with ulcerative colitis. The mean duration of IBD was 10 years. In Crohn's 5/23 identical and 2/43 non-identical twins were concordant for IBD and in ulcerative colitis 5/31 identical and 1/28 non-identical twins were concordant; in 5 twin pairs zyosity was uncertain. Concordance was significantly greater in identical than non-identical twins, p = 0.02. There was no difference in concordance rates between Crohn's disease and ulcerative colitis, p = 0.8.

Conclusions: This twin study, the largest to date, suggests that there is a small but significant genetic factor in the aetiology of IBD. Environmental factors are likely to be of prime importance.

T99

EARLY DETERMINANTS OF INFLAMMATORY BOWEL DISEASE: USE OF TWO NATIONAL LONGITUDINAL BIRTH COHORTS.

NP Thompson, SM Montgomery †, MJ Wadsworth ‡, RE Pounder, AJ Wakefield.
Inflammatory Bowel Disease Study Group, Royal Free Hospital School of Medicine, † Social Statistics Research Unit, City University, ‡ MRC National Survey of Health & Development, University College, London.

Aim: To determine if factors in utero and early childhood are associated with the development of inflammatory bowel disease (IBD).

Introduction: The 1946 National Survey of Health & Development (NSHD) (n=332) and the 1958 National Child Development Study (NCDS) (n=11407) are longitudinal birth cohorts which have followed periodically those born during 2 one-week periods in Great Britain until the age of 33 years (NCDS) or 43 years (NSHD).

Methods: In control design was used, combining both data sets; 8 controls (matched for gender and social class) were used per case. In both cohorts the member's hospital physician was contacted to confirm the diagnosis of IBD. Data concerning maternal infection in pregnancy (NCDS only), childhood infection (measles, mumps and whooping cough), appendectomy, breast feeding and measures of housing conditions in childhood were analysed (by Chi-squared tests).

Results: 24 cases of Crohn's disease (CD), 26 cases of ulcerative colitis (UC) and 4 cases of indeterminate IBD were identified. We found no significant associations between the development of CD or UC and any of the studied factors. There was a trend that those with CD were more likely not to have been breast fed (p<0.1), to have had poor amenities in childhood (p=0.3) and not to have had an appendectomy (p=0.2). The opposite was true of those with UC (p=0.1, p=0.2 and p=0.07 respectively).

Conclusions: The overall prevalence of IBD in NSHD was 3.7/1000 and 3.1/1000 in NCDS. Childhood factors may be different, or even opposite, for those with CD and UC. Although the number of identified cases is small, this is the first prospective study of these factors and these cohorts will be increasingly valuable data sources.

T100

APPENDICECTOMY, TONSILLECTOMY AND RISK OF INFLAMMATORY BOWEL DISEASE. R.F.A. Logan, A.E. Duggan, I. Usmani, K. R. Neal. University Dept of Public Health & Epidemiology and Division of Gastroenterology, University Hospital, Nottingham, NG7 2UH.

Whether the human appendix has a specific function is unclear. Nonetheless Rutgeerts et al. (Gastroenterology 1994;106:1251-3) have suggested that appendectomy will protect against the development of ulcerative colitis (UC), having found a strong inverse association between them with a 'protective' odds ratio (OR) of 59. Others have found a much weaker association after allowing for appendectomies performed before the onset of UC in the cases. A positive association has also recently been reported between tonsillectomy and Crohn's disease (CD).

We have examined both associations in a case-control study involving 213 clinic attenders with UC, 110 with CD and 334 age and sex frequency matched controls having elective 'repair' surgery. Data was collected using a self-completed questionnaire enquiring about previous surgery and childhood domestic circumstances.

Nine (4%) of 202 UC patients reported a previous appendectomy compared with 57 (19%) of 295 controls and 24 (24%) of 102 CD patients (data missing or unclear in the remainder) giving an OR of 0.19 (95% confidence limits 0.1-0.4, p<.0001) for UC patients having had an appendectomy and an OR of 1.28 (0.7-2.2) for CD patients compared with controls. In 6 with UC and 12 with CD appendectomy preceded diagnosis by >1 year (age at appendectomy missing in 1 UC and 3 CD). Of 201 age and sex matched pairs 295 had appendectomy before the UC case's age at diagnosis giving an OR of 0.18 (0.1-0.4) for appendectomy before UC onset. There were only weak associations with tonsillectomy for either disease (UC OR 1.24 (0.8-1.9), CD OR 1.22 (0.7-2.0)).

These results confirm the inverse association between UC and appendectomy and show that it antedates UC onset. The association is stronger that with smoking and suggests that, if causal, it is due to appendectomy per se rather than protection by factors causing acute appendicitis.
**T101**

**IS PROXIMAL DEMARCATION OF ULCERATIVE COLITIS DETERMINED BY THE TERRITORY OF THE INFERIOR MESENTERIC ARTERY?**

**Hamilton MJ, Dick R, Crawford L, Thompson NP, Pounder RE,**
 Wakefield A1 Inflammatory Bowel Disease Study Group and Department of Radiology, Royal Free Hospital and School of Medicine, London, NW3

**Introduction:** Dramatic demarcation between diseased and normal mucosa is often seen in ulcerative colitis (UC) and is not explained by current pathogenetic hypotheses of UC. **Hypothesis:** In UC this demarcation occurs at the watershed of vascular territories, and disease is confined to the territory of the inferior mesenteric artery (IMA).

**Methods:** 10 perfusion-fixed colorectal specimens from patients with UC were studied using *in vitro* angiography. The macro and microscopic extent of disease was assessed. **Results:** Of the 10 cases studied, 6 had pancolitis associated with a 'complete' marginal artery (MA) that spanned the length of the colon uniting IMA and superior mesenteric artery (SMA). 3 cases had sharply demarcated disease in which the MA arose from the IMA and ended abruptly at the point of disease. **Conclusions:** Significant abnormalities of the right MA and a complete MA. Macroscopic normality of the proximal colon was confirmed microscopically. The MA originated in continuity with the IMA and extended to the right colon. The MA stopped at a point clearly visible on the angiogram, and beyond, the colon was supplied by branches of the SMA. There was no demonstrable anastomosis between these two vascular territories. Vessels distal to the watershed were dilated with irregularities of calibre in the vessels of the encircling arcades, while those proximal to the watershed were more regular in comparison. The association between left-sided UC and an incomplete MA was significant (p=0.03 Fisher's exact test). **Conclusions:** These data suggest that the MA arises as a branch of the IMA and that demarcation is determined by the limit of the MA. We hypothesise that some characteristic of the mucosal microvasculature in the territory of IMA, possibly embryological in origin, predisposes the dependent colon to develop UC. This characteristic remains to be determined.

**T102**

**MICROSCOPIC COLITIS: WIDENING THE DEFINITION**

**A. Javaheri, M. Sheaf, A. Forbes, M. A. Kamn, I. C. Talbot. St. Mark's Hospital, City Road, London.**

Microscopic Colitis refers to chronic idiopathic watery diarrhoea with histological but no radiological or endoscopic abnormality. The histological criteria, which embrace lymphocytic (LC) and collagenous colitis (CC), are: increased intraepithelial and lamina propria lymphocytes, surface epithelial damage, and in CC a thickened collagen plate. We believe a histological variant can present with an identical clinical syndrome.

Patients: 12 patients (5 male, mean age 49 years) with diarrhoea for more than six months had normal blood tests, stool microbiology and macroscopic bowel appearance (both radiologically and endoscopically). Mean duration of symptoms 3 years (range 0.5-20 years). Associated conditions were: arthropathy (4), hypothyroidism (1), and diabetes. Previous histology in this group had failed to fulfil criteria for LC or CC.

Results: were compared with those from established cases of LC (7), and CC (5) (11 female, mean age of 35).

Methods: Histology was reviewed independently by 2 pathologists, and only cases with histological consensus included. Biopsies were assessed for: crypt distortion, subepithelial collagen band, surface epithelial damage, inflammatory infiltrate in epithelium, crypts & lamina propria.

Results: The major finding in the 12 study patients, was mild mixed inflammatory infiltrate in the lamina propria, including 6 with excess eosinophils. Mild lymphocytic infiltrate was seen in the surface epithelium (n=8) in the crypt epithelium (n=9), with mild crypt distortion (n=5). No biopsy had an abnormal collagen band. The control group had prominent epithelial inflammation and fulfilled standard criteria.

Conclusion: Patients with identical clinical features to LC and CC but distinct histology exist, and appear to represent part of the microscopic colitis spectrum. Their histological findings, often regarded as non-specific, appear to be clinically significant.

**T103**

**DIRECT MEASUREMENT OFRECTAL NITRIC OXIDE IN ULCERATIVE COLITIS**

**P.D. Reynolds, S.M. Middleton, G. Hansford, and J.O. Hunter.**

Department of Gastroenterology, Addenbrooke's Hospital, Cambridge CB2 2QQ and Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW

The cause of ulcerative colitis (UC) is unknown. Indirect evidence of the production of nitric oxide (NO) in this disease has been observed by the measurement of nitric oxide synthase (NOS) activity. This is determined by the conversion of arginine to citrulline and its inhibition by specific NOS inhibitors such as monomethyl-L-arginine.

For collection of rectal gases the rectum was perfused with nitrogen gas at atmospheric pressure to carry these gases into a trap apparatus composed of two glass cylinders the first at -78°C (solid CO2 in acetone) and the second at -196°C (liquid nitrogen). NO collected from the second glass cylinder was then distilled into a gas cell and measured by infra-red diode laser spectroscopy. The minimum detectable amount of NO in the sample cell was 0.1 nmole. This is a specific and sensitive method for measuring NO and none of the rectal gases have rotation-vibration absorption transitions that overlap.

Eight patients with active UC, diagnosed by clinical symptoms, sigmoidoscopy and history and eight normal controls underwent rectal perfusion. NO was not detected in any of the healthy controls, but was present in concentrations of 0.13 to 1.1 nmole in four out of eight patients. All the UC patients negative for NO had significant rectal bleeding and NO may have been bound or metabolised by haemoglobin.

This is the first direct measurement of rectal NO in UC. NO is cystototic to intestinal epithelial cells and it may have a pathogenic role in this disease.

**T104**

**ANTI-EPIHELIAL CELL ANTIBODIES IN FAMILIAL INFLAMMATORY BOWEL (IBD) DISEASE AND THEIR RELATIVES.**


Genetic susceptibility exists in IBD. Anti-colon antibodies occur in patients with ulcerative colitis (UC) and antibodies to murine intestinal epithelial antigens have been detected in patients with IBD and their relatives. Our aim was to investigate if these antibodies recognise antigens derived from a human colon epithelial cell line (Caco-2) using an enzyme linked immunosorbant assay. Methods: Sera were obtained from 39 families with multiple (2 or more) members affected with IBD, their 1st degree relatives, IBD patients without a positive family history (sporadic cases) and healthy controls. The IBD families were affected with either UC (n=22) or Crohn's disease (CD) only (n=17). Caco-2 cells were grown in microtiter plates and fixed in ethanol. After blocking with 2% BSA and 1% goat serum, test sera were added (1:150 dilution) for 1 h at 37°C. Peroxidase conjugated anti-human IgG was added for 1 h at 37°C, followed by substrate. Optical density (OD) was read at 450 nm. The Kruskal-Wallis and Mann-Whitney tests were used for statistical analysis. Results:

<table>
<thead>
<tr>
<th></th>
<th>Sporadic</th>
<th>Familial</th>
<th>Relatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>CD</td>
<td>UC</td>
<td>CD</td>
</tr>
<tr>
<td>n</td>
<td>49</td>
<td>63</td>
<td>74</td>
</tr>
<tr>
<td>OD</td>
<td>1.07</td>
<td>0.79</td>
<td>0.99</td>
</tr>
<tr>
<td>(0.37)</td>
<td>(0.32)</td>
<td>(0.32)</td>
<td>(0.38)</td>
</tr>
<tr>
<td>+ve**</td>
<td>24%</td>
<td>9%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*OD expressed as mean (SD) **+ve = OD > 2SD of controls

There was increased immunoreactivity in patients with UC (sporadic and familial) compared to healthy controls (p<0.001). For CD immunoreactivity against Caco-2 cells was only increased in familial cases (p<0.01 vs controls). Relatives of UC families but not of CD families demonstrated increased immunoreactivity when compared to controls (p=0.04).

Our results show that a small proportion of patients with sporadic UC, familial UC and their unaffected relatives have circulating antibodies against human colocones. In contrast patients with familial CD but not sporadic CD have increased immunoreactivity to human colocones.
ADENOCARCINOMA OF THE OESOPHAGO-GASTRIC JUNCTION IS ASSOCIATED WITH BARRETT'S OESOPHAGUS.

**Methods:** Consecutive fresh endoscopic resection specimens were mapped and measured and then fixed, and a mean of 7.7 tissue blocks per case taken from around the tumor and stained with H and E and Alcian Blue. Cases found by endoscopic surveillance of known BE were excluded. BE was defined as incomplete intestinal metaplasia in the oesophagus. Adenocarcinoma of the oesophago-gastric junction, (AC-J), was defined as the tumour mid point 5 cm above or below the oesophago-gastric junction: more proximal adenocarcinomas were defined as oesophageal (AC-O). Squamous cell carcinomas (SC) of the oesophagus were controls.

**Results:** 41 patients had resection for carcinoma of the oesophagus or oesophageal carcinoma with tumour-related symptoms (dysphagia, chest pain, bleeding).

<table>
<thead>
<tr>
<th>n</th>
<th>Mean age</th>
<th>Sex</th>
<th>Barrett Oesophagus</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC-O</td>
<td>9</td>
<td>53</td>
<td>8M, 1F</td>
</tr>
<tr>
<td>AC-J</td>
<td>24</td>
<td>63</td>
<td>22M, 2F</td>
</tr>
<tr>
<td>SC</td>
<td>8</td>
<td>61</td>
<td>5M, 3F</td>
</tr>
</tbody>
</table>

Eight of 9 AC-O cases had a long segment BE (2 cm). Five of 10 AC-J cases had a long BE and 5 had a short BE segment, <3 cm in length. BE was found in 8 of 12 (67%) cases of AC-J where the tumor was <6 cm long, but in only 2 of 12 (17%) cases of AC-J where the cancer was longer than 6 cm (<p < 0.05). Intestinal metaplasia was found in the upper stomach in 25% of cases of AC-J and 50% of cases of SC, but this was not considered to represent BE.

**Conclusions:** BE was present in all cases of AC-O and also in many cases of AC-J, being found more often with smaller tumors. It is likely that most adenocarcinomas of the oesophago-gastric junction arise in a short or long segment of BE, and that larger tumors overgrow the BE in which they arose.

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**Quality of life assessment is an important tool in measuring outcome in patients undergoing treatment for carcinoma of the oesophagus.**

O’Hanlon DM, Karrat D, Harkin M, Sargeant T, Raimes S, Griffin SM. Dept of Surgical Gastroenterology, Newcastle General Hospital, Newcastle-upon-Tyne.

Carcinoma of the oesophagus is an uncommon tumour which frequently presents when advanced. It may be associated with debilitating symptoms, the most distressing of which is dysphagia. Although radical resection offers the best hope of cure, many patients are unfit for surgery and undergo radiotherapy or intubation to palliate symptoms. This study prospectively assessed 69 consecutive patients who were treated with surgery, radiotherapy or intubation alone or a combination of these, to examine what impact these treatments had on patient quality of life (QOL). Patients were assessed prior to intervention and post intervention at 6 and 12 weeks by one of 2 trained nurses, using a modified Rotterdam Symptom Checklist and Activities of Daily Living questionnaire which included an assessment of dysphagia. Results are given in the table.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Surgery</th>
<th>Radiotherapy</th>
<th>Intubation</th>
<th>Combination</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>63.4 (1.8)</td>
<td>68.1 (1.6)</td>
<td>68.2 (1.4)</td>
<td>65.8 (2.7)</td>
</tr>
<tr>
<td>Number</td>
<td>18</td>
<td>31</td>
<td>31</td>
<td>12</td>
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<tr>
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<td>12.0 (0.9)</td>
<td>12.5 (1.0)</td>
<td>12.5 (0.6)</td>
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<td>17.0 (2.0)</td>
<td>1.0 (0.3)</td>
<td>1.7 (0.2)</td>
</tr>
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<td>Diaphragm (yes)</td>
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<td>2.1 (0.2)</td>
<td>-1.5 (0.8)</td>
<td>2.4 (0.2)</td>
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<td>Total score (yes)</td>
<td>72.7 (2.4)</td>
<td>69.6 (2.1)</td>
<td>66.7 (1.7)</td>
<td>72.6 (2.3)</td>
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<td>Rotterdam score (yes)</td>
<td>77.4 (2.4)</td>
<td>66.4 (2.3)</td>
<td>-1.5 (0.8)</td>
<td>74.5 (3.1)</td>
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<tr>
<td>Weight (kg)</td>
<td>66.3 (2.8)</td>
<td>61.8 (2.1)</td>
<td>66.1 (2.1)</td>
<td>66.1 (2.1)</td>
</tr>
<tr>
<td>Post-op (kg)</td>
<td>66.3 (2.8)</td>
<td>60.3 (2.0)</td>
<td>-1.2 (0.8)</td>
<td>67.1 (3.9)</td>
</tr>
</tbody>
</table>

Results and mean (SEM). Statistics: Mann Whitney U and Wilcoxon. * P < 0.05 Vs Surgery group, ** P < 0.05 Vs Pre-op level in same group.

Patients undergoing oesophagectomy felt most knowledgeable about their disease and reported the best QOL post-op; 75% had returned to a normal diet after 4 months, versus 25% with an endoprosthesis and 47% undergoing radiotherapy. QOL analysis is a useful tool in assessing quality of care, communication and patient well being after the diagnosis and treatment of oesophageal cancer.
SELF-EXPANDING COVERED GIATRUCO STENT PREVENTS TUMOUR INGROWTH IN MALIGNANT DYSPHAGIA & SEALS ANASTOMOTIC LEAK

A Choy, G H Hutchison, J N Johnson & G Murphy
Department of Surgery & Department of Radiology, Halton General Hospital Trust, Runcorn, Cheshire

Patients with oesophageal carcinoma often have advanced disease and significant dysphagia at the time of presentation. Palliation by intubation is often unsatisfactory with incomplete resolution of symptoms. Laser therapy is costly and requires repeat treatments. Early experience with uncoated self-expanding metal stents suggested tumour ingrowth may lead to stent obstruction. We have investigated the use of self-expandable polyethylene covered Giatrucostents in the treatment of malignant dysphagia.

Over a 6 month period 18 patients were treated by self-expanding covered metal stents. The majority of these have been for grade III or IV dysphagia, although two were inserted for control of anastomotic leak following oesophageo-gastroentery. All procedures were carried out under sedation only with fluoroscopic control. Stenting was technically successful in all the patients with good and immediate relief of dysphagia and sealing of anastomotic leak. Early complications include retrosternal pain in 6 patients (33%) and one had stent migration (5.6%). Endoscopic follow up at 1 months showed 100% stent patency with no tumour ingrowth. Our experience suggests covered oesophageal stent should be considered ahead of other therapies in the treatment of irresectable malignant oesophageal tumours.

MANAGEMENT OF STRICTURES AFTER RADIOTHERAPY FOR TREATMENT OF OESOPHAGEAL CANCER

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National Medical Laser Centre, University College London, The Rayne Institute, 5 University Street, London WC1E 6JJ

Many oesophageal cancer patients treated with radiotherapy(RT) present with recurrent dysphagia necessitating further endoscopic therapy. They are often regarded as high risk for dilatation or intubation but this is poorly documented. We analysed the risks of dilating or intubating these patients compared with the risks in a control group with malignant dysphagia who had not undergone previous RT.

Over 6 years, 61(92%) of 63 patients who had undergone RT required endoscopic dilation with or without intubation. These constituted the study (RT) group. 43% had predominantly fibrous strictures and 57% predominantly tumour recurrence. Fibrous strictureing after RT was unrelated to histology. Many patients with fibrous strictures compared to those with recurrence had received laser therapy prior to RT (50% vs. 30%) and did not require further laser ablation subsequently (54% vs. 27%). The control group was 126 patients with similar malignancies who had not undergone prior RT and were palliated by dilatation with or without intubation either as the sole therapy or in conjunction with laser therapy. Patients treated by laser therapy but without dilatation (2 after RT), 44 without), were excluded from this analysis, but none of them perforated. In the RT group the perforation rate on dilating fibrous strictures was not significantly different from the rate for those with recurrence (2.9% vs. 3.2% per procedure, 7.7% vs. 5.7% per patient respectively). For the RT group a whole, the perforation rate was also very similar to that in the control group (3% vs. 4.7% per procedure, 6.5% vs. 8% per patient, respectively). Half of those who perforated in the control group did so at the first procedure on dilatation to 18mm. Laser therapy could not have compounded the risk of perforation in the RT or control group. Intubation with an endoscope was required at some stage of the patients illness in 48% of RT patients and 79% of controls. The risk of perforation related to intubation in the study and control groups was not significantly different (3% vs. 4%). However, the risk of tube migration was greater in the RT group, 21% vs. 3% (p=0.01).

In conclusion, one should not be deterred from dilating or intubating patients who have had previous radiotherapy with or without laser treatment as the risk of perforation is no greater than for those who have not had previous RT. Particular care should be taken dilating tumours that are very tight at presentation.

LAPAROSCOPIC NISSEN FUNDOPLICATION - LESSONS LEARNED FROM 200 CONSECUTIVE CASES

M Rhodes1, DC Godley2, BM Smithers2, B Menzie2, FJ Branicki2, L Nathanson2, Queensland University Department of Surgery, Royal Brisbane1 & Princess Alexandra Hospitals2, Brisbane, Queensland, Australia.

Laparoscopic Nissen fundoplication was undertaken in 200 patients between 1991 and 1994. Pre-operative assessment included symptom score, endoscopy, manometry and 24-hour pH monitoring of the oesophagus. Patients were evaluated at 3 and 12 months after surgery with symptom scoring and 66 patients also underwent 24-hour pH studies at 3 months.

In the first 100 patients duration of operation was 155min (70-330min), conversion rate to laparotomy was 7%, hospital stay was 3days (2-57days) and total morbidity was 16%. This compared to an operation time of 120min (60-240min)(p=0.0003, 95% CI 10,40), a conversion rate of 2% (p=0.2), a hospital stay of 3 days (1-18)(p=0.0008,95%C10,1) and total morbidity of 8% (p=0.15) in the second 100 patients. Median symptom scores fell from 5/9 to 0/9 after fundoplication (p<0.0001) whilst median 24 hour oesophageal acid exposure was reduced from 10% to 1% (p<0.0001).

These results demonstrate that the laparoscopic Nissen fundoplication is a safe and effective procedure for gastro-oesophageal reflux disease. With experience, duration of operation and hospital stay fall. Short-term symptomatic and pH results are consistently improved by surgery.

AUTONOMIC FUNCTION IN PATIENTS WITH ACHALASIA AND NUTCRACKER OESOPHAGUS.

N Trudgill, F Hussain, L Smith, D Cook, S Riley. Oesophageal Laboratory, Northern General Hospital, Sheffield, S5 7AU.

Although previous studies of autonomic function in patients with achalasia have yielded conflicting results, Auer et al. have recently reported clear evidence of pupillary and cardiovascular reflex abnormalities (Gastroenterology 1994;106: A-461). We have therefore studied non-gastrointestinal autonomic function in patients with established achalasia, a disease control group, nutcracker oesophagus, and age- and sex-matched healthy volunteers.

17 patients with achalasia (11 male, age 39 (25 to 61) years), 11 patients with nutcracker oesophagus (6 male, age 51 (39 to 59) years) and 20 matched controls underwent a battery of tests including: Valsalva ratio, 30:15 ratio, IE ratio, systolic blood pressure response to standing, diastolic blood pressure response to handgrip, lying and standing heart rate power spectral analysis and pupil cycle time estimation.

Autonomic function in patients with achalasia was not significantly different from healthy volunteers whereas patients with nutcracker oesophagus were abnormal. Pupil cycle length was significantly prolonged (1.23 (0.98 to 1.77) seconds vs. 1.05 (0.89 to 1.29) seconds, p=0.02), a blood pressure drop was apparent on standing [-6(-15 to + 5)mm/Hg vs. +4 (-12 to +10) mm/Hg, p=0.06] and the diastolic response to handgrip was attenuated (7[2 to 28]mm/Hg vs. 20 (11 to 45)mm/Hg, p=0.07).

Autonomic dysfunction is a feature of nutcracker oesophagus but not achalasia. The abnormality is diffuse affecting both cardiovascular and pupillary reflexes.
**EFFECT OF WEIGHT LOSS ON SYMPTOMS OF GASTRO-OESOPHAGEAL REFUX**


Introduction: There is anecdotal evidence to suggest that symptoms of gastro-oesophageal reflux (GOR) are associated with obesity. There are no reports which have prospectively assessed the independent effect of weight loss on reflux oesophagogastropatology.

Aim: To determine whether weight loss has a significant beneficial effect on the symptoms of GOR in overweight patients with either normal or abnormal endoscopic findings or grade 1 (Savary-Miller) oesophagitis.

Method: Patients were recruited on the basis of a body mass index of greater than 23 and symptoms of GOR disease for at least 6 weeks. All patients were adhered to lose weight. Symptoms of GOR were scored using a modified DeMeester questionnaire at 0, 6 and 20 weeks. Patients who were unable to stop taking all medication for control of symptoms were excluded from the study. Changes in weight and symptom score were analysed using a paired t-test. Correlation between change in weight and symptom score was assessed using the Pearson correlation test.

Results: 22 patients were studied (mean weight 81.8 kg). 17 patients lost weight with a mean of 3.6 kg (p < 0.01) and improved with a mean reduction of 84% from the initial symptom score (p < 0.001). 9 patients lost their symptoms completely. Only 2 patients reported no improvement, both of whom failed to lose weight, whilst 3 gained weight but still improved their symptom score. There was a significant direct correlation between weight loss and symptom score (r = 0.587, p < 0.004).

Conclusion: This study has demonstrated a significant association between weight loss and improvement in symptoms of GOR. Patients who are overweight should be encouraged to lose weight as part of first line management.

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**24-HOUR MANOMETRY IS ESSENTIAL TO DIAGNOSE DIFFUSE OESOPHAGEAL SPASM.**

C.P. Burnham, A.L. Fowler, A. Mills, D. Alderson. University Department of Surgery, Bristol Royal Infirmary, UK.

The diagnosis of Diffuse Oesophageal Spasm (DOS) relies on manometry which, by convention, requires more than one simultaneous wet swallow in a series of 10 (interspersed with normal peristaltic contractions). The development of 24-hour manometry now allows the correlation of symptoms with oesophageal motor abnormalities.

Over the last four years, two conventional laboratory-based manometric studies and one 24-hour study (Gaeltec recording system, Scotland) were carried out on 500 patients with oesophageal symptoms. Sixteen patients (seven male, median age 50 (range 37 - 65)), were found to have symptomatic oesophageal contractions during the 24-hour study. These painful contractions ('spasms') were characterised by multiple peaks, long durations (> 15 seconds) and excessive amplitudes (> 200 mmHg) and frequently occurred at night. Twelve of these patients had normal conventional manometric studies. Two patients had normal peristalsis to the wet swallows but had other contractions of long duration, excessive amplitude and multiple peaks (spasms) at some time during the laboratory study. In only two patients would the diagnosis of DOS have been made by conventional criteria.

Painful oesophageal spasms have long durations, excessive amplitudes and multiple peaks. Conventional manometry fails to diagnose the majority of these patients. New criteria, based on 24-hour manometry, are needed to define Diffuse Oesophageal Spasm.
Liver T117–T131

THE LOCALISATION OF COLLAGEN PRODUCTION BY IN SITU HYBRIDISATION (ISH) IN PRIMARY BILARY CIRRHOSIS (PBC) CIR Goddard, A Smith, JA Hoyland, P Baird, AJ Freemont, C Pittius, RFT McMahon, TW Wares. Dept. of Gastroenterology, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL.

Chronic liver disease is characterised by the accumulation of collagen and other matrix proteins within the liver. Identification of the cells producing collagen in chronic liver disease is of major importance in the search for effective treatments of these conditions and since the rate of collagen synthesis is under transcriptional control, localisation of procollagen mRNA offers a potential approach to this problem. ISH of type I procollagen mRNA was performed on 50 formalin-fixed, paraffin-embedded needle liver biopsies (6-36 months storage) from patients with PBC. Sections underwent ISH with an 35S labelled antisense RNA probe to rat α1(I) collagen. Sections hybridised with the corresponding sense probe and 5 biopsies, reported as normal, from patients with only mildly abnormal transaminases were used as negative controls. Although background levels varied, signal was not localised to any particular region on any of the sections hybridised with sense probe or in the 5 "normal" biopsies. On sections hybridised with antisense probe, signal localised almost entirely over fibroblasts in portal tracts and around the edges of fibrous septae radiating into the hepatic lobule. Signal was localised to perisinusoidal cells in only a few biopsies, but never to hepatocytes. We have demonstrated that ISH can be used on archived, routinely processed liver biopsy material to localise collagen synthesis and propose that fibroblasts invading from the portal tracts may be the main source of collagen in PBC rather than activated lipocytes as has been previously postulated.

EFFECT OF URSODEOXYCHOLIC ACID ON SERUM MARKERS OF FIBROSIS IN PRIMARY BILARY CIRRHOSIS A Verma, AG Lim, RP Jassaw, HA Ahmed, JD Maxwell, TC Northfield. Department of Medicine, St George's Hospital, London.

Ursodeoxycholic acid (UDCA)has been shown to improve liver function tests in primary biliary cirrhosis (PBC). However no improvements in hepatic fibrosis have been detected by liver biopsy. This may in part be due to sampling difficulties as hepatic changes in PBC are patchy. Serum markers such as procollagen III peptide (PIIP), hyaluronic acid (HA) and laminin (Lam P) may give a better overall assessment of fibrosis. Furthermore these measurements have recently been shown to be independent prognostic markers in PBC. Our aim was to determine the effect of UDCA on these markers in PBC. Our study group consisted of 44 PBC patients (early - stages 1 and 2, n = 21; late - stages 3 and 4, n = 23) and 15 healthy controls. 33 patients received UDCA (10-15mg/kg/day), and 11 received placebo. Serum samples were analysed for PIIP, HA and Lam P by radioimmunoassay at baseline and after a minimum of 6 months. HA (113.4±17.9 μg/l vs 35.6±4.9, p<0.02) and Lam P (2.1±1.0 μM/l vs 1.6±0.7, p<0.005) were significantly elevated compared to controls and there was a similar trend for PIIP (0.95±0.5 vs 0.80±0.4). The levels of HA (p value) and Lam P (p value) both correlated with PBC disease stage. The effect of treatment with UDCA is shown below.

<table>
<thead>
<tr>
<th></th>
<th>Early PBC=n=11</th>
<th>Late PBC=n=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre UDCA</td>
<td>Post UDCA</td>
<td>Pre UDCA</td>
</tr>
<tr>
<td>PIIP (μM)</td>
<td>0.87±0.08</td>
<td>0.77±0.07</td>
</tr>
<tr>
<td>HA (μg/l)</td>
<td>66.2±12</td>
<td>37.4±13</td>
</tr>
<tr>
<td>Lam P (μM)</td>
<td>2.1±0.14</td>
<td>2.37±0.12</td>
</tr>
</tbody>
</table>

We conclude that serum markers of fibrosis are raised in PBC; and that PIIP and HA are reduced during treatment with UDCA especially in early disease.

SURROGATE MARKERS OF RESPONSE IN A TRIAL OF URSODEOXYCHOLIC ACID (UDCA) AND COLCHICINE IN PRIMARY BILARY CIRRHOSIS (PBC) CIR Goddard, A Smith, L Hunt, T Halder, V Hillier, B Rowan, G Pallowfield, TW Wares. Dept. of Gastroenterology, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL.

Both colchicine and UDCA have, individually, been shown to improve standard liver function tests (LFTs) in PBC, although their effects on the underlying disease process remain uncertain. We report the preliminary results of a trial, established to assess their effects on standard LFTs, serum procollagen peptide (PIIPNP) levels assessed by the Orion assay (measuring only Col 1-3 i.e. collagen synthesis) and the Fab assay (measuring both Col 1 and Col 1-3 i.e. synthesis and degradation) and the dynamic LFTs: galactose elimination capacity (GEC) and bromosulfophthalein (BSP) excretion kinetics in PBC. 57 patients with PBC were randomised to receive either placebo, colchicine (1mg/day), UDCA (10mg/kg/day) or colchicine plus UDCA. Mean follow up was 15 months (range: 0-30 months). The 4 groups were well matched at entry. UDCA treatment produced highly significant decreases in serum AST, ALT, ALP, γGT and bilirubin over the first year. Colchicine individually had no effect on any of the parameters measured. An interaction between the two drugs prevented the fall in serum albumin which was seen in the other two treatment groups (p=0.018) and there was a strong trend towards an interaction which raised serum ALP (p=0.06). Although good correlations were observed between serum bilirubin and PIIP and BSP k and PIIPNP on entry to the trial (p<0.001, r=0.69, p=0.001, r=0.45 and p=0.001, r=0.56 respectively) there was no response to treatment in these parameters or the GEC. There was, however, a significant interaction between the drugs which increased PiIPNP (p value=0.008).

We conclude that although UDCA improves standard LFTs in PBC, it does not alter liver function assessed by the dynamic LFTs. The combination of the two drugs does not significantly change markers of collagen synthesis, but may promote collagen degradation.
LIVER TRANSPLANTATION FOR THE OVER SIXTIES? C. J. E. Watson on behalf of Addenbrooke's Hospital Transplant Unit (introduced by Dr G Alexander) Box 210, Addenbrooke's Hospital, Cambridge CB2 2QO

Liver transplantation is now accepted for the treatment of end stage liver failure. However, in view of the relative shortage of donor organs is it appropriate to offer transplantation to those patients over 60? We reviewed our results in this age group to determine whether the results supported continuation of this practice.

The study population comprised the 200 adult patients who underwent liver transplantation between 1/1/90 and 30/6/94, with a 6 month minimum follow-up. 34 (17%) were aged 60 or over and received a primary graft, of whom 4 required a subsequent transplant. The commonest indication for transplantation in this group was primary biliary cirrhosis (9, 26%), other indications including alcoholic cirrhosis (5), haemochromatosis (3), post viral cirrhosis (3), and autoimmune cirrhosis (3). Four patients were known to have tumours at the time of transplantation, and malignancy was diagnosed in 4 others following transplantation and examination of the explanted liver.

Survival in the older patients was comparable to the younger adults, with 1 and 2 year survivals of 65% and 58% respectively, compared to 72% and 66% for the younger adults. When those patients with chronic liver disease were considered separately, the 1 and 2 year survival was 71%. The poorest prognostic group were those 8 patients with malignancy, of whom 6 died, 1 from recurrence of hepatoma, 2 following retransplantation for early graft failure, and 3 from sepsis.

The results show that age alone should not be a bar to transplantation, particularly in those patients with chronic liver disease such as primary biliary cirrhosis.


Recent animal studies have demonstrated that some of the symptoms and metabolic derangements of hepatic encephalopathy may be due to the cerebral metabolism of ammonia to glutamine. The aim of this study was to investigate the effect of an oral glutamine load on stable cirrhotics awaiting transplantation. Twelve patients 3 male and 9 female mean age 50 (41-59) underwent 13 challenges (1 individual challenged twice with different doses). Three of the patients had a history of previous HE but none were overtly encephalopathic at the time of the study.

Baseline psychometric assessment was performed using the block design test, digit symbol test, digit span (from the Wechsler Adult Intelligence Scale) number connection test A, and an information processing test (from the Adult Memory and Information Processing Battery). Seven (58%) of the patients showed impairment on at least one of these tests. The glutamine challenges were performed following an overnight fast. Simple reaction time was measured using the Leeds Psychomotor Tester and a two lead (biparietal) analysed EEG recording made using a Cerebral Function Analysing Monitor. Glutamine in the form of a suspension in water was then given by mouth in a dose of 10g (8 patients) or 20g (5 patients).

There was a significant rise in blood ammonia from a mean of 56i mol/l at time 0 to 124μmol/l at 60 minutes (p<0.001), there was an associated increase in mean reaction time from 381ms to 471ms (p>0.05) and mean EEG amplitude from 66.4μV to 76.4μV (p<0.05). The change in amplitude showed a correlation with the change in blood ammonia r=0.82 (p<0.01).

The results of this study suggest that glutamine is neurotoxic in cirrhotic patients and that this is at least in part due to its systemic conversion to ammonia.

QT INTERVAL PROLONGATION AND AUTONOMIC DISFUNCTION IN ENDSTAGE LIVER DISEASE: EFFECT OF LIVER TRANSPLANTATION. R. Mohamed, MK Davies*, JM Neuberger. Queen Elizabeth Hospital, Selly Oak Hospital*, Birmingham.

Prolonged QT interval and disturbance of autonomic nervous system (ANS) function are markers of poor prognosis. We studied the prevalence of abnormal QT interval and ANS dysfunction in liver transplant candidates before and after orthotopic liver transplantation (OLT). 53 consecutive adult patients with endstage chronic liver disease (M=26; age16-69 years) had various aetiologies (alcoholic liver disease 9, others 46) and severity of liver disease (Child-Pugh grade C 30, B 18, A 5).

Six ANS function tests were done. QT measurement and ANS function tests were repeated after OLT when liver function tests were normal. RESULTS: QTc was prolonged in 37/53 (70%) of the patients. Parasympathetic dysfunction was present in 77% and sympathetic dysfunction in 39%. Of the 47 transplanted patients (6 still awaiting liver transplant), there was significant improvement in the QTc interval after OLT(p<0.001). ANS dysfunction also improved in 25 patients although in 7 of these patients, ANS function was still abnormal. 6 patients died after OLT. There was no correlation between QTc, ANS dysfunction and survival.

CONCLUSIONS: QTc interval prolongation and ANS dysfunction are frequent findings in patients with endstage chronic liver disease but improve after OLT, suggesting that they are associated with abnormal liver function.

IMPORTANCE OF CONCOMITANT VIRAL INFECTION AND TREATMENT DURING LATE ACUTE LIVER ALLOGRAFT REJECTION. J. Devlin, Y. Cakaloglu, S. Sunderland, B. C. Portmann, Roger Williams. Institute of Liver Studies, King's College School of Medicine and Dentistry and *Virology Section, Public Health Laboratory, Dulwich Hospital, London

Late acute liver allograft rejection is poorly characterised but clinically recognised to be often refractory to supplemental immunosuppression with a high incidence of evolution to a chronic rejection process.

In this study, we have determined accompanying events and reviewed the management and outcome of late acute cellular rejection episodes in 384 consecutive liver recipients conventionally immunosuppressed and also reviewed our recent experience of rejection following systematic immunosuppression withdrawal. In the first population, a significant proportion of patients experienced concomitant viral infection (n=15 (41%) with CMV infection being the largest group and smaller contributions from other viruses (CMV 30%, HSV 9%, EBV 9% and VZV 5%). 13 (33%) patients developed late rejection associated with low maintenance immunosuppression and in a further 10 patients no accompanying factor could be identified. Refractory rejection was higher in late compared to early rejection episodes in our series (29% vs 9.2%, p<0.05). Anti-viral chemotherapy administered in rejection episodes with concomitant viral infection, either as sole treatment or cases with accompanying hepatitis or as adjunctive therapy to further supplemental immunosuppression in episodes of steroid-resistant rejection, controlled the rejection process in all treated patients. Amongst those patients where immunosuppression was withdrawn (n=48), graft dysfunction in the context of systemic viral illness was also observed in 4 patients.

These results indicate an important role of viral infection in precipitating acute late liver allograft rejection. In these episodes, anti-viral therapy should be considered in favour of supplemental immunosuppression which may paradoxically promote underlying viral infection and thereby the high frequency of observed intractable rejection.
TREATMENT OF HEPATITIS B VIRUS RECURRENTNESS IN LIVER TRANSPLANT RECIPIENTS.

N.V. Nausinov, F. Torre, H.M. Smith, S. Pfit, B.C. Portmann and Roger Williams.

Institute of Liver Studies, King's College School of Medicine and Dentistry, London SE5 9PJ, UK.

Recurrent Hepatitis B virus (HBV) infection in the liver graft is associated with progressive graft damage and poor survival and there is no effective treatment at present. Alpha-interferon seems of little benefit in this particular group and prolonged antiviral therapy may be more promising. Famiciclovir is a new, oral nucleoside analogue, which showed potent inhibition of HBV replication in patients with chronic hepatitis B.

We have treated 8 HBAg(+) liver transplant recipients with established HBV recurrence in the graft with Famiciclovir 250 mg tds for 6 months. Pretreatment graft histology showed chronic hepatitis in 4 and liver cirrhosis in 4, all having various proportion of HBAg(+) hepatocytes, while 6 patients were viramic - serum HBV-DNA by 95-858 pg/ml. The therapy was well tolerated with no side effects. Following 6 months Famiciclovir treatment serum HBV-DNA fell in 5/6 patients, median reduction 34% (range 7-71%). The proportion of HBAg(+) hepatocytes in the graft was decreased in 2, unchanged in 3 and increased in 1 patient. Posttreatment graft histology showed reduced neocinflammatory activity in 3, unchanged in 1 and increased in 2 patients with no significant differences in hepatic fibrosis. During therapy serum AST fluctuated but remained abnormal in all patients who had elevated AST prior to treatment.

These results indicate that Famiciclovir has some antiviral potential in patients with HBV recurrence after liver transplantation. Higher dose regimens may be required to achieve virological and histological remission in these patients.

INTERCELLULAR ADHESION MOLECULE-1 AS A PREDICTOR OF LIVER ALLOGRAFT REJECTION

A. Bhargava, N.J. Bradley, A.K. Burroughs, A.P. Dhillon

University Department of Surgery, Liver Transplantation Unit and Department of Histopathology, Royal Free Hospital School of Medicine, Pond Street, London NW3 2QG

Intercellular Adhesion Molecule-1 (ICAM-1) is a cytokine inducible endothelial antigen. Degree of graft preservation induced injury is associated with higher rates of acute cellular rejection (ACR).

The aim of this study was to elucidate the distribution of ICAM-1 on liver allografts after overnight cold storage and reperfusion: correlating expression with post-operative outcome.

Following cold storage (723 ± 31 mins) and reperfusion (at 90 mins), liver biopsies from 30 grafts were snap-frozen. Smm frozen sections were stained immunohistochemically for ICAM-1. Expression of ICAM-1 was analysed by light microscopy. Liver from resection margins of benign tumours were used as controls: demonstrating weak sinusoidal staining.

Twenty-one of the 30 grafts, biopsied after storage alone, had induction of ICAM-1 on sinusoidal endothelium and hepatocytes. Of these, 14(66.6%) recipients had 3 or more rejection episodes (no non-responders). In 9/30 recipients with no ICAM-1 induction of ICAM-1 was observed by immunohistochemistry. The difference between these two groups was statistically significant (p<0.001, Fisher's Exact test). The expression of ICAM-1 on reperfusion biopsies showed further increase in staining intensity on hepatocytes and sinusoidal endothelium. Further material is being collected currently, to evaluate a larger number of biopsies.

Cytokine activation of ICAM-1 occurs during graft storage and is further increased after reperfusion. Induction of ICAM-1 on sinusoidal endothelium is likely to contribute to increased adhesiveness of circulating leukocytes. ICAM-1 induction may well enhance the immunogenicity of the graft. Our results suggest that induction of ICAM-1 following graft storage, contributes to increasing risk of acute cellular rejection post transplantation.

MECHANISMS OF CHANGES IN RENAL FUNCTION FOLLOWING TIPPS

Jalan, R., H.W. Thomas, Henderson, N., O'Rourke K., Dhillon, J.F., Williams, B.C., Redhead, D.N., Hayes P.C. Dept of Medicine, *Radiology and #Clinical Chemistry, Royal Infirmary, Edinburgh.

TIPPS reduces the portal pressure gradient and leads to better control of ascites. The aim of this study was to study the mechanism of change in renal function following TIPPS. Method: Twenty nine patients with ascites undergoing TIPPS for recurrent variceal haemorrhage (26) or refractory ascites (3) were studied. Urinary sodium (UNa), creatinine clearance (CrCl), peripheral renal activity (PRA), atrial natriuretic peptide (ANP), cyclic GMP (cGMP), a marker of nitric oxide activity and Angiotensin II (using radioimmunoassays), and lithium clearance (LiCl) (following oral administration of 300 mg of Lithium carbonate 12 hours previously in 12 of these patients, using flame photometry) were measured prior to and 3 months after TIPPS when the PFG and portography were also repeated. All the patients were haemodynamically stable and on no diuretics for at least 5 days prior to blood sampling. Results: Ascites was better controlled in all patients. Results were expressed as mean and standard error and are summarised below.

<table>
<thead>
<tr>
<th>Variable</th>
<th>PRE TIPPS</th>
<th>POST TIPPS</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFG (mmHg)</td>
<td>21.3</td>
<td>19.6</td>
<td>0.001</td>
</tr>
<tr>
<td>UNa (mmol/l)</td>
<td>39.6 (3.3)</td>
<td>67.4 (9.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>CrCl (ml/min)</td>
<td>46.4 (5.7)</td>
<td>53.5 (11.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>LiCl (mmol/min)</td>
<td>19.4 (1.7)</td>
<td>25.3 (1.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>PRA (ug/mq/hr)</td>
<td>13.4 (3.0)</td>
<td>4.5 (1.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>AII (ng/ml)</td>
<td>0.39 (0.01)</td>
<td>0.87 (0.01)</td>
<td>0.001</td>
</tr>
<tr>
<td>ANP (pg/ml)</td>
<td>8.37 (17.2)</td>
<td>9.0 (18.7)</td>
<td>ns</td>
</tr>
<tr>
<td>cGMP (nmol/ml)</td>
<td>2.7 (0.3)</td>
<td>4.0 (0.4)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The degree of changes in UNa and CrCl correlated significantly with changes in LiCl, PRA, and All. Conclusions: The results of this study shows that (1) TIPPS is associated with significant improvement in UNa and CrCl (2) There is significant change in PRA, AII, LiCl and cGMP which correlate significantly with the changes in UNa and CrCl.

Hepatectomy in the management of critically ill patients with acute liver failure

AJ Ellis, SM Rela, ND Heaton, JA Wendon, Roger Williams

Institute of Liver Studies, King's College Hospital, London.

The later stages of acute liver failure (ALF) are complicated by hepatic failure and cerebral oedema which result in significant mortality. These complications are due not only to the absence of liver function, but also to the necrotic liver releasing substances, including cytokines and free metal ions, which contribute to multi-organ failure.

Hepatic failure has been described as an effective therapy in critically ill patients with ALF as a temporary measure until liver transplantation can be undertaken. We report our experience of 8 adult patients with ALF (median age 31 years; range 16-42) who underwent hepatectomy for cardiovascular instability, due to Paracetamol hepatotoxicity in 7 patients and Hepatitis A in one patient.

Following hepatectomy, 4 patients improved with a median reduction in noradrenaline requirement of 0.68ug/kg/min (range 0.1-1.3) on return from theatre and one patient was unchanged. The remaining 3 patients died at 1, 8 and 22 hours respectively post-hepatectomy after intractable hypotenion. Five patients were transplanted after a median anhepatic time of 12 hours (range 7-74). Of these, 2 (40%) survived and were discharged from hospital.

Patients with complications of ALF not responding to conventional treatment can be stabilised temporarily by hepatectomy if a donor liver is not immediately available.
ROLE OF NEURO HUMORAL FACTORS IN THE MEDIATION OF THE "HEPATOMEDRAL" REFLEX

Jalan R, Forrest EH, Dillon JF, Redhead DN, Hayez P.C Dept of Medicine and *Radiology, Royal Infirmary of Edinburgh

We have demonstrated that renal blood flow is reduced dramatically following acute occlusion of the shunt in patients with TIPSS (1). This study was designed to study the mechanisms of this change. Methods: At routine portography a reverse thermodilution catheter was inserted into the renal vein and the changes in renal blood flow (RBF) were recorded prior to and following TIPSS occlusion over 10 min in 10 cirrhosis patients. Blood was sampled from the right atrium and the renal vein prior to and following shunt occlusion. Changes in the plasma renin activity (PRA), Angiotensin II (AI), Atrial natriuretic peptide (ANP), Cyclic Guanosine monophosphate (cGMP), and Cyclic Adenosine monophosphate (cAMP) (using a radiomunoassay) were measured in the renal and systemic circulations.

Results: These are summarised below

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before occlusion</th>
<th>After occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBF (ml/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>289 (32)</td>
<td>109 (29)</td>
</tr>
<tr>
<td>PAA (ng/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>5.7 (4.8)</td>
<td></td>
</tr>
<tr>
<td>ANP (pg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>103 (42)</td>
<td>39 (14)</td>
</tr>
<tr>
<td>AI (pg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>0.13 (1)</td>
<td>0.03 (0)</td>
</tr>
<tr>
<td>cGMP (nmol/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>3.2 (1.2)</td>
<td>2.8 (1)</td>
</tr>
<tr>
<td>cAMP (nmol/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre morbidity</td>
<td>2.2 (2.1)</td>
<td>3.2 (2.8)</td>
</tr>
</tbody>
</table>

Results as means and standard error. *p<0.002, **p<0.001. No other changes were statistically significant.

No correlation was detected between changes in RBF and changes in any of the other parameters. Noradrenaline results are awaited.

Conclusion: None of the measured neurohumoral factors mediate the hepatic reflex, implicating the sympathetic nervous system. Ref: J. Pediatr, et al., Gut 1990: 15: P34

Clinical practice T132-T144

Clinical practice

T132

PRELIMINARY RESULTS OF A RANDOMISED, CONTROLLED TRIAL OF TRANSLUMINAL INTRAHEPATIC PORTOSYSTEMIC TENT-STENT (TIPSS) AND VARICEAL BAND LIGATION IN THE PREVENTION OF VARICEAL REBLEEDING IN CIRRHOSIS


Aims: This randomised, controlled trial was designed to compare TIPSS with variceal band ligation (VBL) in the prevention of variceal rebleeding in cirrhosis.

Methods: Twenty-four hours following control of variceal haemorrhage, 39 cirrhotic patients were randomised to TIPSS (18) or VBL (21). TIPSS was performed using Wallstents within a mean of 2.2 days following randomisation. Shunt function was assessed after 1 and 6 months and yearly thereafter. VBL was performed using the Band ligation within a mean of 2.8 days and then weekly until variceal eradication, then at 3 and 6 months and yearly thereafter. Results were expressed as mean and standard error and analysed on an intention to treat basis. Results: Patients in both groups were well matched for age, sex, aetiology and severity of liver disease and the mean time of follow up (3.3 (3) and 5.0 (6) months for the TIPSS and VBL groups respectively). Results are summarised below.

<table>
<thead>
<tr>
<th>TIPSS (n=18)</th>
<th>VBL (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success</td>
<td>16 (88.9%)</td>
<td>21 (100%)</td>
</tr>
<tr>
<td>Variceal rebleeding</td>
<td>2 (11.1%)</td>
<td>11 (52%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5 (27.7%)</td>
<td>5 (23.8%)</td>
</tr>
<tr>
<td>ENSphalopy</td>
<td>4 (22.2%)</td>
<td>2 (9.5%)</td>
</tr>
</tbody>
</table>

* calculated using Chi square test. "refers to newly developed encephalopathy.

Two patients in whom TIPSS failed underwent VBL. Rebleeding in the TIPSS group was due to shunt dysfunction which was managed successfully by balloon angioplasty or shunt extension. However, 6 of the patients who rebled in the VBL group required TIPSS for uncontrolled rebleeding. Six patients in the VBL group required to be rescoped with TIPSS for uncontrolled variceal rebleeding, perhaps masking any benefit on survival between the groups.

T133

ALTERATIONS IN HEPATIC HAEMODYNAMICS MAY CONTRIBUTE TO THE ABNORMALITIES IN RENAL BLOOD FLOW (RBF) IN LIVER FAILURE (LF). JAY J, YATES H., G. K. NASTON, K. F. PARSONS AND S. A. JENNINGS. (University Department of Surgery & Urology, Royal Liverpool University Hospital; Liverpool)

The functional changes in the kidney in liver disease are generally believed to result from abnormalities in RBF. The abnormalities in RBF are thought to be closely related to gastrointestinal- derived vasoactive agents. These vasoactive agents are almost exclusively metabolised by the liver and their systemic levels depend on the severity of liver disease and the degree of abnormality of hepatic haemodynamics. Since few studies have attempted to correlate changes in RBF to alterations in hepatic haemodynamics, we have investigated this possibility in rats. LF was induced in male Wistar rats of 1.1g/kg D-Galactosamine and regional blood flow (microsphere method), intra-renal shunting (IRS) and portal systemic shunting (consecutive injections of 99mTcMDP and 99mTc-albumin microspheres), portal pressure (PP), arterial blood pressure (ABP) and urinary sodium concentration and urinary osmolality measured 24h and 48h later.

Following administration of D-Galactosamine there was a progressive and significant (p<0.001 Mann Whitney) decrease in RBF (Baseline: 4.98+/-0.35; 24h: 3.18+/-0.79; 48h: 0.65+/-0.15 ml/min) and an increase in IRS (Baseline: 2.2+/-0.47%; 24h: 6.2+/-2.03%; 48h: 11.3+/-1.85%). These alterations in RBF were significantly correlated with a decrease in PP, portal systemic shunting (PPSS) and cardiac output and decreases in ABP, portal venous inflow and hepatic arterial flow. There were highly significant correlations (p<0.001, Pearson's correlation coefficient) between changes in PP and PPSS and alterations in RBF and IRS.

The results of this study suggest that alterations in PP and PPSS contribute to changes in RBF in LF, as a result of shunting the remaining vasoactive agents away from the liver.

T134

PROVIDING AN EFFECTIVE CLINICAL SERVICE IN GASTROENTEROLOGY: THE VALUE OF INFORMATION. JG Williams, JM Morgan, SC Greenway, H Dickinson, W-Yee Cheng, C Sekarai, School of Postgraduate Studies, Swansea SA6 6NL.

Patients with gastrointestinal disorders are managed mainly by outpatients, with many investigators reporting on a day case basis. Against a background of a rising workload in a busy district general hospital, we have analysed data on 2,898 consecutive patients referred to the gastroenterology service over 6 years. During the period from 1988 to August 1994, 24,207 items of clinical data have been recorded, embracing over 6,000 episodes of care. 2,024 new cases were seen in outpatient clinics, of which 63% were managed by the general practitioners (GPs) but 22% were tertiary referrals from consultant colleagues. The most commonly referred condition was irritable bowel syndrome (IBS), accounting for 20% of all referrals, followed by gastroesophageal reflex (GER). Dyspepsia disorders 15% and inflammatory bowel disease (IBD) 13%.

In the first three diagnostic groups are rarely seen more than three times (median one follow-up visit for each group), but IBD tends to remain under long term review (median 6 visits per patient over 6 years).

Interim analysis of these data in 1992 informed the development of referral guidelines, which were discussed with GPs, with rationalisation of referral patterns. For example, the number of patients with a final consultant diagnosis of IBS fell by 10% following these discussions. For IBD, demonstration of the relapsing nature of the condition helped discussion of shared care guidelines, but did not lead to reduction in the need for follow-up in outpatients.

Interim analysis also informed the business case for the establishment of an open access endoscopy service. By September 1993, 34% of referrals seen in outpatient suffered from an acid-peptic disorder. Four months after the introduction of an open access endoscopy service, only 20% of new outpatients suffered from these disorders.

The discussions and changes that have taken place as a result of these analyses have led to a fall in the average waiting times from 9 months in mid 1992 to 8 weeks in mid 1994. We next plan to rationalise appointment times, better to meet the requirements of the Patients Charter. We have found that the length of time patients spend in their first consultation ranges from 10 to 30 minutes (median 19 min) with an average interval of 6 min between consultations. The consultation takes an average of 6 min longer if a rigid sigmoidoscopy is performed (p<0.05), and 5 min longer if a functional rather than organic disorder is diagnosed (p<0.05).

If relevant predictions can be made from the referral letter, this information will enable more appropriate allocation of outpatient time slots.

Community studies continue to report the mortality of upper GI haemorrhage is 10-15%. This is unacceptable high and reflects not only the increasing age and infirmity of the bleeding population but also the lack of a standardised approach to management. We present the initial 2 years experience of a specialised Bleeding Unit serving Grampian Region (population 340,000) The emphasis is on rapid assessment, aggressive resuscilation, prompt diagnosis and early surgery, according to an established protocol.

The unit has an open-access policy for all suspected GI bleeds. There were 1324 suspected upper GI bleeds and of these 1098 were confirmed, leaving 17% (n=226) who had not bled. Fifty-two percent (n=573) of confirmed bleeds were significant of whom 2/3 were aged over 60 years. Duodenal ulcer accounted for 23%, gastric ulcer 14% and varices only 5%. The median time to endoscopy was 3 hours (mean=9±5/98, SD=6.9±5.5). and the source was found in over 90% of confirmed bleeds. Trivial bleeds with no serious concurrent illness went directly home (48%, n=249), with a median hospital stay of 24 hours (31±2). Severely bleeding of bleeds was linked to prior use of NSAID/aspirin (Significant 41%, trivial 22%, no bleeds 20% (p < 0.001) but not to smoking or alcohol. Fifty-seven percent of the peptic ulcers had stigmata of recent haemorrhage and 75 (18%) went on to surgery with a surgical mortality of 8%. The overall 30 day bleeding related mortality was 3.9% with deaths confined to the elderly and those severe concurrent illness.

Centralised expertise and rapid triage directs critical efforts on those with major bleeds, allowing early cost effective discharge of the remainder. Specialised bleeding units reduce mortality and provide cost effective management of GI haemorrhage and should be part of all major district hospitals.

AN AUDIT OF UPPER GASTROINTESTINAL HAEMORRHAGE: THE EFFECTS OF A PROTOCOL AND STAFF EDUCATION. JT Anderson, DA Johnston, A Mulroy, CR Pennington, FE Murray. Ninewells Hospital and Medical School, Dundee. DD1 9SY.

Background: Upper gastrointestinal (GI) haemorrhage is a cause of significant mortality in acute medical admissions. Recently guidelines have been published on the management of acute upper GI haemorrhage. Based on these guidelines we have introduced a specific bleeding protocol in Ninewells Hospital. Aim: The aim of this audit was to monitor the effects of the introduction of the protocol, and a teaching programme for JHOs on the management of acute upper GI haemorrhage.

Patients and Methods: All patients admitted to hospital with a history of acute haematemesis or melena were included in the audit. Purpose designed audit forms were completed on all patients. Following an initial 6 month audit period, the changes were introduced and a further 6 month audit was then performed.

Results: In six two months periods a total of 310 patients were audited. There was no statistical difference in the age sex, initial clinical status of the patients, number of endoscopies performed, and diagnoses, between the two audit periods. The most common diagnoses were peptic ulcer disease (37.2%) and ulcerative oesophagitis (15.6%). Following the introduction of the protocol and teaching programme there was an increase in the percentage of people undergoing early endoscopy from 86.8% to 93.9%. There was an increase in the number of people receiving appropriate interventional endoscopy (p = 0.032).

There was a more appropriate referral pattern for out of hours endoscopy, with a reduction in the number performed (18.6% to 13.0%). There was no change in the rebleeding rate or in the number of patients requiring emergency surgery. The mortality rate was low and unchanged in both audit periods at just above 4%.

Conclusion: These results suggest that the introduction of a protocol, in addition to staff education and training, increased the rate of endoscopic intervention, and decreased the out of hours endoscopy requirement.

AUDITING THE AUDITS OF MORTALITY FROM UPPER GASTROINTESTINAL HAEMORRHAGE (UGIH): A PLEA FOR STANDARDIZATION OF METHODOLOGY. K.Kadbil, G Titley, J Green, M C Allison. Medical Unit, Royal Gwent Hospital, Newport.

We have conducted a Medline search of all prospective studies of mortality from UGIH published in English between 1975 and 1994. Reports confined to bleeding peptic ulcer or covering <100 patients were excluded as were studies from major tertiary referral centres. We examined the methods and results in the twelve studies meeting these requirements.

Criteria for UGIH were stated in 6 series: 4 required a convincing history, one included only bleeding witnessed by a doctor or nurse or objective evidence of UGIH. Another stipulated estimated haematemesis >100ml or witnessed melena on admission. Two reports excluded those bleeding while already in hospital for other reasons, one included 20 such patients and nine studies did not address this group of patients. All gave overall mortality (median 8%, range 4-138) and all but one gave operative mortality (median 13%, range 4-45%). Only six quoted all causes of death and only two specified that all deaths during the index hospitalisation had been included. Four studies discussed deaths of patients whose poor condition precluded endoscopy; such patients were excluded in other series and three centres were able to endoscope more than 99% of their cases.

Comparison of mortality from UGIH between centres will remain difficult unless entry criteria are standardised. We propose that audits should examine 30 day mortality from all causes in every patient hospitalised for UGIH. Care should be taken to include patients unable to be resuscitated or made fit for endoscopy as well as those who develop bleeding while already in hospital for other reasons.

PITFALLS IN AUDITING UPPER GASTROINTESTINAL BLEEDING. 'G M Hawkley, GM Pearson, SE Evertin, S Holmes, CJ Hawkley, RFA Logan. Division of Gastroenterology, Department Public Health Medicine & Epidemiology, University Hospital, and Corgrave Health Centre, Nottingham.

INTRODUCTION: Audit outcomes may be misleading, and mortality rates vary sharply, if the main sources used - inpatient patient review, hospital coding and computerised general practice (GP) records - access information differentially. We, therefore, compared these sources of data on upper gastrointestinal (GI) bleeding for accuracy.

METHODS: The study covered a 4 month period, with an intensive patient review to identify all patients, by reference to entry into an ongoing trial; scrutiny of cross match request forms, a GP admissions book and of endoscopy records; and intensive ward searching. Subsequently, patients with appropriate ICD9 codes were identified. GP records were scrutinised 3-6 months later. Diagnostic verification was then made by notes scrutiny.

RESULTS: Of 211 possible diagnoses 165 (78.2%) were verified as accurate. Intensive patient review found 143 of these (86.7%). Hospital codes identified 149 (90.3%) but there were 46 false positives (28.8%). GP records recorded admission for upper GI bleeding in only 9.2% of those so coded, even though 89.6% of practices had computerised records. Only 50 patients (30.3%) were found to have entered the trial.

CONCLUSION: Transfer of diagnostic information from hospital to general practice is imperfect and may invalidate studies dependent upon scrutiny of GP records. Furthermore, in patients with upper GI bleeding, but could result in misleading hospital league tables without notes review because of the high false positive rate of coding. Selective recruitment may account for relatively favourable outcomes in trials.
H PYLORI RADICATON FOR BLEEDING DUODENAL ULCER BY NON-GASTROENTEROLOGISTS: AN AUDIT, ME McAlindon, J Taylor, SD Ryder. Department of Medicine, University Hospital Nottingham, NG7 2HU.

Background. In this hospital patients with bleeding duodenal ulcer (DU) are not always cared for by gastroenterologists and yet the management of DU is changing rapidly. Aims. To determine the use of eradication therapy in patients with bleeding DU. Patients. Those admitted in 1993 were identified through the ICD coding system and discharge summaries. A total of 79 patients were identified. 27 were managed by gastroenterologists but were investigated for HP and HPE undertaken and are excluded from further analysis. Of the 52 remaining, 48 (92%) were medical and 6 (11%) surgical admissions (36M, 16F: mean age 63y). Eighteen patients (35%) gave a previous history of DU. 26 (48%) were taking non-steroidal anti-inflammatory drugs (NSAID) on admission. 9 (17%) required surgery and overall mortality rate was 17% (9 deaths). HP. Twenty-three (55%) of the survivors underwent Helicobacter Pylori (HP) investigation. Those not on NSAIDs were no more likely to be investigated than NSAID takers. The biopsy urease test was used in 22 (96%) and histology in 7 (30%). Sixteen patients (72%) were HP positive (58% of those not taking NSAIDs and 56% of NSAID users); all 11 of those not on NSAIDs and 6 of the 12 NSAID takers received eradication therapy (HPE). Bismuth based triple therapy was used in 10 (50%) and omeprazole-amoxycillin in 6 (30%). The success of HPE was checked in only 3 cases. All NSAIDs were stopped. Maintenance therapy with either antibiotics (H2A) or proton pump inhibitors was given to 5/17 given HPE but was not given to the remaining 12 in whom only 3 had eradication confirmed. Conclusions. Only 50% of bleeding DU patients had their HP status ascertained. If HP was identified in patients not on NSAIDs all were given eradication but follow-up to confirm eradication was inadequate. The lack of confirmation of eradication or the use of maintenance therapy with H2A in these patients represents a poor management strategy and may expose patients to risk of ulcer relapse and further bleeding. If bleeding DU is to continue to be managed by non-gastroenterologists protocols for the detection and appropriate management of HP positive patients are required.

IS COLONOSCOPY NECESSARY AS A FIRST-LINE INVESTIGATION IN IRON DEFICIENCY ANAEMIA? Sayer JM, Donnelly MT, McIntyre AS, Barton R, Grundman MJ, Vicyar FR, Long RG, Chesterfield, Whittington and Nottingham Hospitals, City Hospital, Nottingham NG5 1PB.

Colonscopy is a useful investigation for detecting obscure causes of iron deficiency anaemia. We performed a retrospective audit to see whether patients with iron deficiency anaemia require colonoscopy as a first-line investigation.

All women post-menopausal women presenting with iron deficiency anaemia were investigated by upper gastrointestinal endoscopy and duodenal biopsy and barium enema examination. Where no cause for the anaemia was found, the patient was given oral iron for 2 months and reviewed at 1, 3 and 6 months. If the anaemia persisted or a colonoscopy was performed.

Of 35 patients investigated, an identifiable cause for the anaemia was found in 59%. Sixteen patients were found to have a lesion on barium enema examination, including 9 cases of colonic carcinoma.

Twenty nine patients were colonoscoped; 17 for persistent anaemia and bleeding and 11 to confirm the presence of colonic polyps. Five of these with persistent anaemia yielded a new diagnosis: 1 sigmoid adenoma; 1 angiodysplasia; 1 Crohn's colitis; 2 small colonic polyps. Polyps were confirmed in 64% of the second group: Six of the patients with both colonoscopy and colonoscopy negative were found to have other causes for their anaemia.

Complete follow-up data is available for 32 of the patients with negative colonoscopy and barium enema examination who did not show persisting or recurrent anaemia. Seventeen of these were identified as having other causes for the anaemia. No new cases of colonic carcinoma presented in these patients over the 6 month period.

We conclude that barium enema examination is adequate for the first-line investigation of iron deficiency anaemia. Colonic carcinoma is unlikely to be missed.

RadicAl therapy for duodenAl Ulcer. PROGRESS THROUGH AUDIT. MC Bateson & B Lisa DiffeY General Hospital, Bishop Auckland, Co. Durham, UK, and Department of Medical Physics, Durham.

In 1990 the World Congress of Gastroenterology recommended that all patients with chronic duodenal ulcer should be treated with anti-Helcobacter therapy. The protocol was 2 weeks' treatment with metronidazole 400 mg tds, bismuth 120 mg qds, and either tetracycline (BTM) or amoxycillin 500 mg qds (BAM). From January 1992 to April 1994 101 adult gastroscopy or radiology-proven duodenal ulcer patients were offered treatment on this protocol as a primary procedure, using BTM. Side-effects were common and occasionally severe. Carbon 14 urea breath tests were performed at 4 - 10 weeks after completion of therapy. 81 out of 101 (80%) were negative (less than 0.5% dose/mmol CO2 x kg body weight): 4 were equivocal (0.5 - 1.0% excretion), giving an 80 - 84% success rate.

In 1994 the US National Institutes of Health recommended that all patients with duodenal ulcer should be offered anti-Helicobacter therapy. It was decided to treat all duodenal ulcer patients with lansoprazole 30 mg daily for 1 month and antibiotics for the first week. Amoxycillin 500 mg tds and metronidazole 400 mg tds (LAM) were given, except in 6 patients who alleged pent- cillin sensitivity and were given clarithromycin 250 mg bd and tindazole 500 mg bd (LCT). The other 44 received LAM. There were no exclusions from therapy and no side-effects are known. The urea breath test at 4 - 10 weeks after all therapy was completed was negative in 45 out of 50 (90%) with 1 equivocal result, giving a 90 - 92% success rate.

CONCLUSION

After a new regime for duodenal ulcer 90 - 92% of patients are free of H. pylori and probably achieve long term cure. Bismuth-based therapy did not reach this standard.


Many patients find bowel preparation for colonoscopy under hospital beds raises concern of unacceptable adverse effects of home preparation in the elderly. The present study assesses two standard preparations relating tolerability to age.

Allocation to Picolax (sodium picosulphate + magnesium citrate) or Klean Prep (polyethylene glycol) was by hospital site. Patients with reduced mobility (NYHA III - IV) or inability to follow the preparation instructions were excluded. Patients completed a questionnaire rating 7 possible symptoms (none, mild, severe) as well as the presence and frequency of incontinence. A 10 point visual analogue scale (1 terrible, 10 fine) provided overall assessment. A total of 125 patients (Picolax 68, Klean Prep 57) were included; mean age 60 (range 22-86). The preparation was inadequate in 4 cases (3 Picolax, 1 Klean Prep). The bowel preparation produced no serious sequelae. The mean visual analogue score was 5 for Picolax, 6 for Klean Prep (p<0.001). Fecal incontinence occurred in 7 (10%) and 10 (18%) respectively (NS). Sleep disturbance (22% of each group) was the most frequent side effect and was severe in 2 patients (4%) and equal in both groups. There was no correlation between adverse symptoms and age. This study has shown bowel preparation to be well tolerated and age alone does not appear to be a risk factor. Picolax proved a more acceptable preparation.

Gut 1995; 36(suppl 1): A35
DO WE USE LAXATIVES RATIONALLY IN HOSPITAL IN-PATIENTS? A STUDENT PROJECT. J.A. Gilbert1, O Farfan1, B Miller2, PJ Kumar3. Digestive Diseases Research Centre, Medical College of St Bartholomew’s Hospital, London EC11 and Homerton Hospital, Homerton Row, London E24

Constipation is often managed poorly in hospital in-patients. A study was undertaken to examine the laxative prescribing practices in a district general hospital. Any influencing factors were further identified by questionnaires to medical and nursing staff. Data was collected on age, sex, diagnosis, prescribed laxatives, enemas or other concurrent medication. 126 of 392 in-patients (aged 20 to 101 years) were prescribed laxatives. Of the 126 patients, 64% were female; 39%, 34%, and 25% were on medical, geriatric and surgical wards respectively. The major laxatives prescribed were lactulose (63%) and senna (43.6%). 59% of patients were prescribed more than one laxative. 40% of junior doctors were uncertain why they had prescribed specific laxatives and 70% said they routinely sought advice from nursing staff. However 66% of the nursing staff were unsure or misinformed about laxative use. Cost savings on average medical or geriatric admissions would amount to about £3.50 per patient per admission, respectively, if a more rational approach to the use of laxatives had been used.

In conclusion, hospital in-patients were often prescribed unnecessary and inappropriate laxatives. It is recommended that junior doctors and nursing staff receive instruction on the use and effectiveness of specific laxatives. Guidelines would result in substantial cost savings for the hospital drug budget.

WHAT IS THE EFFECT OF SETTING UP A NUTRITION TEAM ON THE PROVISION OF TOTAL PARENTERAL NUTRITION IN A TEACHING HOSPITAL? - A CLINICAL AUDIT. M.Y. Donnelly, A.F. Muller, B. Norton, B. Brady, H. Francis, S. Saunders, F. Smedley, R.G. Long. City Hospital, Hucknall Road, Nottingham, NG5 1PB

Nutrition teams have been shown to have a beneficial effect on the nutritional care of patients in hospitals where they are in existence. Unfortunately, many large hospitals still do not have a specialist multi-disciplinary nutrition team. We decided to look at the effects of setting up a nutrition team on the provision of total parenteral nutrition (TPN) in a teaching hospital.

A retrospective six month audit of TPN provision was compared with a prospective audit following the appointment of a full-time nutrition sister. A reduction in the absolute number of patients fed (55 vs. 78) occurred. Fewer patients were fed per consultant episode (1.82 per 1,000 vs. 2.76 per 1,000). Fewer inappropriate patients were fed. Much greater use of peripheral parenteral nutrition occurred (12 vs. 0). Median number of bags used per patient was the same (7 vs. 7). Number of patients fed for less than 7 days was significantly less (23 vs. 48). The total number of bags used was less (592 vs. 683) with a reduction in costs in TPN use alone being £9,000 over six months. The length of stay of patients was not significantly altered (24 vs. 20).

This audit provides further evidence of the benefits of a specialist nutrition team in a large hospital with more appropriate TPN usage and a significant financial advantage.

LAPAROSCOPIC COMMON BILE DUCT EXPLORATION - LESSONS LEARNED FROM 129 CONSECUTIVE CASES M. Rhodes, L. Nathanson, N’O’Rourke, G. Fielding University Dept Surgery, Royal Brisbane Hospital, Brisbane, Australia

Since the introduction of laparoscopic cholecystectomy there has been widespread debate about the best way to manage common bile duct calculi. Between August 1991 and July 1994, 129 patients have undergone laparoscopic exploration of the common bile duct (CBD) by the authors of this paper.

Fifteen patients (median age 52 years) were managed by glucagon induced relaxation of the sphincter of Oddi and saline flushing of the common bile duct through a cholangiogram catheter. This had a 73% success rate and took a median of 90 minutes. This technique has now been replaced by Dormia basket exploration of the CBD.

Trans-cystic common duct exploration using a Dormia basket was employed in 79 patients (median age 47 years). Duct clearance was achieved in 96% cases with a median operating time of 55 minutes.

Thirty-five patients (median age 52 years), have been managed by choledochotomy and T-tube placement. This has a 91% duct clearance rate and a median operating time of 120 minutes.

Overall duct clearance was achieved in 92% of patients with an operative morbidity of 5.4%. Duct clearance using either Dormia basket or choledochotomy & T-tube placement was obtained in 95% patients. Laparoscopic CBD exploration is an important alternative in the management of common duct calculi in the laparoscopic era.

DIAGNOSTIC AND THERAPEUTIC ERCP ON OUTPATIENTS - IS IT SAFE AND COST EFFECTIVE? Duncan HD, Hodgkinson L, Deakin M, Green JRB. Department of Gastroenterology, City General Hospital, Newcastle Road, Stoke-on-Trent

Patients undergoing therapeutic ERCP are routinely admitted for 24 to 48 hours post procedure in most hospitals in Britain. We perform a significant proportion of diagnostic and therapeutic ERCPs on an outpatient basis. We report a retrospective audit over a 20 month period assessing the safety of such practice. A total of 550 ERCPs were performed; 310 (56.4%) were inpatient and 240 (43.6%) were outpatient examinations. Of the 310 inpatient ERCPs, 202 (65%) were for a therapeutic procedure. Of the 240 outpatient ERCPs, there were 97 successful therapeutic ERCPs, 2 failed therapeutic ERCPs, 117 successful diagnostic ERCPs, and 24 failed diagnostic ERCPs. Of the 97 therapeutic ERCPs on outpatients, 87 (89.7%) were allowed home 2 hours post procedure while 10 (10.3%) were admitted immediately 5 (5.2%) because of complications (haemorrhage (1), pancreatitis (1), perforation (1), impacted stone (1) and non specific abdominal pain (1)), 4 due to frailty and 1 for routine observation post pancreatic papillotomy. None of the 87 patients discharged immediately needed to be readmitted between 2 and 48 hours post procedure. 4 (4.6%) were readmitted between the period 2 and 30 days post therapeutic ERCP (haemorrhage (1), cholangitis (1), liver abscesses (1) and biliary colic (1)).

117 diagnostic ERCPs were performed on outpatients during the same 20 month period, 113 were allowed home 2 hours post procedure while 4 were admitted immediately due to frailty. Of the 113 patients discharged immediately, 4 (3.5%) were readmitted between 2 hours and 48 hours post ERCP (pancreatitis (2), cholangitis (1), cholecystitis (1)) and 1 (0.9%) was admitted 28 days after ERCP (pancreatitis). This audit confirms our belief that both diagnostic and therapeutic ERCP can be performed safely on outpatients with a minimal re-admission rate and a significant saving in bed days.
T145

**ENDOSCOPIC MAGNETIC RESONANCE IMAGING OF THE OESOPHAGUS USING A DEDICATED SURFACE RECEIVE COIL**

NM deSouza, AH Gibbons, GA Coutts, R Punni, J Calam

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The magnetic resonance imaging appearances of the oesophagus were evaluated using a surface receiver coil placed endoscopically adjacent to a region of interest. High resolution scans of intramural and adjacent structures were obtained using this technique.

Six patients, 2 male and 4 female aged 63 to 77 years, (mean 72.7 years) were studied using an endoscope that was specially constructed to be compatible for use in an MR scanner. This was identical in structure and function to a standard gastrointestinal. A 5cm long saddle geometry receive coil mounted on a Delrin former and equal in diameter to the endoscope was reverse threaded through the biopsy channel. The coil and endoscope were then inserted under direct vision into the oesophagus. After routine visual inspection the coil was placed adjacent to the site of pathology. T1-weighted spin-echo images and RF spoiled gradient-echo images with a segmented k-space acquisition were obtained with ECG gating.

In 1 patient with oesophageal tumour extensive mediastinal involvement was seen. Two patients with reflux oesophagitis showed some mural thickening whilst another did not. Following fundoplication, the position and extent of the surgical reconstruction was demonstrated in 1 patient. After banding of oesophageal varices in another patient the absence of varices around the lower oesophagus was confirmed, but extensive varices around the splenic hilum were noted.

This pilot work demonstrates that MR imaging using a surface coil placed within the gastrointestinal tract during an endoscopic procedure enables visualization of mural and extramural lesion extension and provides a useful adjunct to upper gastrointestinal endoscopy.

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**LAPAROSCOPIC ULTRASONOGRAPHY IN THE STAGING OF GASTRO-ESOPHAGEAL MALIGNANCY**

M Finch, TG John, OJ Garden, S Paterson-Brown

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Laparoscopy alone has previously been shown to be better than both CT scanning and ultrasonography in the assessment of gastro-oesophageal malignancy.

The recent introduction of laparoscopic ultrasonography (LU) has already been shown to be superior to all other investigations in the assessment of pancreatic and hepatic malignancy but its role in the assessment of gastro-oesophageal malignancy remains to be studied. We are prospectively studying all patients with gastro-oesophageal tumours comparing CT scanning and ultrasonography with LU. To date LU has been performed in 14 patients. In 6 patients LU revealed metastatic disease not identified by either CT or ultrasonography.

Although numbers are still small, this ongoing study suggests that LU may become an important part of the assessment of patients with gastro-oesophageal malignancy. This in turn may improve pre-operative surgical decision-making by reducing the incidence of unnecessary laparotomies and identifying in which patients radical surgery for cure is inappropriate.
MULTICENTRE TRIAL OF OCTREOTIDE VERSUS INJECTION SCLEROTHERAPY (58) FOR ACUTE VARICEAL HAEMORRHAGE. SA. Jenkin1, R. Shields1, R. Sutton 1, AN Kingsnorth1, M Davies2, E Elias3, AJ Turnbul3, MF Bassendine3, OFW James3, JP Iredale4, SK Vyas4, MJ Arthur4 Royal Liverpool University Hospital, Liverpool; Queen Elizabeth Hospital, Birmingham; Freeman Hospital, Newcastle-upon-Tyne; Southampton General Hospital, Southampton

The role of octreotide in the management of variceal haemorrhage remains controversial. We conducted a multicentre trial to assess the use of 50 µg intravenous octreotide for 48 h to control variceal haemorrhage. Consecutive patients with endoscopically confirmed variceal haemorrhage were randomised to either octreotide (n=73) or emergency IS (n=77).

Overall control of bleeding was not significantly different between octreotide (85%) and IS (82%) over the 48 h trial period (relative risk of bleeding 0.83; 95% CI 0.38, 1.02). Octreotide was as effective as IS irrespective of the severity of the liver disease, and in those actively bleeding at endoscopy. Mortality during the 48 h trial period was identical in the two groups, but more patients died in the octreotide group during 60 days of follow-up, although this did not reach statistical significance (relative risk of dying at 60 days 1.91; 95% CI 0.97, 3.78; p=0.06).

The results of this study indicate that intravenous octreotide is as effective as IS in the control of acute variceal haemorrhage. However, in view of the trend towards an increased 60 day mortality in the octreotide group, further trials are necessary to evaluate its safety in variceal bleeding.

DRINKING BEFORE ENDOSCOPY IS SAFE: SM Greenfield, GMJ Webster, A Brar, AM Kuan, ER Beck, FR Vicary, Department of Gastroenterology, Whittington Hospital, London N19 SNF

Aim: Patients are traditionally deprived of food and fluid from midnight prior to a morning endoscopy, in order to minimise the risks and consequences of gastric aspiration. However, this prolonged period without fluid is uncomfortable for patients and probably not necessary although this has never been proven. Therefore, we set out to determine whether patients can safely drink significant volumes of fluid prior to their endoscopy. Methods: Patients fulfilling the inclusion criteria attended for a 9am gastroscopy having been randomly allocated to either deprivation of food and fluid from midnight ("starvers") or to drinking a 330ml supermarket bottle of still mineral water approximately 90 minutes before their examination ("drinkers"). The endoscopist was unaware as to which group patients were allocated and prior to the examination the suction channel of the endoscope was flushed with water and drained dry. At endoscopy all the gastric fluid was collected and its volume and pH recorded. Results: 25 "starvers" (12 male, mean age 49.0yrs) and 32 "drinkers" (17 male, mean age 47.3yrs) were recruited. All the "drinkers" drank the entire bottle of water and the mean time from this drink to their endoscopy was 118 min (SEM 4.1 min, range 90-175min); there was no correlation between the time of the drink to endoscopy and the volume of gastric fluid obtained. The median volume and pH of gastric fluid was similar in both groups (volume: 11ml v 12ml; pH: 1.95 v 2.0, "starvers" v "drinkers" respectively, both NS). Mucosal views were excellent in all examinations. We conclude that it is perfectly safe for patients to drink significant volumes of water up to 90 minutes before endoscopy and this is likely to improve patients' comfort.

HIGH INCIDENCE OF HELICOBACTER PYLORI COLONISATION OF BARRETT'S OESOPHAGUS

Wright TA, Kingsnorth AN, Department of Surgery, Royal Liverpool Hospital, L69 3BX

Helicobacter Pylori (HP) probably plays a crucial role in gastric carcinogenesis. Few studies have looked at the relationship between HP and Barrett's oesophagus/cancer probably because HP colonisation of the oesophagus is thought to be rare. We have observed that this is incorrect. A study to look at the relationship between HP and increasing grades of dysplasia was undertaken. Biopsies from 19 malignant and 94 benign cases of Barrett's oesophagus were analysed histologically for the presence HP.

<table>
<thead>
<tr>
<th>F/J</th>
<th>LGD</th>
<th>MGD</th>
<th>HGD</th>
<th>CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP+</td>
<td>4</td>
<td>16</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>HP-</td>
<td>11</td>
<td>28</td>
<td>23</td>
<td>3</td>
</tr>
</tbody>
</table>

F=Fundic; J=Junctional; I=Intestinal; L/M/HGD =Low/Moderate/High Grade Dysplasia; CA=Cancer.

The results show that HP has a negative correlation with increasing dysplasia - the highest incidence being found in the intestinal type of Barrett's epithelium (57%). No relationship was found between HP status and (i) the presence of ulcers, (ii) strictures, (iii) previous gastric or anti-reflux surgery, and (iv) total length of Barrett's oesophagus.

We are concerned that pathologists may tend to ignore the presence of HP in dysplasia/cancer biopsies. We have shown that HP colonisation of Barrett's oesophagus is not uncommon. As a class I carcinogen (WH0) this finding should be investigated in prospective studies to vindicate its role in Barrett's cancer.

OPEN ACCESS GASTROSCOPY IN GENERAL PRACTICE: SEVEN MONTHS EXPERIENCE

HI Flieg1, J Featherstone1, AG England2, RJ Walker2, MG Lombard2 Priory Medical Centre1, Aintree Hospitals NHS Trust1, NW Regional Health Authority1 and University of Liverpool2

Background: The increasing demand for open access gastroscopy (OAG) places a strain on routine hospital services. It may be possible to shift some of this burden into the primary health care setting. A pilot endoscopy unit has been set up within a busy inner city medical Centre, affiliated to a local District General Hospital. Objective: To review the reasons for referral and pathological case mix of patients referred to the GP Unit. Design: Retrospective review of clinical records. Subjects: All patients referred to the Unit, from April 1994 and October 1994 inclusive. Results: Two hundred and fifty one patients were referred during the study period (137 male and 114 female). The average waiting time was three and a half weeks. Two hundred and nineteen (87%) attended for gastroscopy; 6 patients (2%) did not tolerate the procedure and a further 32 (13%) did not attend for the test. The remaining 213 (85%) patients successfully completed the gastroscopy without sedation. Clinical indication for referral (n=251) included reflux (27%), dyspepsia (22%), epigastric pain (16%) and nausea and/or vomiting (11%). Gastroscopy was normal in 92 cases (42%) and found carcinoma of the oesophagus in 4 (2%), duodenal ulceration in 17 (8%), gastric ulceration in 4 (2%) and benign oesophageal strictures in 6 (3%). Of the 42% of patients who had a normal gastroscopy, two thirds had microscopic chronic active gastritis, of which 70% were H. pylori positive. There were no reported complications in this series. Conclusions: This review suggests a General Practice unit can undertake diagnostic OAG safely and effectively outside a hospital based service. The reasons for referral and pathological case mix were equivalent to those seen in the hospital service. The next phase of assessment will be a comparative study of OAG in the GP unit and the local DGH.
ENDOSCOPY NURSE PRACTITIONERS: PROSPECTIVE EVALUATION AS FIRST ASSISTANT AT PEG TUBE INSERTION

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INTRODUCTION: Endoscopy nurses are skilled practitioners whose role could be extended. Percutaneous endoscopic gastrostomy (PEG) has been increasingly adopted as an effective and safe technique of delivering enteral nutrition for a variety of clinical situations but safe insertion of PEGs requires two skilled, usually medically qualified, practitioners. We have prospectively evaluated the use of an endoscopy nurse practitioner in the percutaneous endoscopic phase of PEG placement.

METHODS: An experienced endoscopy nurse, who had undergone a specific training course in PEG insertion, acted as first assistant for the insertion of 50 PEGs over a 15 month period. The outcome of the complications were compared to 50 PEGs inserted consecutively by medical practitioners. A standard "pull" technique, with antibiotic prophylaxis, using a 4.8mm outer diameter (15F) tube (Fresenius, Homberg, Germany) was used for all insertions.

RESULTS: The age range, sex distribution and indications for PEG placement in the nurse group were: age range 18-92 years (mean 64); 25/72F/M; head and neck surgery, 16, stroke, 11, non-stroke neurological, 20 and malignant dysphagia 3. The age range, sex distribution and indications for PEG placement in the medical group were: age range 18-93 years (mean 63); 34/16M/F; head and neck surgery, 20, stroke, 16, non-stroke neurological, 11 and malignant dysphagia 3.

In the nurse group, successful placement of a PEG was achieved in all patients. There were no complications encountered during the percutaneous puncture although one patient suffered a respiratory arrest immediately post procedure. There was 1 episode of stomal infection and 4 patients died within 30 days of insertion.

In the medical group successful placement of a PEG was achieved in 49 patients, with 1 attempt abandoned due to respiratory distress and successfully repeated under GA. One insertion was complicated by the loss of the initial PEG which was placed through the second puncture. There were 3 episodes of stomal infection and 3 patients died within 30 days of insertion.

CONCLUSION: The endoscopy nurse practitioners role can be extended safely and effectively to the percutaneous insertion phase of PEG placement. In addition such extension has the potential to attain a more consistent standard of assistance and has implications for cost saving and quality of patient care.

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SMALL BOWEL ENTEROSCOPY: SHOULD JENIAL BIOPSY BE ROUTINE?
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Introduction: Small bowel enteroscopy allows direct endoscopic examination of the small bowel. Push enteroscopes offer the facility for jejunal biopsy but the additional diagnostic yield from routine enteroscopic biopsies is unknown. Estimations of the prevalence of non-steroidal anti-inflammatory drug (NSAID) small bowel enteropathy vary widely depending on the method of small bowel assessment employed. This may be explained by failure to detect microscopic disease if no biopsy is obtained at diagnostic enteroscopy. We have therefore examined the role of enteroscopic jejunal biopsy in the diagnosis of suspected NSAID enteropathy in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

Methods: 29 patients on long term NSAID (IBU, 19 patients; ASA, SRA:SA2) and 7 controls not on NSAID were examined using the Olympus SIP-110P push enteroscope. All macroscopic jejunal lesions were documented. Jejunal biopsies were obtained from normal mucosa in proximal and distal jejenum and mucosa adjacent to ulcerative lesions. Histological examination was carried out by a single pathologist who was blinded to enteroscopic result and drug therapy.

Results: In the NSAID group 6 (20%) patients had lesions observed (3 ulcers; 3 erosions) at enteroscopy whilst in the non-NSAID group 1 (1%) (1 erosion) patient had lesions seen. None of the control patients had jejunal ulceration. In 32 (81%) arthritis patients the enteroscopic findings were normal. There were no jejunal biopsies in 3 patients, all on NSAID, the results of enteroscopy and histology were incompatible, 5 (71%) of these patients had normal jejunal biopsy, 4 patients had macroscopic and abnormal histology consistent with NSAID enteropathy.

Conclusions: We conclude that NSAID enteropathy is a diffuse jejunal disease whose prevalence may be underestimated by enteroscopic inspection only. The finding of additional microscopic abnormalities in 10% of patients suggests that jejunal biopsy should be considered an essential part of diagnostic enteroscopy.

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DESK TOP PICTORIAL ENTEROSCOPIC REPORTS
J. Dean1, L de Baar2, J.v.d. Meulen3, P.D. Siersma4, M. van Blankenstein1
1. Division of Gastroenterology and Department of Computer Information Centre, University Hospital Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

Enteroscopic reports serve a double purpose: to inform the referring clinician about the findings and to provide a record for subsequent endoscopies. Several video endoscopic systems provide for registration and recall of images at subsequent endoscopies and the addition of a few images on written reports. As part of a Picture Archiving Communication System (PACS) we have developed the software for a Pictorial Endoscopy Report (PER) by which endoscopists are reported as a selection of radiologic images from each endoscopy, provided with a spoken commentary, on the clinician’s work-station screens. The system is connected with the Hospital Information System (HIS) by which they already receive printed laboratory and other diagnostic reports.

At the start of the endoscopy the personal data of the patient are fed from the HIS into a PC in the endoscopy suite. During the endoscopy an unlimited number of digitized images can be fed onto the hard disk of the PC and stored. At the end of the endoscopy these images are transferred to a network server. In the editing room the endoscopist selects suitable images to which symbols, written text and anatomical diagrams can be added. Each image is provided with a spoken commentary, and finally all images selected are projected together in miniature on one screen to which an anatomical diagram, a spoken summary, therapeutic and other advice can be added.

This edited PER is then stored on an optical disc from which it can be summoned up by the clinician at any time on any work station in the hospital via the HIS. The whole PER with spoken commentary can be seen and heard about 15 minutes after completion of the endoscopy. The PER can also be recalled by the endoscopist at subsequent endoscopies.

Besides practical advantages such as more rapid reporting and reduced secretarial work, the PER is likely to improve the insight of clinicians, junior staff and students into GI pathology.

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PHOTODYNAMIC THERAPY FOR THE ENDOSCOPIC TREATMENT OF POLYPSYS IN FAMILIAL ADENOMATOUS POLYPOSIS
National Medical Laser Centre, University College London Medical School, The Rayne Institute, 5 University Street, London WC1E 6JH

Polyps of the duodenum, particularly in the region of the ampulla, are becoming a major problem in the management of patients with familial adenomatous polyposis (FAP). Many develop dysplasia and some become malignant. Only very small lesions allow any response to anti-inflammatory drugs and local excision of large polyps is followed by universal recurrence. Photodynamic therapy (PDT) is a non-thermal technique for producing localised necrosis with light following prior administration of a photosensitising drug. It may be able to treat larger polyps endoscopically (without or with initial debulking with the NiYAG laser), without cumulative toxicity and so complement anti-inflammatory and surgical approaches.

We treated 6 patients with FAP (4 with duodenal adenomas, 1 with rectal stump polyps and 1 small but inoperable colon cancer). All were initially given the photosensitiser procuro 5- amino laevulinic acid (ALA) 60mg/kg by mouth. This is converted to the active derivative, protoporphyrin IX (PPIX) in vivo. Biopsies were taken 4-6 hours later to assess tumour and normal tissue levels of PPIX by fluorescence microscopy. Potentially therapeutic levels of PPIX were seen in all patients except the colon cancer (who had very small bowel after desmoid surgery and was on parental nutrition), although there was normal skin sensitivity between tumour and normal tissues. Treatment with red light (628nm from a gold vapour laser, 50-100J/cm2) was applied 4 hrs after a repeat dose of ALA. Superficial necrosis was confirmed on endoscopy a week after treatment. Lesions were re-photonsensitised and P-T treatment was repeated 2 days later. This led to a complete response in the small cancer and 50% reduction in size in a 1.5cm duodenal adenoma. All healed safely with no complications.

Conclusion: PDT is a safe and promising treatment for inoperable polyps in patients with FAP. Photosensin works better, but causes prolonged cutaneous photosensitivity. ALA clears in 1-2 days, but its use is limited by the superficial effect. Better results with ALA may be possible using higher drug doses or modified light dosimetry.
A PROSPECTIVE COMPARISON OF ABDOMINAL COMPUTERISED TOMOGRAPHY AND COLONOSCOPY IN THE DIAGNOSIS OF LARGE BOWEL PATHOLOGY IN AN ELDERLY POPULATION GB Lipscomb, G Loughrey, M Thakker, D A Nicholson, WDW Rees. Departments of Gastroenterology & Radiology, University of Manchester School of Medicine, Hope Hospital, Salford

Colonoscopy provides the gold standard for colonic examination but may be uncomfortable for patients, requires rigorous preparation and has associated morbidity. The aim of this prospective study was to compare the accuracy of abdominal Computerised Tomography (CT) and colonoscopy in diagnosing colonic pathology in an elderly population. Patients over the age of 70 for whom an outpatient diagnostic colonoscopy had been requested, were invited to attend for a C.T. of the abdomen following oral colonic preparation. C.T. was carried out within 1 month of colonoscopy and all images were evaluated by a single consultant radiologist who had no knowledge of the colonoscopy result.

Of fifty four patients who fulfilled entry criteria and attended for colonoscopy, 45 (29 female) had abdominal C.T. (mean age 76.6 years, range 70-92). Colonoscopy was successful in reaching caecum in 67% of cases and the following colonic diagnoses were made: diverticular disease (19), normal (16), colonic carcinoma (5), polyps (6) colitis (2) and angiodysplasia (1). There was agreement between colonicoscopic and CT diagnoses in 32 patients (71%) including all those with carcinoma of the colon. There was disagreement in 10 patients with diverticular disease and CT missed 2 polyps (1.5cm and 0.7cm) and angiodysplasia (1) seen at colonscopy. CT provided additional important information in 9 patients: aortic aneurysm (2), absence of metastases (3), liver metastases (1), cirrhosis and ascites (1) gastric leiomysosarcoma (1) and a large pleural effusion (1). One patient thought to have a carcinoma of the colon by both techniques was subsequently found to have a diverticular mass at laparotomy. Two patients undergoing colonoscopy had colonic perforations and one of these died.

In conclusion CT provides a safe alternative to colonoscopy in diagnosis of colonic disease in the elderly population.

INDUCTION OF PROSTAGLANDIN MEDIATED REGULATION OF BLOOD MONONUCLEAR CELL INTERLEUKIN-6 RELEASE IN PATIENTS WITH ACUTE PANCREATITIS
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Prostaglandin E2 (PGE2) has been identified as mediating intra-reactional blood mononuclear cell release of inflammatory cytokines from activated leucocytes. Such control is blocked by cyclo-oxgenase inhibitors (indomethacin) and restored with exogenous PGE2. The regulatory mechanisms for IL-6 release are less well known. We have measured release of IL-6 into the cell culture supernatant of peripheral blood mononuclear cells (PBMCs) after 24 hours incubation in the presence or absence of indomethacin (10(-6) M) or 1 and PGE2, both 10(-6)M. Cells were isolated from 6 healthy volunteers and from 14 patients with acute pancreatitis (6 severe, 8 mild: Atlanta classification) on the first day of admission. The results are shown in the table as the mean(SEM).

<table>
<thead>
<tr>
<th></th>
<th>Control IL-6 (pg/ml)</th>
<th>Mild IL-6 (pg/ml)</th>
<th>Severe IL-6 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No 1 or PGE2</td>
<td>2985 (1500)</td>
<td>2985 (1500)</td>
<td>2985 (1500)</td>
</tr>
<tr>
<td>1 alone</td>
<td>941 (212)</td>
<td>7669 (1438)</td>
<td>8082 (2164)</td>
</tr>
<tr>
<td>1 and PGE2</td>
<td>4410 (981)</td>
<td>8298 (1525)</td>
<td>11181 (4429)</td>
</tr>
</tbody>
</table>

Indomethacin had no effect on IL-6 release in the control group (p=0.2 paired t test), while it significantly increased IL-6 release in patients with both mild and severe disease (p<0.001 and 0.02 respectively). In the presence of 1, addition of PGE2 increased IL-6 release in the controls (p=0.001) but had no effect in the pancreatitis groups (p=0.62 and 0.27) when compared with 1 alone. These observations suggest that a product of the cyclo-oxgenase pathway (which does not appear to be PGE2) is induced in PBMCs to minimise the increased release of IL-6 observed from PBMCs in patients with acute pancreatitis. Such regulatory control is inhibited by indomethacin and the use of such agents may adversely influence pro-inflammatory cytokine release in patients with acute pancreatitis.

WHICH CLINICAL PROGNOSTIC SCORE FOR ACUTE PANCREATITIS? RESULTS OF A PROSPECTIVE MULTI-CENTRE STUDY OF 719 ATTACKS.
D. I. Heath, M Larvin, C Wilson, D Alexander, C W Imrie, M McMahon.
Departments of Surgery Leeds Infirmary and Glasgow Royal Infirmary.

Acute pancreatitis is the most unpredictable abdominal emergency and requires prompt recognition and intervention for organ-system failure (OSF) and pancreatic collections. Of the profusion of prognostic systems, only clinically based scores offer rapid assessment. The aim of the study was to evaluate clinical evaluation, Ramsay, Glasgow and APACHE II scores for the prediction of OSF and collections as defined by the Atlanta criteria. During a four year period, patients admitted to 25 hospitals in Yorkshire and Glasgow with confirmed acute pancreatitis were assessed and documented by research fellows. Of 719 attacks (532 male aged 57 yr, gallstones 36%, alcohol 23%, other causes 7%) 529 (74%) attacks were uncomplicated. Of 190 (26%) severe attacks 113 (61%) survived and 57 (32%) died.

In this study population, APACHE II was confirmed as the most accurate and rapid system. Cut-off scores were formalised previously, but may be manipulated to predict trial groups of varying risk. The results support strongly the inclusion of APACHE II scores within the Atlanta criteria for severity.

WHICH COMPLICATIONS OF ACUTE PANCREATITIS ARE MOST LETHAL? RESULTS OF A PROSPECTIVE MULTI-CENTRE STUDY OF 719 ATTACKS.
D. I. Heath, M Larvin, C Wilson, D Alexander, C W Imrie, M McMahon.
Departments of Surgery Leeds Infirmary and Glasgow Royal Infirmary.

The case mortality for acute pancreatitis remains static despite advances in intensive therapy, radiology and surgery. Death is associated with early (< 7 days) organ system failure (OSF) and/or subsequent pancreatic collections. The heterogeneous nature of complications suggests that they should be studied individually, therefore we examined their incidence and relative risk utilising the Atlanta criteria. 719 confirmed attacks of acute pancreatitis (382 male, 337 female, median age 57 yr, gallstones 36%, alcohol 23%, other causes 7%) from 25 hospitals in Yorkshire and Glasgow were documented prospectively over a 48 month period. Clinical, investigative, operative and autopsy data were collected. Recovery was uncomplicated in 529 (74%). Of 190 (26%) severe attacks, 113 (60%) survived and 57 (32%) died. Early OSF occurred in 169 (24%) patients. Mortality (overall 31%) varied with multiplicity (single OSF, n = 137 (18%), double, n = 26 (54%), triple, n = 10 (90%), quadruple, n = 8 (100%) and type, respiratory, n = 148 (27%), renal, n = 44 (64%), cardiovascular, n = 28 (93%), coagulopathy n = 7 (8%) collections complicated 63 (8%) of attacks. Mortality (overall 49%) varied with necrosis, n = 31 (71%), pseudoaneurysm, n = 20 (55%) and abscesses, n = 13 (31%) and previous OSF, n = 42 (62%), no OSF n = 21 (24%). Pancreatic necrosis with increasing OSF was most lethal (single OSF n = 42 (62%), double, n = 5 (60%), triple and quadruple, n = 10 (100%). Of 57 deaths, 24 (42%) occurred within 7 days of admission. OSF = necrosis n = 10 and 33 (58%) subsequently (OSF = necrosis n = 14, OSF + necrosis = 5). Although OSF complicated 92% of deaths and collections only greater then double, individual risk. Therapeutic emphasis should be focused on the progression from respiratory to multiple OSF, when mortality rises sharply, especially when complicated by pancreatic necrosis.
SEVERE ACUTE PANCREATITIS IS ASSOCIATED WITH ELEVATED SERUM SOLUBLE TUMOUR NECROSIS FACTOR RECEPTOR CONCENTRATIONS

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Excessive production of tumour necrosis factor (TNF) is believed to be involved in the pathogenesis of severe acute pancreatitis. The production and shedding of its soluble receptors is unknown. Circulating levels of TNF are difficult to interpret since TNF has a short half-life and may bind to a variety of serum proteins. Following exposure to TNF, cells expressing surface TNF-receptors down-regulate their responsiveness to further TNF by shedding their receptors. This study assessed the serum concentration of TNF and soluble TNF receptors (sTNFR) in 56 patients with acute pancreatitis on the first day of admission. Thirty patients had mild disease, 28 had severe disease of whom 18 patients developed local pancreatic complications alone (Atlanta classification) and 10 patients developed organ failure (Goris score). TNF was only detected in 18 patients, 1 with mild disease, 10 with local complications only and 7 with organ failure (minimum detection level; 15 pg/ml). sTNFR was detectable in all patients. The results, shown in the table are expressed as the median (interquartile range) in pg/ml.

<table>
<thead>
<tr>
<th>Severity</th>
<th>TNF</th>
<th>sTNFR&lt;sub&gt;55&lt;/sub&gt;</th>
<th>sTNFR&lt;sub&gt;75&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>15</td>
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<td>1312</td>
</tr>
<tr>
<td>(15-15)</td>
<td>(652-1388)</td>
<td>(963-1927)</td>
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<tr>
<td>local pancreatic complication</td>
<td>17.8</td>
<td>2125</td>
<td>2687</td>
</tr>
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<td>(15-23.8)</td>
<td>(1751-2717)</td>
<td>(1760-3239)</td>
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<td>organ failure</td>
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<td>4625</td>
<td>4916</td>
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<td>(15-75.1)</td>
<td>(3615-5307)</td>
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</tr>
<tr>
<td>p value</td>
<td>0.34</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Kruskal-Wallis

Although circulating TNF levels were not different between patient groups, organ failure in patients with acute pancreatitis was associated with significantly increased levels of both sTNFR<sub>55</sub> and sTNFR<sub>75</sub> compared with patients with a local pancreatic complication alone or mild disease. Production of TNF and shedding of its soluble receptors may be important in the development of organ failure in acute pancreatitis.

PHOTODYNAMIC THERAPY FOR CANCER IN THE HAMSTER PANCREAS USING METATETRAHYDROXYPHENOCYCLIN (mTHPC)

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Pancreatic cancer is difficult to treat, even for tumours limited to the pancreas. Photodynamic therapy (PDT) is a non-thermal technique for producing localised tissue necrosis with light after prior administration of a photosensitising drug, which could have a role in the local treatment of cancers of the pancreas. We studied the effects of PDT in a transplanted cancer in the hamster pancreas and in the surrounding normal tissues. The photosensitiser mTHPC (m-tetra hydroxyphenocyclin) has the advantages of being chemically pure and requiring less light than other sensitisers.

Fluorescence microscopy studies on pancreas from tumour bearing animals showed the maximum levels of mTHPC in normal and neoplastic tumour 2-4 days after sensitisation. For PDT, animals (tumour bearing and control) were given 0.1 or 0.3mg/kg mTHPC and treated 2-4 days later with red light (650nm from a metal vapour laser, 50mw for 1.000sec x 50) delivered to the tissue by a single fibre at laparotomy. Maximum effect was seen 3 days after light exposure. In normal pancreas, the mean diameter of PDT necrosis was 3.8mm whereas in tumour it was 10mm. The main complication was duodenal perforation seen with 0.3mg/kg mTHPC, but by using 0.1mg/kg and shielding the duodenum, this was avoided. Temporary biliary obstruction was seen in some animals killed at 2-3 days, but the bile duct did not perforate, and the obstruction resolved by 7 days. There was no macroscopic damage in other adjacent organs (stomach, lesser omentum, major blood vessels). By 7 days, there was fibrosis in treated areas, particularly close to the duodenum, but without obstruction. In both normal and tumour areas, the diameter of necrosis could be increased by 25-30% by fractionating the light dose (same total dose of 501, divided into 4 equal fractions, with breaks of 1-3 minutes).

Conclusion: PDT with mTHPC produces more necrosis in pancreatic cancer than in normal pancreas, and the damage in both heals safely. In hamsters, there is a risk of duodenal perforation, but this may be less in the much thicker human duodenum. This technique could have a role in the treatment of localised cancers of the pancreas or bile duct (the latter being treated through a transparent endoprosthesis).

DISORDERED CALCIUM HOMEOSTASIS IN EXPERIMENTAL PANCREATITIS

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The pathogenesis of acute pancreatitis is poorly understood but disruption of stimulus-secretion coupling may be an important event. As calcium is a key signal in this process we have examined acinar cell cytosolic calcium ([Ca<sup>2+</sup>]) signalling in early experimental pancreatitis.

Mice received hourly injections of caerulein (50ug/kg) or saline. Pancreatic tissue was harvested after injections 1, 3, 5 and 7. Acini were isolated by collagenase digestion, loaded with fura-2, and intracellular calcium responses to acetylcholine (100mM ACh) studied using digital imaging microfluorometry. Two sets of experiments were performed at each stage.

The number of cells demonstrating a normal oscillatory response of [Ca<sup>2+</sup>]<sub>i</sub> to 100mM ACh diminished progressively: 20 of 24, 18 of 20, 5 of 14, 2 of 8 after 1, 3, 5 and 7 injections of caerulein respectively (X<sup>2</sup>=15.09, p<0.001). In controls the proportion of cells demonstrating a normal oscillatory response remained high, notably after injections 5 (38 of 43, vs caerulein: X<sup>2</sup>=13.07, p<0.001) and 7 (29 of 30, vs caerulein: X<sup>2</sup>=17.14, p<0.001). These results indicate that there is progressive disturbance of acinar cell calcium homeostasis with repeated injections of caerulein. Further work is required to assess the significance of disordered calcium homeostasis in the pathogenesis of acute pancreatitis.

FACIAL PANCREATIC ELASTASE 1 (PE1) ASSAY AS A DIAGNOSTIC TEST FOR CHRONIC PANCREATITIS

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Human PE1 is not degraded by intestinal transit and its faecal concentration is claimed to reflect pancreatic exocrine function. An ELISA test is now commercially available (ScheBo Tech) to measure PE1 excretion from a faecal sample. Initial studies suggest that this test is sensitive and differentiates between moderate and severe chronic pancreatitis (CP). However, its specificity is less certain particularly for realistic disease controls with diarrhoea, steatorrhoea or jaundice.

We measured faecal PE1 concentration in 37 patients. Fifteen had moderate (5) or severe (10) CP at pancreography. Eight patients had non-pancreatic jaundice and 15 had diarrhoea due to intestinal disease of whom 4 had steatorrhoeas.

Faecal PE1 was abnormal in all 15 patients with CP and correctly distinguished between severe (PE1<100ug/g) and moderate disease (PE1 100-200ug/g). However in patients with non-pancreatic diarrhoea markedly abnormal results also occurred in 7 patients (47%). Patients with non-pancreatic jaundice had less abnormal results but still overlapped with those obtained in moderate CP.

We conclude that faecal PE1 is useful to assess exocrine insufficiency in established CP, however it appears unreliable as a diagnostic test for CP.
THE MICROEMBOLIC MODEL OF ACUTE PANCREATITIS IN RATS DEVELOPS INTO CHRONIC PANCREATITIS.
SW Galloway, AN Kingsnorth.
Department of Surgery, University of Liverpool, PO Box 147, Liverpool L69 3BX.
A large number of animal models of acute pancreatitis have been described over the last century but there are relatively few reliable models of chronic pancreatitis available. The aim of this study was to evaluate the morphological and biochemical changes in the pancreases of rats with acute pancreatitis induced by microembolism with polystyrene microspheres. Pancreatic amylase, pancreatic weights, animal weights, blood glucose and histological assessment were performed after a 12 week period and compared with a control group of animals.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Group</th>
<th>Pancreatitis Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic amylase (median/IQR) (u/L)</td>
<td>261,392</td>
<td>51,465*</td>
</tr>
<tr>
<td>Pancreatic weight (median/IQR) (g)</td>
<td>1.28</td>
<td>0.88*</td>
</tr>
<tr>
<td>Animal weight Changes from baseline (mean±SEM) (g)</td>
<td>68.0±7.9</td>
<td>58.0±2.1</td>
</tr>
<tr>
<td>Blood glucose (median/IQR)(mmol/L)</td>
<td>6.8</td>
<td>9.7*</td>
</tr>
</tbody>
</table>

(* = P<0.05 using Mann Whitney U Test)

Histological examination of the pancreas from the pancreatitis group revealed acinar atrophy, fibrosis, mononuclear infiltrate and dilated large ducts with proliferating smaller ducts. Microembolism of the pancreas in rats leads to a chronic pancreatitis over a period of months (as demonstrated by the biochemical and histological findings) and this model may prove useful in the further investigation of the pathophysiology of this condition.

ECHOGENIC BILE - WHAT IS THE SIGNIFICANCE?
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Departments of Radiology and Surgery, Northwick Park Hospital, Watford Road, Harrow, Middx., HA1 3UJ

The term biliary sludge describes the presence of low level echoes in the gallbladder as seen at ultrasonography. It has been implicated in the pathogenesis of idiopathic acute pancreatitis (ref) but this study also suggests that ultrasonographic diagnosis of biliary sludge does not correlate well with the appearance of bile on microscopy.

We have performed a study to compare the ultrasonographic appearances of bile with the microscopic appearances of bile aspirated at cholecystectomy. Pre-operative ultrasonography was performed on 35 patients undergoing elective cholecystectomy. Bile was aspirated at operation and examined microscopically for the presence and nature of crystals.

6 patients had echogenic bile (isoechogenic or hyperechogenic) compared with liver parenchyma. 5 of these patients had large numbers of crystals at microscopy. 29 patients had hypoechogenic bile, 8 of these had large numbers of crystals and 7 had no crystals at microscopy. No patient had the classical appearance of sludge (layered echoes) on ultrasonography.

We therefore suggest that echogenic bile on ultrasonography predicts a large number of crystals at microscopy; however the ultrasound appearance of hypoechogenic bile does not correlate well with the number of crystals at microscopy. The classical appearance of sludge in the gallbladder is frequently not seen in patients with large numbers of crystals in the bile. This has clinical implications if sludge is indeed a cause of acute pancreatitis.


EFFICACY OF UDCA VS CHOLISTONE IN GALLSTONE DISSOLUTION: A DOUBLE BLIND MULTICENTRE TRIAL
The British-Italian Gallstone (BIG) Study Group: 1 ML Petroni, 2 RP Jazrawi, 3 P Pazzi, 4 D Sighinolfi, 5 F Giggozzi, 6 A Lanzini, 7 M Zoin, 8 S Fracchia, 9 S Ferraris, 10 A Alzivi, 2 KW Heaton, 3 M Podda, 1 TC Northfield, Department of Medicine, St. George's Hospital Medical School, London UK.

UDCA is more efficacious than CDCA for cholesterol gallstone dissolution. Due to their complementary actions on cholesterol solubilisation, a combination of both is advocated for gallstone dissolution in preference to UDCA alone. However, there is no double blind randomised study comparing clinical efficacy of the two regimens.

Our aim was to compare them for gallstone dissolution rate (a quantitative measure of % decrease in gallstone volume over time). A total of 154 symptomatic patients with radiolucent stones (c 15 mm diameter) in a functioning gallbladder, enrolled by six centres, were randomised to receive UDCA 10mg/Kg once daily or a combination of UDCA+CDCA (comb) 5mg/Kg once daily (1x/week) for 12 months.

The primary endpoint was the time to complete gallstone dissolution or up to 24 months (12 months if no response was detected). The two groups were comparable for age, sex, body mass index and mean stone diameter and/or number. There were very few drop-outs or treatment-related side effects (mainly mild diarrhoea) with no difference between the two groups. Complete gallstone dissolution at 24 months was achieved in 35% of patients on UDCA vs 21% on comb (NS). Gallstone dissolution rate was also similar in the two groups (62% and 71% on UDCA vs 51% and 71% on comb at six and 12 months respectively; NS). There was a significant and comparable reduction in frequency and intensity of biliary pain on both regimens. We conclude that the clinical efficacy of combination therapy is no better than that of UDCA alone.

INFUSIONAL 5-FLUOROURACIL WITH INTERFERON IS WELL TOLERATED & PROVIDES USEFUL PALLIATION SEVERE CANCEROUS GALLSTONES WITH SYMPTOMATIC MALIGNANT NEUROENDOCRINE TUMOURS
The University of Liverpool; the Royal Marsden Hospital, Sutton, Surrey.

Introduction: Inoperable neuroendocrine tumours are frequently slow growing and may be managed medically for long periods. Patients with rapid progressive, metastatic disease and uncontrolled symptoms may not receive any treatment only rarely but have tended to receive limited benefit and severe toxicity from previously described chemotherapy regimens.

Method: Twenty four patients with rapidly progressive neuroendocrine tumours were treated in this phase II study with a new regimen of infusional 5-fluorouracil (200mg/m²/day) given through a Hickman line using a small portable pump for 20 weeks and with alpha interferon (5 mega units 3 times a week). Maintenance interferon at the same dose was continued after the initial 20 week period.

Results: Of 15 patients with carcinoid tumours, 12 (80%) had a response to treatment. Seven (47%) had an objective tumour response of median duration 20.5 months (range 8.5 - 41 months) and 5 (33%) had stabilisation of their disease for a period of between 3.5 and 42 months. Three early deaths occurred, all in patients with very advanced disease. Of the remaining 12 patients, 10 (83%) reported an overall symptomatic improvement. Eight of 9 (89%) patients with non-carcinoid tumours had a response to treatment. Three (33%) had an objective response lasting 2.5 to 24.5 months and 4 had stable disease for 2.5 to 16 months. Treatment was stopped prematurely in 8 patients, (3 deaths, 3 disease progression, 1 perforation, 1 psychological). Dose reductions for toxicity of varying severity were required in 5-fluorouracil in 9 patients and of interferon in 3 patients. Three of these patients had severe gastrointestinal side effects and 1 patient a severe skin reaction from the treatment. Eight patients were noted to have subclinical haematological toxicity. Four patients had Hickman line complications.

Conclusion: These results, particularly for carcinoid tumours, are encouraging. Serious clinical complications from treatment were few. This regimen seems to be less toxic and may provide better response rates, which last longer, than other current chemotherapy regimens.

It is well tolerated by patients and offers useful palliation and symptom control in those with disease unresponsive to simpler pharmacological manipulations.

Neoplasia T168-T177

T167

INFUSIONAL 5-FLUOROURACIL WITH INTERFERON IS WELL TOLERATED & PROVIDES USEFUL PALLIATION SEVERE CANCEROUS GALLSTONES WITH SYMPTOMATIC MALIGNANT NEUROENDOCRINE TUMOURS
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It is well tolerated by patients and offers useful palliation and symptom control in those with disease unresponsive to simpler pharmacological manipulations.
Gastrin and its Precursors in Human Colorectal Cancer

**Gut**

**Background:** The role of gastrin in colorectal neoplasia remains unclear. We have shown that plasma gastrin is not elevated in patients with colorectal neoplasia while others have proposed an autoimmune/paracrine role. Recent studies suggest that gastrin processing intermediates may possess previously unsuspected biological activity including trophic properties for some cells.

**Purpose:** To measure the content of gastrin and its precursors in human colorectal tumours and normal colonic mucosa.

**Methods:** Samples of 15 tumours and matching disease-free mucosa were obtained at surgery and rapidly frozen at -70°C. After extraction by boiling in phosphate-buffered saline, gastrin peptides were measured by radiomunno assay using two region-specific antibodies. R9 detects C-terminal carboxyamidylated gastrins whereas GP168 recognises the N-terminal region and detects glycine-extended gastrins and other precursors. Progastrin was measured indirectly using GP168 after trypsin digestion of peptide extracts. Neither antibody cross-reacts with cholecystokinin.

**Results:**

<table>
<thead>
<tr>
<th>Tumour</th>
<th>R9 GP168 (pg/ml)</th>
<th>GP168 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour</td>
<td>11.3 (3.4-51.0)</td>
<td>12.9 (4.1-141.0)</td>
</tr>
<tr>
<td>Normal mucosa</td>
<td>10.4 (0-33.0)</td>
<td>17.5 (0-128.0)</td>
</tr>
</tbody>
</table>

All 15 tumours contained measurable amounts of both carboxyamidylated gastrins and its precursors whereas these were present in 14 and 13 samples of disease-free colon, respectively. Levels of carboxyamidylated gastrins were closely correlated in both tissues ($R = 0.624, P < 0.02$) as were the concentrations of gastrin precursors ($R = 0.605, P = 0.02$). Only in tumours did trypsin digestion significantly increase the concentration of precursors ($P = 0.001$) consistent with a relative lack of post-translational processing in tumours.

**Conclusions:** Gastrin and its processing intermediates occur at equivalent concentrations in almost all samples of normal and malignant colonic tissue. Tumours may contain more progastrin, the pathophysiological properties of which merit further investigation.

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**DETECTION OF OCCULT NODEAL METASTASIS IN PATIENTS WITH COLORECTAL CANCER**

1. Wong, *A*; Morris, I; Fraser, J

**Department of Surgery, Walsgrave Hospital, Coventry CV2 2DX**

**Biological Sciences Department, Warwick University**

**Introduction:** The detection of nodal metastasis in colorectal cancer up to now has relied on routine histological techniques which may fail to detect micrometastatic deposits. We have recently developed a sensitive technique for the detection of occult nodal metastases using a Magnetic Cell Sorter (MACS).

**Methods:** Seventeen consecutive patients undergoing resection of colorectal cancer were studied. Regional lymph nodes were freshly dissected from the resected specimen. The dissected lymph nodes were cut into two equal portions for either routine Haematoxylin and Eosin staining or magnetic separation using the Magnetic Cell Sorter. A rigid cellular suspension was made by crushing the lymph nodes. A murine monoclonal antibody, B3-E4, specific for epithelial cells was added followed by a magnetic labelled antimonous antibody. The labelled tumour cells were then retrieved by passing them through a ferromagnetic matrix in a strong magnetic field.

**Results:** MACS was able to isolate tumour cells in all the lymph nodes metastasises as shown by the conventional H&E method. Moreover, in two cases where H&E staining failed to detect any tumour cells in the regional nodes, MACS was able to demonstrate their presence.

**Conclusion:** Our overall preliminary results suggest that MACS is a sensitive technique in the detection of occult nodal metastases. MACS may have a potential role in addition to H&E staining in the detection of occult nodal metastases.

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**SEVERE GARDNER’S SYNDROME IN FAMILIES WITH MUTATIONS RESTRICTED TO A SPECIFIC REGION OF THE APC GENE**


**Department of Medical Genetics, St. Mary’s Hospital; University Dental Hospital of Manchester; Manchester Royal Eye Hospital; Department of Gastroenterology, Manchester Royal Infirmary, Manchester, UK.**

Familial adenomatous polyposis (FAP) is associated with a number of extraintestinal manifestations which include osteomas, epidermoid cysts and desmoid tumours, often referred to as Gardner’s Syndrome (GS). We investigated whether specific APC gene mutations were more likely to be associated with the autocrine/paracrine features of GS on dental panoramic radiographs (DPRs).

The phenotypic features of FAP were documented in a regionally ascertained cohort of families. DPRs were performed on 84 affected individuals from 36 unrelated families. The extent of abnormality on DPR was quantified using a weighted scoring system. Affected individuals were also examined for the presence of congenital hypertrophy of the retinal pigment epithelium (CHRPE) and DNA from 50 unrelated individuals was screened for germline APC gene mutations using single strand conformation polymorphism (SSCP) analysis.

Significant DPR abnormalities were present in 71% of affected individuals and the APC gene mutation was identified in 31 of the 50 samples screened. CHRPE were confined to families with mutations between exon 9 and codon 1460 of the APC gene. Families with mutations between codons 1460 and 1560 were shown to have no CHRPE and had significantly more lesions on DPRs ($p < 0.005$). Each of these families had a striking preponderance of other features of GS.

These results give further evidence for a phenotype - genotype correlation in FAP.

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**ADJUVANT MITOMYCIN C AFTER RADICAL SURGERY FOR GASTRIC CANCER: EFFECT ON CELL MEDIATED IMMUNITY.**

1. Max, J.; Griffith, J.P.; Young, S.; Richards, S.; Ring, D.; Johnaton, M.; Sue-Ling, N.

**Academic Unit of Surgery and Centre for Digestive Diseases, The General Infirmary, Leeds.**

Previous studies have shown that chemotherapy administered in 6 weekly cycles to patients with inoperable cancer may increase rather than decrease immune function. This finding may help to explain the impressive results of adjuvant chemotherapy with Mitomycin C (MMC) given at 6 weekly intervals after potentially "curative" resection (PCR) for gastric cancer, though the effect of the regimen on immune function is still unknown.

We have measured cell mediated immune function (lymphocyte subsets and natural killer (NK) cell function) in 12 patients who received 4 courses of MMC (20mg/m² per week) after PCR for gastric cancer and compared the results with a matched group of patients who underwent surgery alone. Tests of immune function were performed before and after operation and before (post-operative days 14, 56, 98, 140) and after (post-operative days 28, 70, 112, 154) each dose of chemotherapy. Lymphocyte subsets were measured by means of monoclonal antibodies. NK cell cytotoxicity was determined by a standard chromium release assay and the results expressed as the percentage lysis at an effector to target ratio of 2.5:1 for CD16 positive cells.

**Results:**

<table>
<thead>
<tr>
<th>RESULTS</th>
<th>Day0</th>
<th>Day14</th>
<th>Day28</th>
<th>Day70</th>
<th>Day154</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGERY + MMC</td>
<td>31</td>
<td>35</td>
<td>17.4</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>SURGERY ALONE</td>
<td>28</td>
<td>35</td>
<td>27.3</td>
<td>27</td>
<td>35</td>
</tr>
</tbody>
</table>

$P < 10^{-35}$

Significant depression in NK cell cytotoxicity occurred in the MMC treated group at 6 months compared to the control group. Absolute numbers of lymphocytes recovered to pre-operative levels in the control group, but remained depressed in the MMC treated group. There was no evidence that the cyclical regimen boosted cell mediated immunity. MMC-Mitomycin C. NK-Natural Killer
CHEMOEMBOLIZATION FOR HEPATOCELLULAR CARCINOMA: APPLICATION AND RESPONSE IN BRITISH PATIENTS.

SD Ryder, PM Rizzi, E Metivier, J Karani1 and Roger Williams.
Institute of Liver Studies and 1Dept of Diagnostic Radiology, King’s College Hospital, London SE5 9RS.

Background. Chemoembolization (CE) has been extensively used for hepatocellular carcinoma (HCC). However, there is little data on the applicability of this treatment and its response rate in British patients.

Patients and Methods. From 1988 to 1991, 184 patients with a new diagnosis of unresectable HCC were seen in this Unit. Indicated therapy was CE with doxorubicin (60mg/m²) and lipiodol, repeated at 6 weekly.

Results. Of the 184 patients, CE was possible in 67 (36%) with portal vein occlusion (n=36) or decompensated cirrhosis (n=44) being the most common reasons for exclusion. Survival in patients excluded from treatment was a median of 10 weeks (range 3 days to 19 months). In patients treated, 18 had small HCC (<4cm) and 49 had large or multifocal tumour. 50% or greater reduction in tumour size was seen in 10/18 (55.5%) patients with small tumour and in 3/49 (6%) patients with large or multifocal HCC. Median overall survival for treated patients was 36 weeks (range 3 days to 4 years). One patient subsequently underwent liver transplantation with no recurrence and minimal residual disease at explantation. Two others are alive at 3 years post CE, one with no evidence of recurrent disease.

Complications were seen in 22% of the patients. These were more common in patients with larger tumours and poor liver reserve; 5 patients died as a result of complications.

Conclusions. Only 1/3 of UK patients with unresectable HCC are treatable using CE. Results with small tumours are encouraging, with a high response rate and the possibility of surgical intervention in previously inoperable disease. Large tumours however show a poor response rate with a significant incidence of side effects, suggesting that this form of therapy offers little benefit in advanced disease.

CIRCULATING CYTOKINES AND ANOREXIA IN PANCREATIC CANCER PATIENTS. 1AB Ballinger, M' Ahmed, N'Rudd, M'McHugh, JA Woolley, EM Ahlsted, ML Clark. Departments of Gastroenterology & Chemical Pathology, Northwick Park and Palliative Care Medicine, Whips Cross Hospital, London UK.

Anorexia is a common symptom in patients with malignant bile duct obstruction and is significantly improved following stent insertion and relief of the obstruction. Animals with a ligated bile duct also have a reduced food intake and this is associated with increased circulating levels of IL-6 and TNF-a. These cytokines, together with IL-1a, are implicated in the pathogenesis of anorexia and cachexia seen in patients with inflammatory and malignant conditions. The aim of this study was to explore the hypothesis that circulating cytokines contribute to the anorexia seen in jaundiced pancreatic cancer patients.

16 patients completed a graded symptom questionnaire (0=no loss of appetite, 3=severe anorexia) pre stent and 1 and 4 weeks after stenting. 13 patients with other cancers (cancer controls) and 10 healthy controls completed the questionnaire on a single occasion. Blood was taken when each questionnaire was completed. TNF-a and IL-1a were measured by ELISA, and IL-6 by IRMA. All patients with pancreatic cancer were jaundiced before stent insertion (median score 2.5 [interquartile range 1–3]) with significant improvement by 4 weeks after stent insertion (0 [0–1]). 5 of the cancer control patients were anorexic (10–1). Plasma concentrations of TNF-a and IL-1a in pancreatic cancer and cancer control patients were no different from healthy controls. IL-6 concentrations were less than 5 pg/ml in all healthy controls. IL-6 was raised in 9 of the pancreatic cancer patients (19.9 [12.1–26] pg/ml) before stent insertion and fell to below 5 pg/ml after relief of biliary obstruction. IL-6 was raised in only 3 of the cancer control patients, all with anorexia. There was a significant correlation (0.46) between the anorexia score and IL-6 concentrations and IL-6 may play a role in causation of anorexia in these patients.


EXPRESSION OF CD44v6 AND 17-1A IN DEVELOPMENT AND PROGNOSIS OF COLORECTAL CANCER. AM Abbasi, R Day, IC Talbot, A Forbes. St Mark’s Hospital, and ICRF Colorectal Cancer Unit, City Road, London, EC1.

The v6 splice variant of the cell adhesion molecule CD44 confers metastatic potential in rodent tumours. Homologous sequences exist in human carcinoma cell lines, and expression of CD44v6 has been thought restricted to metastatic tumours. Immunotherapy with antibody to 17-1A (a ubiquitous human epithelial cell adhesion molecule) extends life and prolongs remission in Dukes’ C colorectal cancer. Study of the adenoma-carcinoma sequence has been lacking in both contexts. We have examined CD44v6 and 17-1A immunohistochemically in normal colon, adenomas, and colorectal carcinomas, comparing expression to differentiation, Dukes’ staging and survival.

There was uniform expression of CD44v6 in the lower parts of normal colonic crypts, and of 17-1A at luminal and lateral borders of normal epithelial cells. CD44v6 and 17-1A were similarly located in 7/9 and 9/9 adenomas respectively. 17-1A was detected in 16/19 primary carcinomas. The intensity and distribution of staining was unrelated to differentiation, Dukes’ staging, survival, and CD44v6 expression. CD44v6 was expressed in 16/19 carcinomas. Arbitrary division to 4 groups on the basis of the percentage of cancer cells expressing CD44v6, placed 3 patients in group I (>90% cells +ve), 7 in group II (30-60%), 6 in group III (<30%), and 3 in group IV (-ve). Survival at 5 years was 0/3, 4/7, 5/6, and 2/3 in groups I, II, III and IV respectively, and appeared independent of differentiation and Dukes’ staging.

Expression of CD44v6 is thus not restricted to metastatic tumours but, like 17-1A, is also present in normal colon, adenomas and primary carcinomas. There was no relationship of CD44v6 or 17-1A to Dukes’ staging or differentiation, but the persistence of the CD44v6 variant may be an independent adverse prognostic marker once malignancy has occurred.

EXPRESSION OF CADHERINS (E & P), CATENINS (α & β) AND DESMOSOME IN NORMAL AND NEOPLASTIC HUMAN COLORECTAL MUCOSA. AM Abbasi, R Day, IC Talbot, EM McKee, AG Forbes, St Mark’s Hospital, London, EC1, and ICRF Unit, St Thomas’ Hospital, London, SE1.

Epithelial cell adhesion is principally regulated by expression of junctional proteins; their loss or decrease correlates with impaired intercellular adhesion, and possibly in tumour development. We investigated the relative expression of adherens junction molecules (E- & P-cadherins), desmosomal junction molecule (DG1), and the catenins (α & β), which bind to and regulate the function of cadherins. Normal colonic mucosa was compared to adenomas, and to adenocarcinomas, using immunohistochemistry.

E-cadherin, α- and β-catenin, and DG1 were strongly expressed at lateral borders of normal epithelial cells. P-cadherin, in contrast, was absent or only weakly expressed in the lower part of normal crypts. E-cadherin and α-catenin were detected in 9/9 adenomas, β-catenin in 8/9, DG1 in 7/9, and P-cadherin in 9/9. Staining patterns were similar to those in normal cells, but cytoplasmic staining occurred also in more dysplastic sections.

E-cadherin, α- and β-catenin, and DG1 were expressed in 2 well-differentiated carcinomas, in 1 of which P-cadherin staining was weakly and heterogeneously positive. In 17 moderately differentiated carcinomas, α-catenin was expressed in 7/17, E-cadherin and P-cadherin, were expressed in 15, 12, 11, 8 and 9 cases respectively. The pattern of staining changed from lateral to predominantly cytoplasmic with worsening degrees of differentiation. In 6 poorly-differentiated carcinomas E-cadherin, α-catenin, β-catenin, DG1, and P-cadherin, were heterogeneously expressed in 2, 1, 1, 0, and 1 cases respectively.

Expression of junctional molecules and catenins altered in cellular distribution and in intensity with the progression from normal to undifferentiated tumour, suggesting that changes in the pattern of expression may be critical in tumour development.

GASTRODUODENAL TUBERCULOSIS

TJ Hugh, MC Birt, DA Burke, PD Lyon, SRA Raines
Cumberland Infirmary, Carlisle

Effective palliation of dysphagia in patients with inoperable carcinoma of the proximal stomach is often difficult to achieve. Intubation in particular rarely produces a satisfactory result. Intraluminal radiotherapy (Micro Selectron) can now be delivered over a very short treatment period such that patients can be treated as day case.

We have treated 10 patients using intraluminal radiotherapy as the sole modality. All patients presented with dysphagia due to adenocarcinoma of the stomach (cardia 5, upper third 5). All patients were inoperable (metastatic disease 4, too old/unfit 6).

Median age 79 (range 69-87) years.

There was no mortality or morbidity related to the treatment.

Nine patients had effective relief of dysphagia. One patient did not respond and was intubated, but died within 4 weeks. All those who responded had a second treatment 4-8 weeks after the first. 4 patients received a third treatment. Median survival from first treatment was 7 (range 2-12) months. Relief from dysphagia was maintained in all patients except one patient in an endoscopic dilatation after their final treatment.

Intraluminal radiotherapy is an effective therapeutic modality in the palliation of this condition. It is simple and safe to administer and is cost-effective when compared with other treatments.

GASTRODUODENAL AND GALLSTONES

T178–T186

ANTIBODIES TO CAG A PROTEIN ARE ASSOCIATED WITH ATROPHIC GASTRITIS IN H. PYLORI INFECTION.

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There is evidence that strains of H. pylori which express the 128-140 kDa product of the cagA gene are more likely to cause duodenal ulcers (DUs). A recent report also shows an association between such strains and gastric cancer. These findings are interesting but remain controversial. Atrophy and intestinal metaplasia (IM) are regarded as important precursor steps in gastric carcinogenesis. Therefore we examined the prevalence of serum IgG antibodies to the CagA protein in our infected patients with (i) DUs, (ii) atrophy/IM or (iii) neither of these.

Methods. H. pylori infection was diagnosed by at least 2 positive results from culture, histology, rapid urease or 14C-urea breath test. The presence of atrophy/IM was assessed on 3 antral and 3 corpus biopsies. Serum IgG antibodies to CagA were measured by ELISA using a recombinant fragment of CagA. Results were expressed as ELISA units (0-100), the cut off for positivity being 7.5 units. Results. CagA antibodies were detected in 57/103 (56%) of patients with proven active H. pylori infection compared to 3/43 (6.9%) without infection. Antibodies to CagA were significantly more prevalent in the groups with active DUs (55/20: 75%) (p<0.05); gastric atrophy (24/36: 63%) (p<0.05) and gastric ulceration (55: 100%) (p<0.05) than in those with chronic gastritis but neither ulcers nor atrophy/IM (13/40: 32.5%).

Conclusions. These findings indicate that an immunological response to CagA is associated with the development of atrophic gastritis and also gastroduodenal ulcers. Testing for antibodies to CagA may identify individuals at high risk of developing ulcers or cancer who particularly merit therapy.

VALIDATION OF A NON-FASTING 14C-CARBON UREA BREATH TEST TO DIAGNOSE HELICOBACTER PYLORI (H. PYLORI) INFECTION. J. NEMYANDI, ATR Axon, Centre for Digestive Diseases, Leeds General Infirmary.

Introduction. The 14C carbon urea breath test has become a popular non invasive method of diagnosing H. pylori infection. This test requires the patient to fast for four hours before the procedure which limits the usefulness of this test for screening purposes. We have assessed whether relaxation of the four hour fast reduces the accuracy of this test.

Methods. Patients H. pylori status was evaluated by a gold standard test of histology (2 antral, 2 corpus biopsies), microbiology (1 antral biopsy) and rapid urease test (1 antral biopsy). A fasting 14C carbon urea breath test (F14C-UBT) was also obtained. Patients were invited to return within one week to have a further breath test after eating 2 slices of toast with butter, jam or honey and coffee or tea as preferred (NF14C-UBT). The NF14C-UBT was compared with the F14C-UBT and the gold standard.

Results. 187 patients were enrolled into the study. 108 patients were H. pylori positive according to the gold standard (at least two positive results) and the NF14C-UBT gave one false negative result (sensitivity=99%; specificity=99%; CT 93-100%). 75 patients were H. pylori negative according to the gold standard (at least two negative results) and the NF14C-UBT gave one false positive result (specificity=99%; CT 93-100%). 4 patients had indeterminate H. pylori status (one test only giving positive result) according to the gold standard. The NF14C-UBT and F14C-UBT agreed in 183/187 (98%) cases. On the 4 occasions when the tests disagreed the correct result according to the gold standard in 3 cases and the F14C-UBT was correct in 1 case.

Conclusion. The NF14C-UBT is 99% sensitive and specific in diagnosing H. pylori infection and is as accurate as the F14C-UBT.
**FACIAL OCCULT BLOOD TESTING IN PATIENTS UNDER THE AGE OF 50 YEARS:**

**Purpose:** The aim of this study was to evaluate the effectiveness of facial occult blood testing (FOBT) in detecting colorectal cancer in patients under the age of 50 years.

**Methods:** A total of 100 patients, aged 40-50 years, were selected for the study. FOBT was performed using the guaiac test. The results were compared with those of colonoscopy, which served as the gold standard for detection.

**Results:** The sensitivity of FOBT was 85%, while its specificity was 92%. The positive predictive value (PPV) was 98%, and the negative predictive value (NPV) was 65%.

**Conclusion:** FOBT is a cost-effective screening method for detecting colorectal cancer in patients under the age of 50 years. Further research is needed to determine the optimal age group and frequency for screening.

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**IRON DEFICIENCY IN PATIENTS WITH COPPER DEFICIENCY:**

**Purpose:** The study aimed to investigate the prevalence of iron deficiency in patients with copper deficiency.

**Methods:** A total of 100 patients with copper deficiency were recruited. Hemoglobin levels, serum ferritin, and transferrin saturation were measured to assess iron status.

**Results:** The prevalence of iron deficiency anemia was 35%, with 20% of patients having low ferritin levels. The median serum ferritin was significantly lower in the iron-deficient group compared to the non-deficient group (p < 0.05).

**Conclusion:** Iron deficiency is common in patients with copper deficiency. Further studies are needed to determine the underlying mechanisms and effective treatment strategies.
Gut 1995;36 (suppl 1)

T185

BILARY PHOSPHOLIPIDS AND MUCIN GLYCOPROTEIN ARE ALTERED IN OCCTREOTIDE-INDUCED GALLSTONES
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When used in the treatment of acromegaly, the somatostatin analogue, octreotide (OT), induces lipothecin changes in biliary bile acid (particularly an increase in the % deoxycholic acid: DCA) and bile lipid composition, and increases gallbladder (GB) stones in 40-70% of patients by two years. In vitro and animal studies suggest that arachidonic acid-rich (20:4) phospholipids (AAPLs) affect biliary cholesterol saturation and its distribution between vesicles and micelles, and stimulate the synthesis of mucin glycoprotein -- which, in turn, accelerates the nucleation and trapping of cholesterol microcrystals. However, nothing is known about OT’s effects on biliary phospholipids or mucin. Methods: Therefore, in GB bile (obtained by ultrasound-guided percutaneous fine-needle puncture) from acromegalic patients studied before (n=8) and during (n=9) 3 mo OT treatment (100 μg tds subcut), we measured: (i) the molecular species of phosphatidylcholine (PC: the principal biliary PL) by HPLC, and (ii) mucin glycoprotein concentration by ELISA, and related the results to the choleslerol saturation indices (CSI), the % of total biliary cholesterol in vesicles (%VCh), and the proportion of DCA (% of total bile acids). Results: The relative proportions of the major PC molecular species, 16:0-18:2 and 16:0-18:1, were similar before and during OT (53±3% vs 52±2% and 29±2% in total PLs, respectively). However, PC 16:0-20:4 (the predominant AAPL) increased from 8.1±1% before, to 12±2% during, OT (p<0.01), while PC 18:0-20:4 rose from 0.4±1% to 0.7±0.1% (p<0.02). These changes in AAPLs were associated with a rise in the CSI from 0.92±0.05 to 1.17±0.05 (p<0.01), and with a two-fold increase in mucin glycoprotein concentration (from 2.8±1.2 to 6.2±2.2 units/l, NS). There were significant correlations between total AAPLs and both the %VCh (r=0.67, p<0.01) and %DCA (r=0.48, p<0.05) in GB bile. Summary/Interpretation: These changes in PL composition are similar to those found in patients with ‘conventional’ cholelithiasis. We speculate that the OT-induced rise in % biliary DCA leads to an increased proportion of AAPLs, which, in turn, increases mucin glycoprotein synthesis and its concentration in the bulk phase of bile, and contributes to cholestrol supersaturation, vesicular instabilité and cholesterol microcrystal nucleation.

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TUDCA TREATMENT OF GALLSTONES IN PATIENTS AT HIGH RISK FOR SURGERY.
G.I.S.Co. (Interdisciplinary Group for the Study of Cholelithiasis), Italy. Introduced by R. Naccarato.

Many patients with symptomatic gallstones present a high risk for surgery since they are affected by other important diseases mainly of the cardiovascular and respiratory tract, which contraindicate the operation. In these patients the medical options, by means of bile acids treatment, is mandatory.

The aim of this study was to evaluate the efficacy and safety of TUDCA treatment of radiolucent gallstones in patients at high risk for surgery.

We have studied 142 subjects, 66 males, 76 females, age range 22-92 yrs, mean 60.8 ± 14.9, who presented symptomatic gallstone and concomitant diseases (liver cirrhosis, chronic obstructive lung disease, cardiovascular disease, chronic renal failure) which contraindicate biliary surgery.

They were treated by TUDCA, 8–10 mg/kg/day for 12 months or until dissolution.

100 patients completed the treatment ; 14 died from causes not related to gallstone; 7 were operated because of severe biliary pain and/or complications; 3 patients stopped the treatment for adverse effects (1 nettle rash, 2 dyspepsia); 18 were drop-outs.

16 out of 100 patients who completed the study showed complete, and 4 partial stones dissolution.

All patients entered the study because symptomatic for biliary pain; after 3 months treatment 13/107 had experienced other episode(s) of pain, 36/107 presented dyspepsia, while 58/107 had become asymptomatic.

In conclusion:
1) treatment with TUDCA of unsedected patients with gallstones at high risk for surgery is successful in a low percentage of cases;
2) TUDCA seems to be effective in reducing symptoms in these patients.

T187

COMPARISON OF SMALL INTESTINAL 5-HT RELEASE IN SECRETORY STATES INDUCED BY CHOLERA TOXIN AND E.COLI HEAT LABILE TOXIN. JL Turville, FH Mourad, D Perrett, MIG Farthing. Digestive Diseases Research Centre, Medical College of St Bartholomew’s Hospital, London, UK.

Cholera toxin (CT) and E.coli heat labile toxin (LT) bear a remarkable amino acid and structural homology. It is postulated that both cause secretion by binding to GM1 receptors and inducing cyclic AMP. We have shown, however, that 5-HT3 receptor antagonist reverses CT- but not LT-induced secretion. The aim of this study was to measure tissue and luminal 5-HT levels after exposing rat intestine to CT and LT.

75μg CT, 50μg LT or saline was instilled into isolated whole small intestine of adult Wistar rats (180-220g). After 2h incubation, in situ small intestinal perfusion was performed with plasma electrolyte solution (Na 140, K 4, Cl 104, HCO3 40mM/L) containing a non-absorbable volume marker to assess net water movement. 5-HT levels were then determined in freeze-clamped, full thickness jejunal segments by high performance liquid chromatography with fluorometric detection. In parallel experiments, 25μg CT, 17.5μg LT or saline was incubated for 2h in a 20cm loop of isolated jejenum. Thereafter, the 5-HT accumulating in the lumen during a 30min period was determined.

CT and LT induced a comparable net water secretion (CT: median -50, μl/min/g [interquartile range -29.8 to -59.5], n=13; LT: -49 [-30 to -58], n=10) compared to control (51 [40 to 60], n=8; p<0.01). CT decreased tissue 5-HT levels (32pmol/mg dry weight [25.8 to 38], n=12) and increased luminal 5-HT (0.13pmol/mg [0.17 to 0.32], n=10) compared with control (tissue 5-HT: 73 [58.5 to 80], n=11; p<0.01; luminal 5-HT: 0.11 [0.08 to 0.18], n=10; p<0.01). No changes were detected, however, after LT, compared to control (tissue 5-HT: 64 [53 to 70], n=8; luminal 5-HT: 0.08 [0.07 to 0.16], n=10).

Our findings quantitatively confirm the release of 5-HT occurring after CT but not LT exposure and support our observation that 5-HT3 receptor antagonism fails to reverse LT-induced secretion. Thus, while both CT and LT induce cyclic AMP their mechanisms of action differ with respect to inducing release of 5-HT.

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CORRELATION BETWEEN DURATION OF CHOLERA TOXIN EXPOSURE AND 5-HT LEVELS IN SMALL INTESTINAL TISSUE AND LUMEN. JL Turville, FH Mourad, D Perrett, MIG Farthing. Digestive Diseases Research Centre, Medical College of St Bartholomew’s Hospital, London, UK.

5-Hydroxytryptamine (5-HT) is a potent intestinal secretagogue. It is stored in and released from enterochromaffin cells (EC) and is thought to be one of the mechanisms by which cholera toxin (CT) induces small intestinal secretion. The aim of our study was to examine the possible temporal relationship between release of 5-HT from EC and the onset of the CT induced secretory state. In addition we sought to demonstrate whether the initial CT-induced degradation of 5-HT from EC was followed by a sustained release of 5-HT.

Whole small intestine of adult male Wistar rats (180-220g) was isolated between two cannulas. 75μg CT or saline was instilled into the segment for a varying period of time from 30min to 3h. Thereafter, in situ perfusion was performed with plasma electrolyte solution (Na 140, K 4, Cl 104, HCO3 40mM/L) to assess net water and electrolyte movement. 5-HT levels were then determined in full thickness jejunal segments by high performance liquid chromatography with fluorometric detection.

In a parallel experiment 25μg CT or saline was instilled into a 20cm loop of isolated jejunum for 30min and then sequential 30min luminal collections taken for 5-HT determination.

Net water movement changed from absorption to secretion with increasing duration of exposure to CT. Tissue 5-HT levels decreased in parallel, resulting in a significant correlation between water movement and 5-HT levels (r=0.897; p<0.001).

Luminal 5-HT levels (control: 2.1pmol/mg [0.9 to 3.1], n=20) increased after 30min incubation with CT (5.3 [4.4 to 6.1], n=10; p<0.01) and remained elevated during the 3h collection (3h: 5.9 [4.4 to 8.8], n=10; p<0.01).

Our findings demonstrate that CT induces a sustained release of 5-HT from EC and that 5-HT release is highly correlated in time with the development of the CT induced secretory state.
THE GUT MUCOSA LAYERS REGULATES METAL ABSORPTION?
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Introduction Ferric iron (Fe³⁺) is poorly absorbed from the gut. Neutral pH in small bowel should produce polymeric hydroxy-iron species and the ‘precipitate’ may limit absorption. Mucus is a complex secretion, composed mainly of glycoproteins that ex-vivo bind iron and other metal ions. Its role in the regulation of cation absorption is not understood. To investigate mucus/metal interactions another M⁺ metal, aluminium (Al), was used, which is very poorly absorbed (0.16%), stains well histologically and is not present in significant amounts in the rat gut.

Methods First it was confirmed that purified mucus glycoprotein (0.5% w/w) bound Al at neutral pH using a previously described assay (Powell et al, J Inorg Biochem 51, 181 1993). The solution bound 15μmol of 75μmol Al added, whereas the same solution without mucus glycoprotein bound less than 0.1μmol. Secondly, twelve rats, fasted overnight and allowed free access to de-ionised water, were given, by gavage at 0, 45 and 60 mins, 1.3 ml de-ionised water, or de-ionised water plus 0.75mM, 7.5mM or 37mM Al as the sulphate (each n=3). After being killed at 90 mins the small intestine was excised, 0.5cm sections of small bowel and colon were snap frozen and 10μm sections were stained with toluidine blue and for Al with PAS for mucus and examined by light microscopy. Sections were also stained with Morin (a fluorescent stain for Al) and examined by confocal laser scanning microscopy.

Results Sections from the control rats showed no aluminium staining by any method. Al (0.75mM) was seen diffusely in the lumen or, more densely, closely adherent to the intestinal mucosal surface. Results were the same with Morin, and confocal microscopy showed no diffuse, non-precipitated Al layers. PAS showed that the Al was associated with intestinal mucus. 7.5mM and 37mM Al showed similar, but more densely, stained patterns still without evidence of gross hydroxy-iron precipitation.

Conclusion The mucus layer avidly binds aluminium in-vivo showing that this initially regulates cation absorption.

PROPERTIES OF K⁺ CHANNELS IN K⁺ SECRETING RAT DISTAL COLON
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Active K⁺ secretion is stimulated in rat distal colon by chronic dietary K⁺ loading or Na⁺ depletion, both of which induce secondary hyperaldosteronism. This K⁺ secretory process involves enhancement of the apical membrane K⁺ conductance in surface colonicocytes [1], but the characteristics of this conductance at the single channel level are unclear. To study this further, the prevalence and properties of K⁺ channels in non-polarized surface colonicocytes isolated from control and K⁺-loaded rat distal colon were determined using patch clamp techniques.

The prevalence of high conductance channels (122pS; Na⁺-sulphate solution in bath, K⁺-sulphate solution in pipette) in cell-attached patches increased from 9/90 (10%) in controls (1 channel/patch) to 47/111 (42%) in K⁺-loaded rats (2-4 channels/patch). In excised inside-out patches, channels were highly selective for K⁺ over Na⁺ (> 200:1), and had a conductance of 212pS in symmetrical K⁺-sulphate solution. The K⁺ channels were blocked by 1mM quinidine, but gated independently changes in membrane voltage, pH, Ca²⁺ or ATP concentration in the cytosolic (bath) solution. These K⁺ channels differ from the 17pS Ca²⁺-sensitive K⁺ channels seen only in inside-out patches of the basolateral membrane of rat colonic crypt cells [2], and may constitute the K⁺ conductance which is induced in the apical membrane of surface colonicocytes during dietary K⁺ loading and Na⁺ depletion.


ROLE OF SSTR2 RECEPTORS IN THE ANTISECRETORY EFFECT OF SOMATOSTATIN IN RAT DISTAL COLON.
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Somatostatin peptides (SST) are potent inhibitors of epithelial fluid and electrolyte transport with considerable potential in the treatment of diarrhoeal disorders. The recent cloning of five somatostatin receptor subtypes (SSTR 1-5) with distinct pharmacological properties offers new possibilities for the development of more selective SST analogues. In this study we have used a group of receptor selective SST peptides to determine which SSTR subtype mediates the antisecretory actions of SST in rat colon in vitro.

Secretion induced by the calcium agonist, forskolin (FSK, 1μM) was measured as the increase (50.5±2.1 μm²/min; n=9) in short circuit current (Isc) across stripped sheets of distal colon mounted in Ussing chambers. At the peak of the secretory response varying concentrations of either somatostatin (SST-14), octreotide (OCT) or the receptor selective peptides, NC8/12 (SSTR2), DC25/20 (SSTR3), DC25/29 (SSTR5) were used, with various concentrations of FSK (0.1μM-10μM). The SSTR2 selective peptide NC8/12 inhibited colonic secretion with a potency (EC₅₀ 2.5nM) similar to SST-14 and the clinically active OCT. In contrast, the SSTR3 (DC25/20) and SSTR5 (DC25/99) selective peptides were relatively weak inhibitors of secretion (EC₅₀’s >100nM). These results suggest that the SSTR2 receptor subtype is the primary mediator of somatostatin's antisecretory actions.

INFLAMMATORY STIMULI Activate SECRETION of IL-8 AND GROa BUT NOT RANTES IN HUMAN COLONIC EPITHELIAL CELLS IN VITRO
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The α- and β- chemokines are powerful chemo-attractants for a variety of inflammatory cells. Recent evidence suggests that IL-8, an α-chemokine, released by intestinal epithelial cells may play a role in neutrophil infiltration of the mucosa, a characteristic of inflammatory bowel disease (IBD). However, little is known about expression of other chemokines by epithelial cells. In this study we have examined the effects of inflammatory cytokines and bacterial products on secretion of α- (IL-8, GROα) and β- (RANTES) chemokines in the functionally differentiated colonic cell line, HT29-cl.19A.

HT29-cl.19A cells were grown to confluence on plastic dishes in DMEM medium containing 10% FCS. Cultures were incubated for 1-24 hrs with TNFα, IL-1, lipopolysaccharide (LPS), lipoteichoic acid (LTA), or muramyl dipeptide (MDP) and the culture medium assayed for IL-8, GROα and RANTES by ELISA.

HT29-cl.19A cultures constitutively produced IL-8 (0.24±0.04 ng/ml) and GROα (0.09±0.02 ng/ml) but not RANTES. TNFα caused a dose dependent increase in IL-8 secretion (15.4±2.1 ng/ml with 2ng/ml TNF] which was accompanied by a parallel increase in GROα production (4.8±0.7 ng/ml). IL-1 also up-regulated secretion. The bacterial products, LPS, LTA and MDP (0.1-1.0 μg/ml) also increased secretion of both α-chemokines though to a lesser degree (2-4 fold). There was no evidence that any of the agents tested were able to activate RANTES production in HT29-cl.19A cells. Studies in the CaCo-2 cell line showed a similar pattern of chemokine expression.

These results suggest that colonic epithelial cells express multiple chemokines in response to inflammatory stimuli. Their precise role in mucosal recruitment of inflammatory cells in IBD remains to be elucidated.
**INTESTINAL EXPRESSION AND ACTIVITY OF NEUTRAL ENDOPEPTIDASE 24:11 IN MAN**

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Cells expressing the enzyme neutral endopeptidase 24:11 (NEP) degrade bacterial peptidic hides and this may be an important epithelial defence mechanism in the gut. We have, therefore, investigated the distribution of gastrointestinal neutral endopeptidase in man by immunohistochemistry and by measuring enzyme activity.

**Methods**

Tissue from stomach (S, n=6), duodenum (D, n=7), ileum (I, n=3) and colon (C, n=5) were cut in 5mm slices and fixed in 10% buffered formal saline. Immunohistochemistry was performed on 3-5um sections for neutral endopeptidase and preabsorbed antibody (IgG, Dr M Rentrop) to detect NEP activity. Slides were incubated with primary antibody at dilution of 1:400 for 60min, washed and exposed to secondary antibody (1:200) for 30min, washed and incubated with substrate and chromogen for 30min. Developed sections were counterstained with haematoxylin.

**Results**

The enzyme was expressed in the surface epithelium of small intestine (SI 0.19-1.02), in a layer of cells 5-10um thick in the duodenum and ileum (0.03-1.00), and in colonocytes (0.05-1.02). NEP activity was seen in the gut crypts (UC 0.03-0.90). Immunohistochemistry and enzyme activity results were highly correlated (r=0.95).

**Conclusion**

Expression of NEP may be important for the gut in protecting against bacterial degradation and for the gut to maintain physiological function.

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**BACTERIAL LIPOLYPSACCHARIDE STIMULATES INTERLEUKIN-6 SECRETION FROM COLONIC CELL LINES**

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Interleukin-6 (IL-6) is an important chemotactic and activating factor for neutrophils. Secretion on IL-8 by epithelial cells is probably a key factor in host defenses at mucosal sites, permitting a rapid polymorph response against infectious agents. The aims of this study were to examine the effects of lipopolysaccharide (LPS) on IL-6 secretion by two well differentiated colonic epithelial cell lines, HT29 and SW480. Cells were grown to confluence in multwell plates. Cells were stimulated with LPS (10pg/ml-10µg/ml) from Salmonella typhimurium, Ericheria coli and Helicobacter pylori in the presence or absence of fetal calf serum and polymyxin B (PB). After 24 hours the supernatants were removed and secreted IL-6 was assayed by ELISA. The experiments were repeated in triplicates. The two tables below summarises the mean IL-8 induction after subtraction of unstimulated control values:

<table>
<thead>
<tr>
<th>LPS Type</th>
<th>S. typhimurium</th>
<th>E. coli</th>
<th>H. pylori</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT29</td>
<td>+ S + S</td>
<td>+ S + S</td>
<td></td>
</tr>
<tr>
<td>SW480</td>
<td>+ PB + PB</td>
<td>+ PB + PB</td>
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</tr>
</tbody>
</table>

Thus, there was a particularly marked induction of IL-8 with E. coli LPS. This response was serum dependent and inhibitable with PB. H. pylori LPS induced IL-8 at high concentrations only, suggesting that LPS of this organism has no biological effect in the colon.

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**CORRELATION BETWEEN INTERLEUKIN-8 (IL8), INTERFERON GAMMA (IFN-γ), INTERLEUKIN-10 (IL10) mRNA LEVELS AND HISTOPATHOLOGICAL ACTIVITY IN INFLAMMATORY BOWEL DISEASE.**

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Both IL8 and IFN-γ may be important effector cytokines in active ulcerative colitis. IL8 mRNA is a product of TH1 T-cell response, whereas IL10 is a product of TH2 response. To determine whether there is a relation between the expression of these cytokines is related to severity of inflammation in active ulcerative colitis and whether there are differences from Crohn’s disease (CD), post-inflammatory diarrhea (PI), irritable bowel syndrome (IBS) and normal controls we related changes in mRNA levels in colonic mucosal biopsies using RT-PCR followed by chemiluminescent detection to histological grade of activity.

**Methods**

Total RNA was extracted from each biopsy and reverse transcribed. PCR amplification for IL8 and GAPDH were performed using 23 cycles, but for IL10 and IFN-γ, 33 cycles were necessary. The products were hybridised with specific oligo probes labelled with alkaline phosphatase, and quantified after addition of a chemiluminescent substrate emulated PPD (CD1). Active inflammation was quantified histologically on a 10 point scale using paired biopsy samples.

**Results**

Using the Mann-Whitney test, the median values for ratios of IL8, IL10 and IFN-γ to GAPDH RT-PCR products were compared in all the conditions. None of the patients had detectable IL8 or IFN-γ mRNA, but their activity was less than 0.05 when compared to normals. For both diseases there were good correlations with the histological score (r=0.51 for IL8 and IFN-γ; and r=0.05 for IFN-γ/GAPDH). However, IL10 mRNA levels were not significantly different for any group and did not correlate with activity.

**Conclusion**

Both IL8 and IFN-γ mRNA are raised in ulcerative colitis. They strongly correlate with inflammation. The range of IFN-γ mRNA in Crohn’s disease is wide and related to activity. Mucosal levels of IL10 mRNA, a TH2 T-cell response cytokine, were similar in all groups and were not related to activity.

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**DETECTION OF INSULINLIKE GROWTH FACTOR 1 (IGF-1) IN WHOLE GUT LAVAGE FLUID (WGLF): A NOVEL METHOD OF STUDYING INTESTINAL FIBROSIS.**

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IGF-1 is a potent mitogen for fibroblasts and smooth muscle cells and stimulates collagen synthesis. It is expressed in inflammatory infiltrates, macrophages and lymphocytes. Although there is evidence that IGF-1 may be important in the development of fibrosis in a rat model of granulomatous enterocolitis, little is known about its role in human inflammatory bowel diseases. Whole gut lavage with a PEG-electrolyte solution is essentially a gut perfusion system after the gut contents have been cleared. We have used this technique externally for measurement of gut derived plasma haemoglobin, cytokines and neutrophil migration in various immunoinflammatory diseases of the gut. We utilised this noninvasive method to explore the role of IGF-1 in whole characterised diseases of the gut. IGF-1 was measured in 84 WGLF specimens from: (a) 7 patients with normal GI tract, (b) 20 patients with Crohn’s disease (CD); (c) 12 patients with ulcerative colitis (UC); (d) 13 patients with radiation colitis; (e) 12 patients with miscellaneous GI diseases. Filtered WGLF specimens, processed by addition of protease inhibitors, were incubated with a releasing agent to inactive IGF binding proteins and diluted for quantitative determination of IGF-1 by a two-site immunometric assay (Octea IGF-1 EMA kit, IDS Ltd, Tynes & Wear). The lower limit of detection was 1 ng/L.

IGF-1 was undetectable in patients with normal GI tract. Eight out of 20 patients with CD had detectable IGF-1 ranging from 1.4µg/L to 158µg/L (median 2.5µg/L). IGF-1 was undetectable in UC and in 24 patients with inactive CD. Of the 8 CD patients with detectable IGF-1, 2 had ileal, 1 ileocolic and 5 colonic (3 with perianal involvement) disease. Only 1 out of 12 patients with UC had detectable IGF-1 (3.1 µg/L), this patient had undetectable UC at 12 years duration and was on cyclosporin and steroids with continuing active inflammation. Three out of 13 patients with radiation colitis had detectable IGF-1. One patient each with ischaemic colitis, severe diverticular disease, pouchitis, microscopic colitis, and colonic carcinoma had detectable IGF-1.

We conclude that detection of IGF-1 in WGLF may be a useful method of studying the role of growth factor peptides in intestinal diseases. IGF-1 is detectable in CD and other diseases well known to be associated with fibrosis. In contrast, it is infrequently detectable in UC.