The British Society of Gastroenterology

The 1988 Spring Meeting of the British Society of Gastroenterology was held at the University of Leicester under the presidency of Dr JJ Misiewicz. Below are printed abstracts of the 57 oral and 103 poster communications selected by the Programme Committee for presentation at the meeting.

ENDOSCOPY

T1

AIDS and endoscopes – evaluation of a new biopsy channel valve

J D HARRISON AND D I. MORRIS (Department of Surgery, Queen’s Medical Centre, Nottingham) AIDS is becoming an increasing problem in medical practice and although the spread of AIDS by a contaminated endoscope has not been reported, it is a possibility due to the presence of blood, gastric juice and saliva on the endoscope and within its channels. We have evaluated a new negative pressure chamber biopsy channel valve designed by one of the authors (DLM) to reduce the aerosol emission during insertion and removal of the biopsy forceps, thus protecting medical and nursing personnel. In order to compare the efficacy of the new valve with a standard Olympus valve, a balloon containing 10 ml 0.5% indigocarmine solution was secured over the end of an OES Q10 gastroscope such that its tip was always submerged in dye solution. The biopsy forceps were then passed through the centre of a 180 mm sheet of filter paper which was held in contact with the valve exit whilst the forceps were passed into and back out of the dye solution five times with each valve. The area of the dye on the paper was then measured in each case. The median (range) area in square millimetres for the standard valve was 4968 (7261–89175), whilst for the new suction valve the area was 5.4 (1.4–9.2); Mann Whitney U = 0.00, p = 0.012. We conclude that the new valve is a highly efficacious means of reducing emission of biological fluids from endoscopes.

T2

Controlled study of heater probe (HP) in bleeding peptic ulcers

G M FULLARTON, G G BIRNIE, A MACDONALD, AND W R MURRAY (University Department of Surgery, Western Infirmary, Glasgow and Department of Medicine, Gartnavel General Hospital, Glasgow) A prospective, randomised controlled trial of endoscopic HP therapy was performed over a 16 month period (August 1986–November 1987). Six hundred and thirty patients presenting with suspected upper GI haemorrhage were endoscoped within 24 hours of presentation. One hundred and seventy (27%) were found to have a peptic ulcer. One hundred and twenty seven had either minor or no stigmata of recent haemorrhage (SRH) at the time of endoscopy. Forty three patients had accessible single peptic ulcers with either active haemorrhage or major SRH and were entered into the trial. These patients were stratified for age (<60, >60), ulcer site (GU/DU) and shock (present/absent on admission) and were randomised to receive either HP therapy (n = 20) or sham treatment (n = 23). All patients received conventional medical management. HP and sham patients were well matched on entry to the study with regard to prognostic criteria. No rebleeding occurred in the HP treated group (0/20), while 5/23 (22%) of the sham treated group rebled (p = 0.05). None of the seven ulcers with visible vessels in the HP group rebled while three of four rebled in the sham group. Urgent surgery was required for three of five (60%) of the sham treated patients who rebled. No HP or sham patients died. These results suggest that the HP may be effective in reducing rebleeding rates in peptic ulcers accessible to endoscopic therapy.

T3

A one minute endoscopy room test for Campylobacter pylori

A S ARVIND, R S COOK, S TABAQCHALI, AND M J G FARTHING (Depts of Gastroenterology and Medical Microbiology, St Bartholomew’s Hospital, West Smithfield, London) The presence of urease in C pylori has been used as a diagnostic test for identifying these organisms in gastric mucosal biopsy specimens. Currently available urease tests can give a result within one hour, but a positive result may not be obtained for up to 24 hours. We have reduced the reaction time of this test by placing the biopsy in 1 ml unbuffered 10% urea in deionised water, pH 6.8 containing phenol red as a pH indicator. Antral mucosal biopsy specimens were obtained from 40 patients and results of the ‘one minute test’ were compared with microbiological culture, Gram stain and a standard urease test using Christensen’s urea broth. Microbiological culture identified C pylori in 21 (52%) of the 40 biopsies. In the one minute test, 19 of these 21 biopsies were positive and there were no false positives (sensitivity 91%, specificity 100%). The conventional urease test was less reliable, for although there were 20 positive biopsies, three were false positives; there were four false negatives (sensitivity 84%, specificity 86%). Gram stain detected 16 of the 21 positive biopsies and there were no false positives (sensitivity 81%, specificity 100%).

Thus the one minute test is able to detect more than 90% of C pylori positive patients with extreme rapidity, almost certainly because the reaction takes place in the absence of a buffer. The immediate availability of this result while the patient is still in the endoscopy room can facilitate clinical management.

COLORECTAL

T4

Fully automated computer analysis of intracolonic pressures

J ROGERS AND J J MISIEWICZ (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) A PC
compatible computerised system for analysis of colonic pressure activity has been developed and tested. The system acquires intraluminal pressure data from a polygraph during colonic motility studies and stores it on magnetic disk. Subsequent analysis by custom written software is fully automated for the following variables: mean amplitude (MA), % duration of activity (%DA), activity index (AI) (area under curve), motility index (MI) and number of pressure peaks for operator-specified epoch lengths. Analysis of an eight hour colonic pressure record was done manually and by the automated system for 48 10 minute epochs. Strict peak definition and analysis criteria were used. Time taken for manual analysis was 889 min v 14 min for automated. Values are expressed as mean (SD). Mean difference (bias) (2 SD ‘limits of agreement’): 95% CI for the bias; and [range of values by both methods] for each variable follow: MA (mmHg): -0.5 (36.8); -5.8 to 4.8; [0–289]. %DA: -0.9 (13.4); -2.9 to 0.9; [0–100]. AI (mmHg.min): 39.9; (127.7); 21.4 to 58.5; [0–2073]. MI (MA.%DA): -55 (2072); -356 to 245; [0–26220]. Number of peaks: –20 (91); –44 to 3.5; [1–211], 30 min epoch. Results by the two methods show good agreement for MA, %DA, MI and number of peaks. Agreement for area under curve had a large bias. Automated analysis of colonic pressure activity is fast and agrees well with labour intensive manual analysis.

T5 Oncogene expression and proliferation in colorectal neoplasia

N CARMITAGE, J WRIGHT, AND J D HARDCastle (Department of Surgery, University Hospital, Nottingham) The role of oncogenes in colorectal neoplasia is not clear although the expression of the oncogenes ras and myc, tends to be highest in adenomas and localised tumours.

The proportion of cells expressing the oncogenes was measured by flow cytometry in 16 cancers, a large adenoma and 29 normal samples taken at 5 cm intervals from the tumour in six specimens, using monoclonal antibodies specific for the oncogene products p21ras and p62myc. The proportion of proliferating cells was measured using Ki67 a monoclonal antibody recognising an antigen expressed by all proliferating cells.

Tumour expression of ras and myc was variable – median 16% (0–68%) for ras and 14% (0–69%) for myc. Expression of ras and myc correlated (Spearman coefficient, r = -0.69, p<0.01) as did expression of both oncogenes and the proportion of proliferating cells (r = ras: 0.57, myc: 0.53, p<0.05). Rectal tumours had higher expression of ras (median 53%) than right sided tumours (median 9%) (U = 4-5, p<0.04). Normal samples at intervals from the same specimen tended to express both oncogenes similarly (r; 0.57, p<0.01). Expression of ras and the proportion of proliferating cells correlated (r; 0.71, p<0.01).

Expression of both oncogenes, ras and myc, is correlated in tumour and normal tissue and is related to proliferative activity.

T6 Does blood transfusion affect recurrence in cancer of the colon and rectum?

J B EYNOY, P W DAVIES, P BILLINGS, J L CHANNER, H UMLEPBY, N J MC MORTENSEN, AND R C N WILLIAMSON (Department of Surgery, Bristol Royal Infirmary, Bristol) A retrospective study of 519 patients undergoing curative resection for colorectal and rectal cancer has been conducted. Recurrence was diagnosed in 214 patients (41.2%); 179 (34.5%) had been transfused and 35 (6.7%) had not. The incidence of recurrence was significantly higher in the transfused patients (p<0.001). After transfusion there was an increased risk of local recurrence (p<0.02) and distal (p<0.001) recurrence.

Exclusion of the right hemicolon tumours showed that 135 (33.9%) were transfused and 25 (6.3%) non-transfused patients developed recurrence (p<0.001). Recurrence in patients only transfused during surgery (n=201) was significantly higher (p<0.001). All patients transfused during surgery (n=297) had a significantly increased risk of recurrence (p<0.001). There was no increased recurrence observed in patients receiving pre (n=39) or postoperative (n=37) blood transfusion.

Additionally in patients with rectal cancer treated by abdominoperineal resection there was a significantly increased risk of recurrence (p=0.02) which was not observed in those patients treated by sphincter saving resection (p=0.2).

T8 Factors influencing motor function after restorative proctocolectomy

K YOSHOKA, W KMIOT, AND R B KEIGHLEY (The General Hospital, Birmingham) We have studied ileo pouch anal function in 24 patients after restorative proctocolectomy using a 4 lumen perfused catheter with side holes 2, 6, 12, and 20 cm from the anal verge for assessment of pressures, compliance and motility response to pouch distension. Saline infusion tests were also done. None of the patients had a rectoanal inhibitory reflex. The following abnormalities were observed: resting anal pressure <40 cm H2O; n=10, anal squeeze pressures <80 cm H2O; n=9, resting pouch pressures >anal pressures; n=3, basal ileal pressures >45 cm H2O; n=4, compliance >5 ml/cm2; n=5, pouch distension accompanied by high amplitude ileal pressures; n=8, first leakage of saline <300 cc; n=14, residual volume >500 cc after a 1 litre infusion; n=11. Seven patients with poor functional results had 34 abnormalities (4-8/patient) compared with 27 of the remaining 17 patients (1-6/patient) (p<0.02). Pelvic sepsis (n=7) was associ-
ated with a significantly higher number of abnormalities: 4/2/patient, compared with those without sepsis: (n=17), 1/8/patient (p<0.05). When pouch design was compared in patients who had no pelvic sepsis, abnormalities were recorded in 1/9/patient after J pouch (n=11) compared with 1/5/ patient after W pouch (n=6) (NS). These results suggest that pelvic sepsis rather than pouch design has a greater influence on physiological parameters associated with impaired functional results after restorative proctocolectomy.

T9    Diarrhoea in human immunodeficiency virus (HIV) antibody positive patients

G M CONNOLLY and B G GAZZARD (St Stephen's Hospital, London) Eighty consecutive HIV antibody patients with diarrhoea for more than a month had daily stool volumes, rectal biopsy, six stool cultures and colonoscopy, or barium enema. Most patients also had jejunal biopsy, Xylose test, Schilling test and barium meal and follow through. In all but 12 patients a potential infection was found which was an opportunist in 44 (cryptosporidium (30), Mycobacterium avium-intracellulare (11), cytomegalovirus (three)), and a non-opportunist in 24. Average stool volumes and degree of weight loss was significantly higher in those with opportunistic infections.

Neoplastic causes of diarrhoea were rare – Kaposi’s sarcoma (two), squamous carcinoma (two). In six patients in the whole series no potential cause for diarrhoea was found but these had electron microscopy evidence of HIV infection or preneoplastic changes on rectal biopsy. Although non-specific abnormalities of malabsorption tests, rectal and duodenal biopsy histology were common these were not of value diagnostically. Radiology and colonoscopy did not add to the diagnosis.

Treatment of cryptosporidium with macrolide antibiotics resulted in significant reduction of daily stool volumes. Mycobacterium Avium-intracellulare or entamoeba did not respond to treatment. Other infectious causes of diarrhoea often remitted spontaneously (50%) and only responded in 25% to specific antibiotic therapy.

T10    How useful are upper gastrointestinal biopsies in patients with Crohn’s disease?

B J Z DANESH, R H R PARK, R UPADHYAY, A HOWATSON, F LEE, AND R I RUSSELL (Gastroenterology and Pathology Department, Royal Infirmary, Glasgow) Histological confirmation is essential for the diagnosis of Crohn’s disease. The disease is patchy and can affect any part of the gastrointestinal tract and, therefore, may be inaccessible for biopsy. We have investigated the clinical value of doing routine upper GI endoscopies with biopsies in 48 patients with Crohn’s disease. Biopsies were considered to be positive for CD if there was focal inflammation with either crypt damage and/or granuloma. Fifteen patients (31%) had positive biopsies – 13 had granulomas (oesophageal one, gastric 11, and oesophageal, gastric and duodenal one). Endoscopic appearances in the positive group were normal (seven), oesophageal ulcers (one), gastric aphthoid-serpiginous ulcers (three), duodenal serpiginous ulcers/duodenitis (two), gastro-duodenal ulcers (two). Ten patients (66%) of the positive group had upper GI symptoms, and of these seven had abnormal endoscopies. Only 10 of the negative group (30%) were symptomatic. Three patients in the positive group, all of whom had disease affecting the terminal ileum and proximal colon, had normal rectal biopsies. Microscopic involvement of the upper GI tract is common in patients with CD (33%) and 17% have endoscopic abnormalities suggestive of CD. Upper GI biopsies can, therefore, provide histological diagnosis of CD when rectal biopsies are negative, thereby avoiding more invasive tests.

T11    Vindaloo and you

INGVAR BJARNASON, SASSOON LEVI, PAUL SMETHURST, IAN MENZIES, AND JONATHAN LEVI (MRC Clinical Research Centre, Harrow, Middlesex) Recent studies show that many apparently normal Asian subjects have higher permeation of poorly absorbed permeability probes (lactulose, 51CrEDTA) than normal caucasians but the cause is unknown. The aim of this study was to assess whether dietary factors are important in altering small intestinal function.

Ten caucasian volunteers ingested after an overnight fast a 100 ml solution containing 3-O-m-glucose (0.2 g), D-xylose (0.5 g), L-rhamnose (1.0 g) and 51CrEDTA (100 μCi) followed by a five hour urine collection to assess active and passive carrier mediated transport and trans- and paracellular permeability before and after Indian meals on three consecutive evenings. The ‘hotness’ of the feeds increased for each subject, from mild, medium to hot as judged by generally accepted criteria.

Baseline mean (SE) excretion was 49.1 (3.8)% 30.9 (2.2)% 15.2 (2.3)% and 0.50 (0.08)% respectively. Excretion following the feast was 63.4 (3.6)% 36.9 (1.8)% 22.4 (2.7)% and 0.83 (0.20)% all of which were significantly increased from baseline (p<0.05) 51CrEDTA/L-rhamnose excretion ratio (which reflect intestinal permeability) did not however change significantly [0.034 (0.004) v 0.036 (0.005) p<0.1].

We conclude that Indian food alters intestinal function significantly. The mechanism is uncertain but the data are consistent with suggestions that the effect is mediated by increased mucosal blood flow as a consequence of hyperaemia.

T12    How rapidly does the stomach empty oral rehydration solutions in acute cholera?

B J COLLINS, F P L VAN LOON, A MOLLA, AND N H ALAM (International Centre for Diarrhoeal Diseases Research, Bangladesh) No study has reported gastric emptying patterns in acute cholera and yet the use of oral rehydration solutions to maintain hydration during an acute attack of cholera has been strongly advocated. Gastric emptying of rice powder electrolyte solution (400 ml) and of glucose electrolyte solution (400 ml) was measured by a marker dye double sampling technique in 14 and in 16 adult patients respectively after intravenous rehydration during an acute attack of cholera. A repeat study was done with the same test meal 16 days later in six who received the rice based solution and in seven who received the glucose electrolyte solution. Gastric emptying of both solutions was very rapid in acute cholera, most patients emptying over half the test meal within 10 minutes of meal ingestion. Emptying rates were comparable with those seen in the recovered patients. Rice and glucose electrolyte solutions emptied at equivalent rates in acute cholera and in the recovered patients (Mann Whitney U test). This study indicates that gastric emptying is not impaired in acute cholera and provides further support for the promotion of oral rehydration therapy as an effective treatment in acute cholera.
Intraluminal calcium and colonic cancer: possible mechanisms of action

G V N Appleton, E E Wheeler, R W Owen, D N Challacombe, and R C N Williamson (University Department of Surgery, Bristol Royal Infirmary, Bristol and Somerset Children's Research Unit, Musgrove Park Hospital, Taunton, Somerset) Dietary supplementation with calcium reduces the incidence of colorectal tumours in rats and decreases intestinal cell turnover in man and animals. Sprague-Dawley rats (n=99) received either 80% mid-small-bowel resection or jejunal transection. Half the animals in each group had calcium lactate 24 g/l added to the drinking water. Seven weeks postoperative faeces were collected for estimation of free bile acid and free fatty acid levels. Colonic mucosa from controls was maintained in organ culture in three different concentrations of calcium, with subsequent stathmokinetic measurement of crypt cell production rate (CCPR). Calcium reduced faecal bile acid concentrations by 53-62% [1.76 (0.44) v 0.82 (0.23) mmol/l dry wt of faeces; p<0.001; 2.74 (0.24) v 1.03 (0.42); p<0.001], but calcium increased the faecal levels of both saturated and unsaturated fatty acids by 110-131% [3.09 (1.45) v 6.50 (2.47); p<0.001; 2.63 (0.93) v 6.07 (2.38); p<0.001]. Calcium soaps of bile salts were not detected. In organ culture calcium 2-4 mmol/l reduced colonic CCPR by 22-68% (4.80 v 1.56-2.75 cells/cret/h; p<0.0001-0.02). Intraluminal calcium has both direct and indirect antitrophic effects on large bowel mucosa. Calcium does not bind bile acids, but may lower colonic levels of these harmful compounds by binding fats.

Hyperglucogonaemia with necrolytic migratory erythema in coeliac disease: a 'pseudo-glucagonoma'

C P Kelly, C F Johnston, N Nolan, P W N Keeling, and D G Weir (Department of Clinical Medicine, Trinity College and St James Hospital Dublin, and Department of Medicine, Queen's University, Belfast) Necrolytic migratory erythema (NME) is the distinctive skin rash seen in the glucagonoma syndrome. Its presence is virtually pathognomonic of pancreatic neoplasia. Conversely, raising of plasma enteroglucagon, without NME, is well recognised in coeliac malabsorption. We have studied a patient with hyperglucogonaemia and NME complicating untreated coeliac disease. Our findings show that NME is not an exclusively paraneoplastic phenomenon but can result from excess production of enteroglucagon by the small intestinal mucosa.

The patient presented with severe diarrhoea. 15 kg weight loss and the rash of NME. Serum zinc was 5-6 mmol/l (11-17). Fasting plasma glucagon concentrations (by RIA) were: N-terminal (total) 1725 ng/l (0-250) and C-terminal (pancreatic) 250 ng/l (0-150). Skin and distal duodenal biopsies showed changes of NME and coeliac disease respectively. Immunofluorescence staining employing a primary antiserum to enteroglucagon (YY118) raised in our laboratory demonstrated numerous (19-6 cells per mm² of mucosa) enteroglucagon positive small intestinal crypt cells. All symptoms resolved on gluten free diet. Plasma glucagon returned to normal. Repeat duodenal biopsy confirmed histological improvement and a normal enteroglucagon staining pattern (0.2 cells/mm² mucosa).

There have been occasional reports of NME occurring in the absence of a pancreatic tumour but until now this phenomenon has been poorly characterised and authors have not differentiated between pancreatic and enteric sources of glucagon. This patient may represent an example of a syndrome of 'pseudo-glucagonoma' characterised by classical NME, diarrhoea and weight loss in association with excess circulating enteroglucagon. Pancreatic neoplasia and marked rise of pancreatic glucagon, hallmarks of the true glucagonoma syndrome, are absent.

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T16
Does the cessation of smoking predispose to ulcerative colitis by reducing colonic mucus production?

G F Cope, R V Healey, and J Kelleher (University Department of Medicine, St James's University Hospital, Leeds) Former smokers appear to be at a higher relative risk of developing ulcerative colitis than either 'never-smokers' or 'current smokers'. We have examined colonic mucus production in vitro by colonic biopsies during 24 hours of organ culture with [3H]glucosamine. The radiolabelled precursor is incorporated into newly synthesised mucus glycoproteins. Biopsies were obtained from patients attending for routine colonoscopy, who completed a detailed questionnaire regarding present and previous smoking habit. There were 82 patients with ulcerative colitis and 64 who had no evidence of inflammatory bowel disease, and were found to have a normal colonic mucosa.

Total colonic mucus production in 'controls' was highest in those who had never smoked (n=25, median 141 DPM/mg protein x 10⁴), lower, but not significantly so in 'current smokers' (n=21, 120 DPM/mg protein x 10³), and significantly lower in 'ex-smokers' (n=18, 116 DPM/mg protein x 10³)(p<0.05). In the colitic patients 'never smokers' had the
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lowest rate of incorporation (n=49, 86.2 DPM/mg protein × 10⁻³); which was increased in ‘ex-smokers’ (n=22, 105.7 DPM/mg protein × 10⁻³); and still further in ‘current smokers’ (n=11, 112.8 DPM/mg protein × 10⁻³).

This study indicates that cessation of smoking disrupts the capacity of the normal colon for mucus production, and may be one factor which reduces the colonic mucosal defence resulting in the onset of ulcerative colitis in susceptible individuals.

T17 Failure to record and recognise growth retardation in children with inflammatory bowel disease

J R BARTON AND A FERGUSON (Gastrointestinal Unit, University of Edinburgh and Western General Hospital, Crewe Road, Edinburgh) As part of an epidemiological and clinical study of Scottish children with Crohn’s disease or ulcerative colitis, hospital case notes of a representative sample of 105 patients aged ≤16 years at disease onset have been examined. To investigate relationships between disease severity, treatment and growth, information on height, weight, bone age and sexual development was collected. Mean follow up was 7.2 years; however, parameters of growth had been very poorly documented. Height was never recorded in 36 children and once only in 21. Bone age had been assessed in only 19 children; sexual maturations were described in 29. Documentation of weight was better, with a median of five measurements per patient. Nevertheless in nine children weight had never been recorded.

From the information available, around the time of diagnosis of Crohn’s disease only four of 42 children were above the 50th centile for height and five of 57 above the 50th centile for weight. In contrast, height and weight distribution in children presenting with ulcerative colitis were normal. Many young patients with IBD attend adult medical or surgical clinics. Surgeons and gastroenterologists should recognise the importance of regularly recording simple anthropometric data so that retardation of growth and sexual development in teenagers may be recognised and treated.

T18 Crohn’s disease in the city of Derby 1951–1985

I W FELLOWS AND G K T HOLMES (Derbyshire Royal Infirmary, Derby) Most recent surveys of Crohn’s disease in the UK have been carried out in coastal areas. This study shows the epidemiology of Crohn’s disease in an inland British city. Cases were sought from records held by Hospital Activities Analysis, the Department of Histopathology and consultants. The case notes of all patients were reviewed. The diagnosis was established on clinical, radiological and histological grounds. The population of Derby varied from 196,256 in 1951 to 215,300 in 1985. The duration from onset of symptoms to diagnosis did not differ significantly during the study. Two hundred and twenty three persons developed Crohn’s disease between 1951 and 1985. The mean incidence over successive quinquennia increased progressively from 0.71/10⁵/year (1951–55) to 6.67/10⁵/year (1981–85). From 1981–85 the highest age-specific incidence was 14.62/10⁵/year in patients aged 70–79 years. Between 1978 and 1985 there was no significant difference in the incidence of Crohn’s disease in West Indians or Asians compared with the rest of the population. At the end of 1985, the prevalence of Crohn’s disease in Derby was 85.93/10⁵.

This study shows a marked increase in the incidence of Crohn’s disease, similar to that observed in coastal areas. There is no evidence of genetic resistance to the disease in West Indians or Asians.

T19 A randomised comparison between the J or W pouch for restorative proctocolectomy

M R B KEIGHLEY AND W KMIOT (The General Hospital, Birmingham) Superior results have been claimed using a W pouch compared with the J or S pouch in restorative proctocolectomy, but changes in design of the pouch have coincided with increased experience of the operation and lower sepsis rates. We have designed a randomised controlled trial to compare a stapled J pouch against a sutured W pouch. All ileocolan anastomoses were sutured excising the anal transition zone and operations done by one individual. So far 26 patients have been entered and followed up for a median of 20 months (4–44): J pouch (n=13), W pouch (n=13). The groups did not differ for age, diagnosis covering ileostomy or follow up. Previous colectomy had been performed in eight patients having a J compared with only five having the W pouch. Operating time was significantly less for patients having the J (190 minutes range: 170–240) compared with the W pouch (230 minutes range: 194–290). Complications and functional results were similar, median frequency of defecation during 24 h was five for the J compared with five for the W pouch but fewer patients needed anti-diarrhoeal agents following the W pouch. Physiological studies failed to show impaired compliance in J compared with W pouch. So far the longer operating time needed for construction of the W pouch is not associated with superior clinical results.

T20 Results of anal sphincter repair in Crohn’s disease

A D SCOTT, P R HAWLEY, AND R K S PHILLIPS (St Mark’s Hospital, City Road, London) Surgical repair of the anal sphincter after injury gives good functional results. Patients with anorectal Crohn’s disease may require surgery for abscess or fistula and hence are particularly prone to operative sphincter injury, but may be denied sphincter repair because of fear of fistula formation or poor wound healing.

We have reviewed the case records of the seven patients at St Mark’s Hospital with Crohn’s disease who have undergone sphincter repair (six women, one man; mean age 30 years; range 12–40) after previous operative (86%) or obstetric (14%) injury. Of these patients, six also had intestinal Crohn’s disease (three ileocolic, two colonic, and one ileal) requiring operation at some time (three right hemicolectomy, three total colectomy). A defunctioning proximal stoma (three ileostomy, three colostomy) was present at the time of sphincter repair in six patients (86%). Postoperatively five patients were continent of solid and liquid stool, one patient was intermittent of liquid stool and required permanent colostomy, and one patient returned home overseas and was lost to follow up.

We therefore conclude that anorectal Crohn’s disease is not a contraindication to surgical repair of the external sphincter.

T21 Olsalazine versus sulphasalazine (SASP) in first attacks of ulcerative colitis (UC): a double blind study

S S C RAO, C D HOLDSWORTH, K P PALMER, P A CANN, S A DUNDAS, AND C L CORBETT (Royal Hullandshire Hospital, Sheffield, Western General Hospital, Edinburgh, and District General Hospital, Worksop, Nottingham) We have compared Olsalazine (2 g/day) and
SASP (3 g/day) in a double blind double dummy trial in 37 patients presenting with first attacks of distal UC. Sigmoideoscopic appearances, rectal biopsies, and symptom and stool diary records were used to assess benefit and adverse effects on entry and at four weeks. The groups were well matched for age and sex distribution. Both groups showed a similar reduction in stool frequency (p<0.01). The percentage of unformed stools was also significantly reduced, but to a lesser extent in the Olsalazine group (78% v 55%, p<0.001) compared with the SASP group (72% v 29%, p<0.001). In contrast, the proportion of stools containing blood was reduced to a significantly greater extent in the Olsalazine group (62% v 21%, p<0.001) than in the SASP group (66% v 38%, p<0.001). Sigmoideoscopic appearances and histological grading of rectal biopsy specimens improved significantly and to a similar extent in both groups. Intolerance was encountered in two on Olsalazine (one diarrhoea, one headache) and four on SASP (two dyspepsia, one diarrhoea, one myalgia). Thus, oral Olsalazine was at least as effective as SASP in treating new patients with mild or moderately active distal UC. The significantly greater reduction in the proportion of bloody stools (p<0.001) together with better tolerance would favour the choice of Olsalazine.

**T22**

**Alkaline intra-oesophageal pH in peptic oesophagitis: is it really caused by gastro-oesophageal reflux?**

R Penagin, H Yuen, and J J Misiewicz (Dept of Gastroenterology, Central Middlesex Hospital, London, and Cattedra di Patologia Medica III, University of Milan, Italy) Alkaline intraoesophageal (IO) pH has been suggested as marker of reflux of alkaline duodenal secretions into the oesophagus. Salivary pH, however, can be alkaline as well. To solve the problem, IO and intragastric (IG) pH have been measured simultaneously for 22 h in seven patients with peptic oesophagitis (PO), eight patients with a peptic oesophageal stricture (POS) and seven patients with peptic oesophagitis and a previous Billroth II partial gastrectomy (BII). An alkaline gastro-oesophageal reflux episode was considered to occur only if a rise in IO pH above 7 was observed during a rise (pH>7) in IG pH. Non parametric tests for multiple comparisons (Kruskal-Wallis followed by Sachs test) have been used for statistical analysis. Values are expressed as mean (SE).

Per cent time IO pH<4 was 12.0 (6.5), 14.3 (2.6), and 5.7 (3.0) in PO, POS, and BII respectively (p=ns). IO pH was alkaline for variable time in the three groups (% time IO pH>7: 16.9 (4.8), 27.5 (7.6), 21.0 (7.7) in PO, POS, and BII respectively, p=ns), but alkaline reflux episodes never occurred in any patient. Intragastric pH>7 was never recorded in PO and POS. Per cent time IG pH>7 was 10.3 (5.3) in BII (p<0.01 in comparison with PO and POS), however episodes of alkalinisation of IO pH were never observed during alkalinisation of IG pH.

In conclusion, alkaline intra-oesophageal pH is unlikely to be because of gastro-oesophageal reflux, even in patients prone to alkalinisation of intragastric pH (BII). It is probably consequence of swallowed fluids.

**T23**

**Patterns of acid exposure in reflux oesophagitis**

I R Jenkinson, T J Norris, and A Watson (Royal Lancaster Infirmary, Lancaster) Nocturnal acid exposure is generally considered to be more relevant to the pathogenesis of reflux oesophagitis because of impairment of normal protective mechanisms. Studies evaluating daytime and nocturnal exposure in isolation have challenged this concept but produced conflicting results. This study was undertaken to investigate the combination of daytime and nocturnal exposure in the pathogenesis of reflux oesophagitis.

Sixty two patients with symptomatic gastro-oesophageal reflux underwent endoscopy, manometry and 24 h ambulatory pH monitoring. Oesophagitis was present in 54 patients, the remaining eight patients having abnormal acid exposure (refluxers). Twenty eight of 32 patients with mild disease (refluxers or grade I oesophagitis) had greater daytime than nocturnal exposure (median % total time pH<4: day=9.7; night=6.0; p<0.001). In contrast, 11/15 patients with severe disease (grades III and IV oesophagitis) had greater nocturnal than daytime exposure (median % total time pH<4: day=26.4; night=35.3; p<0.05). Patients with intermediate disease (grade II oesophagitis) were distributed between the two patterns (p=NS).

This study confirms that daytime and nocturnal acid exposure are increased in patients with gastro-oesophageal reflux. It has, however, shown that mild disease is associated with proportionately greater daytime reflux and severe disease with prolonged nocturnal acid exposure.

**T24**

**Computed tomography in the pretreatment evaluation of oesophageal cancer**

St J Kirk, R A J Spence, R J Moorehead, E McIlrath, and J P R Gibbons (Royal Victoria Hospital, Belfast and Belfast City Hospital, Belfast) Computed tomography (CT) was prospectively carried out on 36 patients with oesophageal carcinoma (adenocarcinoma 25, squamous cell carcinoma eight, anaplastic carcinoma two, melanoma one). The aim of this study was to determine the value of CT scanning as an adjunct to traditional investigative procedures in carcinoma of the oesophagus. An oesophageal protocol was established, the scanning and reporting being done by three consultant radiologists. On the basis of the scan results an opinion was expressed regarding operability.

Computed tomography correctly identified seven of the 12 patients with invasion either periesophageal or perigastric, and 23 of the 24 patients without invasion (accuracy 83%). Computed tomography was accurate in staging nodes in 13 of the 24 patients with node involvement (accuracy 54%). 12 patients had negative nodes. CT had predicted that this would be the case in 23 patients (accuracy 52%). Computed tomography correctly identified metastatic disease in two of four patients and excluded accurately metastatic disease in 34 of 34 patients (accuracy 95%).

In summary, our study shows that CT scanning may be useful in assessing the operability of oesophageal carcinoma, but does not give an accurate assessment of nodal involvement preoperatively, and is therefore not a preoperative indicator of prognosis or survival.

**T25**

**Campylobacter pylori and history of dyspepsia in healthy blood donors**

J I Wyatt, B J Rathbone, R V Heatley, and M S Losowsky (Departments of Pathology and Medicine, St James's University Hospital, Leeds) Chronic gastritis is a common condition in the general population, although its significance as a cause of dyspeptic symptoms is unclear. Chronic gastritis is very strongly associated with...
Campylobacter pylori (CP), which can be detected serologically by a specific ELISA technique. We have investigated the prevalence of CP in a healthy blood donor population, 247 of whom completed a questionnaire concerning consultations and investigations for dyspepsia, antacid and alcohol consumption, smoking, and family history of dyspepsia.

Seventy four of 247 (30%) donors who completed the questionnaire were CP+ve. The prevalence of CP increased from 19% in the under 30's to 51% of donors over 50. 13.5% CP+ve and 17% CP--ve donors had had a peptic ulcer. Consultations and investigations for dyspepsia, family history of dyspepsia and antacid ingestion also increased with age; after correcting for age only investigation for dyspepsia in the >40's was significantly associated with CP. Campylobacter pylori showed no association with smoking, drinking, or blood group. 47 (64%) CP+ve and 136 (78%) CP--ve donors gave no history of clinically significant dyspepsia.

We conclude that the majority of CP+ve subjects have never had clinically important dyspeptic symptoms.

T26
Campylobacter pylori gastritis in children – a common cause of symptoms?

J Thomas, E J Eastham, T S J Elliott, C M Dobson, and D M Jones (University of Newcastle upon Tyne and Public Health Laboratory, Manchester) The aim of this study was to assess the incidence of Campylobacter pylori antibody in a paediatric population and relate this to symptoms, and the presence of gastritis. Three groups were studied. Group I – 51 consecutive symptomatic patients (5–16 years) undergoing upper GI endoscopy. Group II – 51 aged matched hospital controls with no significant GI symptoms. Group III – 150 well schoolchildren. Specific serum IgG antibodies were measured using a sensitive ELISA technique. Antral biopsies were cultured from all patients in Group I and examined histologically. Twenty per cent of patients in Group I had significant titres and in all cases >1:1600. C pylori was present on the gastric mucosa in all of this subgroup and in no other, and histological gastritis was present in all but two cases. In contrast only 4% of Group II and 5% of Group III had significant antibody titres and in all cases <1:1600.

We conclude that a high specific IgG titre to C pylori indicates active gastritis and that a significant proportion of children with upper GI symptoms have such an association. Unlike adults, few normal children appear to have been exposed to this organism.

T27
Reduced hydrophobicity of gastric mucosa in duodenal ulcer

R Spychal, J Marrero, S Saverymuttu, C Corbishley, and T C Northfield (Department of Medicine, St George’s Hospital Medical School, London) In 1910 Schwarz suggested that peptic ulcer results from an imbalance between autodigestion by gastric juice and mucosal resistance. Animal work has revealed that gastric mucosa is very hydrophobic, repelling aqueous solutions including acid. We therefore applied this approach for the first time to human endoscopic gastric biopsies, using a goniometer to measure contact angles of liquid droplets at the air/liquid/biopsy interface. We studied three groups of subjects: (I) duodenal ulcer (DU, n=18); (II) normal controls with endoscopically and histologically normal gastric mucosa (n=22); and (III) disease controls without DU but with histological gastritis of similar grade to I (n=20). Intra and interobserver variation was <5% for contact angle. Contact angles in DU [mean (SE); 55.8 (0.8)] were less than in healthy controls [70.8 (1.1), p<0.001] and disease controls [64.8 (1.0)° p<0.001]. Repeat measurements after DU healing with H2 blockers showed no change [n=9, 54.8 (1.1)° v 54.2 (1.3)°]. We conclude that surface hydrophobicity of gastric mucosa is reduced in DU. This reduction is greater than can be accounted for by gastritis alone, and is unaffected by DU healing, suggesting an underlying mucosal defect.

T28
Prednisolone fails to delay granulocyte migration to inflamed bowel in inflammatory bowel disease (IBD) in vivo

S H Saverymuttu, V S Chadwick, and H J F Hodgson (St George’s Hospital, London and Hammersmith Hospital, London) We have investigated whether steroids affects granulocyte function in vivo by a new technique for assessing the early stages of granulocyte migration to inflamed bowel using dynamic gamma camera imaging after injection of 111 Indium granulocytes, with computer analysis of regions of interest. A measured and a calculated migration delay are obtained. Twenty four patients with active IBD were studied either before, on maintenance, or within 48 h of commencing steroids and were restudied after 10 days therapy. At initial study all patients showed rapid migration of granulocytes to inflamed bowel with a measured maximal migration delay of five minutes, and a calculated delay consistent with no delay in 21/24 (88%). After 10 days therapy 13 patients had sufficient activity to allow measurement of migration delay and in all cases was less than five minutes with no significant change in calculated delay. These studies show that therapeutic doses of corticosteroids do not influence the early stages of granulocyte migration in IBD.

T29
Distinction between Crohns colitis and ulcerative colitis by 111Indium granulocyte scanning

S H Saverymuttu, V S Chadwick, A E A Joseph, T C Northfield, J D Maxwell, and H J F Hodgson (Department of Medicine, Royal Postgraduate Medical School and Department of Medicine II, St George’s Hospital Medical School, London) Studies have suggested that 111Indium white cell scanning may be superior to radiology in the assessment of disease extent and activity in inflammatory bowel disease. One area of assessment where radiology plays an important role is the distinction between ulcerative colitis and Crohns colitis. We have prospectively examined the usefulness of 111Indium granulocyte scanning in the differential diagnosis of 84 patients with active colitis (36 Crohns colitis, 39 ulcerative colitis, nine indeterminate colitis). Five patterns of scanning were used to diagnose Crohns (ileo) colitis – skip lesions, predominantly right sided colonic activity, rectal sparing, perianal disease, and ileal disease. Ulcerative colitis was diagnosed by the absence of these features and presence of continuous involvement of activity from the rectum. On the basis of these criteria 31 of 36 (86%) of Crohns (ileo) colitis and 35 of 39 (90%) ulcerative colitis were correctly diagnosed. Six of the nine patients with indeterminate colitis had a pattern suggestive of Crohns disease. 111Indium granulocyte scanning can distinguish between Crohns colitis and ulcerative colitis with an accuracy comparable with that reported for radiology and should be used in the differential diagnosis of colitis.
T30

How good are clinical, laboratory, and scan assessments for monitoring inflammatory activity in Crohn's disease?

S H SAVRUMUTT, V S CHADWICK, AND H J F HODGSON (St George's Hospital, London and Hammersmith Hospital, London) Accurate assessment of gut inflammation is essential for monitoring therapeutic trials in Crohn's disease. Faecal 111 Indium granulocyte excretion (FE) provides a precise assessment of gut inflammation but is only available in a few academic centres. To determine the value of more widely available assessments we have compared the Crohn's Disease Activity Index (CDAI), with laboratory assessments (ESR, C-reactive protein [CRP], albumin) and 111 Indium granulocyte scans with FE measurements in 78 serial studies in Crohn's disease. The assessments were compared for their ability to assess remission (FE<5%) and significant changes in gut inflammation (changes in FE>5%). For assessing remission scanning was most accurate (90%) followed by CRP (79%), ESR (73%) CDAI (71%), albumin (65%). For assessing changes in disease activity scanning was again the most accurate (73%) followed by ESR (67%), CDAI (66%), CRP (62%), albumin (60%). These studies show that conventional assessments are associated with a substantial error rate both for assessing remission and significant changes in gut inflammation in serial studies.

T31

Standard blood tests as a guide to rational ordering of the small bowel enema

I A EYE-BROOK, K ROGERS (INTRODUCED BY PROFESSOR A G JOHNSON) (Department of Surgery, Northern General Hospital, Sheffield) Because only 16% of small bowel enemas (SBE) in this hospital show evidence of small bowel Crohn's disease (SBC) we have reviewed the notes of 97 patients with SBC seen since 1978 to seek guidelines for more restrictive policy of SBE ordering. Of 97 patients, 93 (96%) had abnormalities demonstrated on full blood count (FBC), erythrocyte sedimentation rate (ESR), serum albumin or plain abdominal radiograph. No abnormality was shown in four patients but in three of them with a palpable abdominal mass an FBC was the only test done. The fourth patient had all the tests normal but his serum vitamin B12 level was low. Abnormalities included low haemoglobin (68%), low mean cell volume (39%), low mean cell haemoglobin (47%), raised platelet count (48%), raised white cell count (26%), raised ESR (76%), low serum albumin (61%), and small bowel distension on plain abdominal radiograph in 18 patients.

Barium enemas were done in 55 patients. Free ileal reflux was achieved in 37 barium enemas and SBC was identified in all these cases. We conclude that SBE can be avoided when FBC, ESR, serum albumin, serum vitamin B12 and plain abdominal radiograph are all normal, particularly when a barium enema has displayed a normal terminal ileum. Such a policy would reduce SBE ordering in this hospital by 50%.

T32

Prognosis for patients presenting with proctosigmoiditis (PS)

D E LONG, I D JUBY, M F DIXON, AND A T R AXON (Gastroenterology Unit, and University Department of Pathology, The General Infirmary, Leeds) The outcome for patients presenting with PS varies between a benign clinical course with no further attacks and major surgery. This study identifies features of the presenting attack which may indicate the future course of disease. One hundred and one patients with PS were referred between 1975 and 1985. Sixty have been followed up for at least five years or have required surgery, and have been classified as follows: group A—asymptomatic after presenting attack (n=14), group B—symptoms after presenting attack for <10% of follow-up (n=25), group C—symptoms for >10% of follow-up (n=11), group D—surgical intervention (n=10). Data on sex, age, length of history, disease extent, length of first attack, and therapy were analysed. There was no significant difference in the length of history; approximately half the patients in each group presented with disease confined to the rectum. The mean ages in the study groups A-D were 40, 45, 30, and 24 years respectively. The ages of groups A and B were not significantly different, but differed from group C (p<0.05) and from group D (p<0.05). The length of the first attack was significantly shorter (p<0.01) in groups A and B (2.5 and 2.6 months respectively) than in groups C and D (7.3 and 7.0 months respectively). Thus age at presentation and the length of the first attack are helpful prognostic indicators in PS.

T33

Dysplasia in ulcerative colitis – an assessment of Riddell's classification

D M THOMAS AND M ISAREL FILIPE (Queen Mary's University Hospital, Roehampton, London and UMDS (Guy's Campus), London) Of 374 patients with longstanding, extensive ulcerative colitis who underwent colectomy and ileorectal anastomosis between 1952 and 1976, 104 presented for regular follow up rectal biopsies over a five year period to 1986. These patients have been followed for an average of 28 years since the onset of the disease (range 11–56 years) and provide a unique model for the study of the development of carcinoma in ulcerative colitis. Four hundred and forty three biopsies have been examined and epithelial morphology assessed according to the classification of Riddell et al (1983). Five patients developed carcinoma during the period of study of whom only two showed dysplasia in biopsies taken a year or more before the diagnosis. Of the remaining three patients, one showed dysplasia in the resected specimen while in two patients carcinoma arose in the absence of dysplasia. Of 20 biopsies designated 'indefinite for dysplasia, probably negative', 80% were associated with subsequent resolution while of nine 'indefinite probably positive' biopsies, 66% were subsequently associated with carcinoma.

The results emphasise the danger of absolute reliance upon dysplasia in assessing individual cancer risk in longstanding ulcerative colitis and appear to demonstrate the validity of Riddell's classification.

T34

Chromosome damage in human lymphocytes in vitro: the effect of sulphasalazine and its sulphapyridine metabolites

J M MACKAY, D P FOX, P W BRUNT, G M HAWKSWORTH, AND J E BROWN (Department of Genetics, Medicine, and Pharmacology, University of Aberdeen, Aberdeen) Sulphasalazine remains the treatment of choice for the longterm management of colonic inflammatory bowel disease (IBD). We have previously shown that IBD patients receiving sulphasalazine therapy have raised concentrations of sister-chromatid exchange (SCE) and micronuclei (MN) in their circulating blood lymphocytes compared to age and sex matched healthy controls. This indicates that these patients have a raised level of DNA damage and we have shown that this level is directly related to sulphasalazine dose, the length of time on sulphasalazine and acetylator phenotype status. In extensive in vitro experiments we have now shown unequivocally that sulphasalazine itself is capable of inducing SCE...
and MN in human lymphocytes and that sulphasalazine and its acetylated metabolites can induce SCE, 5-aminosalicylic acid, the therapeutic moieties of sulphasalazine, and its acetylated metabolite did not induce either SCE or MN at the concentrations tested. These results agree well with our previous observations in IBD patients and clearly show that sulphasalazine therapy causes genetic damage in man. This adds impetus to the evaluation of 5-aminosalicylic acid analogues as an alternative to sulphasalazine therapy in IBD.

Supported by the Scottish Hospital Endowments Research Trust grant HE/RT 657.

T35
Blood transfusion – primary therapy for inflammatory bowel disease?

R H R PARK and R I RUSSELL (Gastroenterology Unit, Royal Infirmary, Glasgow)

Blood transfusion therapy has been shown to alter the clinical response in certain clinical conditions, notably renal transplantation, possibly by an effect on the immune system. It is unclear whether a similar mechanism occurs in patients with active inflammatory bowel disease (IBD). We analysed all the clinical details of patients with active IBD requiring inpatient treatment over the past seven years. Eighty seven patients (25 with Crohn’s disease [CD], 35 with ulcerative colitis [UC]), were admitted over this period of time. Twenty patients (11 with CD, nine with UC) required blood transfusion (group I). The patients in group I were matched for age, duration of illness, disease extent and severity, and treatment during the admission with the other patients not requiring a blood transfusion (group II). On follow up there were no significant differences (group I v II) in the duration of treatment and the duration of disease remission.

In conclusion, it is common for patients with active IBD to require a blood transfusion (23%). Blood transfusion therapy does not appear to have a primary role in altering the disease activity in active IBD.

T36
Enterovesical fistulae in Crohn’s disease

N S AMBROSE, P W DYKES, R N ALLAN, F HHEYEN, J ALEXANDER-WILLIAMS, AND M R E KEIGHLEY (The General Hospital, Birmingham)

Although urinary symptoms in Crohn’s disease are common (21%), urinary fistulae are rare. Fifteen enterovesical fistulae have been treated in a series of 785 patients (0.019%) seen between 1947 and 1986. Only five presented with pneumaturia, one with haematuria, and one with recurrent cystitis, the rest were diagnosed by contrast study or at laparotomy, one was associated with a carcinoma of the rectum. Thirteen were men (86%) and ages ranged from 16–65 years. Six developed spontaneously from a segment of intestinal Crohn’s disease. Four arose in previously bypassed or defunctioned bowel. Four occurred after resection. Seven were ileovesical, three colovesical, and four were complicated ileocolo-vesical fistulae and one was rectovesical. Ten fistulae have been resected and one has recurred. Two healed spontaneously (one on steroids, one postoperatively). Three fistulae were managed conservatively (1954, 1954, 1958) but all three have died from septicemia. In view of the risk of fatal septicaemia in untreated patients we believe that surgical treatment should be offered to all patients with enterovesical fistulae complicating Crohn’s disease.

OESOPHAGO/GASTRO/DUODENAL POSTERS I
T37–57

T37
Plasma gastrin, secretin, and somatostatin responses to cephalic stimulation and a meal in health and duodenal ulcer disease

CA ERIKSEN, K D BUCHANAN, AND A CUSCHIERI (Department of Surgery, Ninewells Hospital, Dundee and Department of Medicine, Queen’s University, Belfast)

Vagal release of gastrin is inhibited by somatostatin and, via duodenal acidification, by secretin. This inhibition is considered defective in duodenal ulcer (DU) patients. We studied 20 healthy subjects and 22 patients with active DU. Fasting plasma gastrin (GAS), secretin (SEC) and somatostatin (SMS) concentrations and responses to cephalic stimulation (MSF) and a meal were measured.

The fasting GAS of DU was significantly higher than controls (medians: 55.0–20.0 ng/l, p<0.01) and showed definite bimodal distribution. Hypergastrinaemic DU (H⁺G, n=11) and normogastrinaemic DU (N⁺G, n=11) exhibited median fasting GAS 70.0 and 30.0 ng/l respectively. Only H⁺G showed a significant rise in GAS after MSF (median peak 90.0 ng/l, p<0.02). All three groups experienced significantly raised GAS after the meal (p<0.001). The SEC responses were small and similar for H⁺G, N⁺G and controls. N⁺G showed significant higher fasting SMS (median: 17.0 ng/l, H⁺G 15.0, p<0.05), controls 10.0, p<0.01) and stronger MSF and meal responses. Postprandial SMS was persistently raised in N⁺G.

Duodenal ulcer patients exhibit significantly higher GAS than controls and two populations of DU exist. H⁺G show vagal hyperactivity and defective SMS-induced inhibition of GAS release. The physiological role of secretin in inhibiting gastrin is doubtful.

T38
Serum antibody titres before and after therapy in patients with campylobacter associated gastritis

D VAIRA, J H HOLT, M FALIZON, N I MCNEIL, S R CAIRNS, J F DOWSETT, A POLYDOXOUS, AND P R SALMON (Departments of Gastroenterology, Microbiology and Histopathology, The Middlesex Hospital, London) One hundred and ninety four gastric and duodenal biopsies were taken from 66 dyspeptic patients. Campylobacter pylori (CP) was assessed, before and after therapy, by histology, culture, CP-TEST and serum antibody measurement. All biopsies showing gastritis had CP, which was never seen overlying histologically normal mucosa. CP-TEST and culture compared with histology had a sensitivity 94% and 74% respectively, specificity 100%. Clearance of bacteria was associated with histological improvement of gastritis. Significantly higher IgG and IgA titres were found in CP positive than negative patients (p<0.001, p<0.001 respectively). Forty per cent of patients with macroscopically normal mucosa had both gastritis and CP found on histology as well as significantly higher IgG and IgA anti-CP titres than CP negative with normal mucosa (p<0.001, p<0.001 respectively). Colloidal bismuth subnitrate cleared CP in 68% of patients and significantly lowered IgG and IgA anti-CP concentrations (p<0.001, p<0.001 respectively) whereas ranitidine or metronidazole failed to clear CP or lower antibody titres.

These findings show that increased concentrations of IgG and IgA antibodies to CP provide evidence of active CP infection. Anti-CP antibodies are useful in determining the response to treatment and detecting relapse.

T39
Failure of endogenous PGE secretion in duodenal ulcer

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Explants from corpus and antrum, stripped in vivo, remained viable for approximately 10 hours as assessed by light microscopy and autoradiography. Correction for adsorption was made by comparison with dead tissue controls. Incorporation of H-glucosamine into the acid-precipitable fraction was linear for eight hours. This effect was significantly enhanced between two and three hours after the in vitro addition of PGE, 10^{-4} (12.3 (0.9) v 8.7 (1.1) dpm/mg protein x 10^{-3}, p<0.05) but not by forskolin 10^{-5}, a non-receptor mediated activator of adenylate cyclase. In the presence of IBMX (0.5 mm), both agents caused a greater than 10-fold rise in tissue cAMP levels but the stimulatory effect of PGE on mucus synthesis was not further enhanced.

These data show that PGE stimulates gastric mucus synthesis in vitro. The precise mechanism, however, is unclear but may be independent of tissue cAMP production.

**T42 Is suppression of nocturnal acid important for the healing of duodenal ulcers?**

M ROGERS, J HOLMFIELD, J PRIMROSE, T GLEDHILL, AND D JOHNSTON (University Department of Surgery, The General Infirmary, Leeds) Since its reintroduction by Dragstedt in 1943, vagotomy has been widely recognised to heal duodenal ulcers (DU's) by reduction of acid secretion. Suppression of nocturnal acid is thought to be particularly important.

We have compared the effects of highly selective vagotomy (HSV) and ranitidine (RAN) using ambulatory intragastric pH (IGPH) monitoring. Sixteen patients had their 24 h IGPH recorded 1> when taking RAN 300 mg at 10 pm, 2> when taking placebo (PL), and 3> four to 13 weeks after elective HSV for DU. Diet and cigarette consumption were identical on each occasion.

Median (quartiles) 24 h IGPH was 2.1 (1.7-2.9) on RAN, 2.8 (1.9-3.7) after HSV, and 1.4 (1.2-1.5) on PL (p<0.001 and p<0.0001 respectively compared with PL).

Twenty four hour [H+] (calculated from area under the [H+]time curve) was reduced by a median 68% (quartiles, 57-82%) by HSV, and 50% (33-66%) by RAN (NS). Daytime [H+] (0800-2400) was reduced 80% (60-93%) by HSV and 30% (12-45%) by RAN. Night time [H+] (0000-0800) was reduced only 57% (47-82%), however, by HSV compared with 89% (60-93%) by RAN. Thus HSV suppresses daytime [H+] more than RAN (p<0.0001), but suppresses night time [H+] less than RAN (p<0.01).

Because HSV and RAN are similarly effective in healing DU's; suppression of nocturnal [H+] may not be of paramount importance for the healing of duodenal ulcers.

**T43 Use of an ammonia electrode for rapid quantification of C pylori urease – lack of inhibition by bismuth subsalicylate**

S HUGHES, M STEWART AND JONATHAN M RHODES (University Departments of Medicine and Medical Microbiology, Walton Hospital, Liverpool) It is important to know whether bismuth salts inhibit urease as there is considerable interest in C' and C' urea breath tests for identifying relapse of C pylori gastritis and because a role for urease in the pathogenesis of ulceration has been postulated. Bismuth salts interfere with colorimetric and fluorimetric techniques for urease assay, so we have developed an assay for C pylori urease using ammonia electrode. C pylori obtained from human gastric biopsies, were grown on selective media, harvested and sonicated in PBS buffer (pH 7.2). One millilitre of this extract containing 2684 units urease (where 1 unit metabolises 1 mmole H in 1 min at 15°C) was added to PBS containing 0.5 M urea and ammonia released measured using an ammonia electrode (Russell Ltd) after addition of excess NaOH. The method proved rapid and reproducible (38 ppm NH₃ produced within 5 mins). Serial dilutions of bismuth subsalicylate (50, 5 mg/ml, 50, 50 mg/ml) were added to C pylori urease extracts before incubation with urea buffer. Bismuth subsalicylate 50 mg/ml caused 25-7% inhibition at 20 mins, but lower concentrations caused no significant inhibition (<3.7%). Addition of bismuth subsalicylate after incubation, as control, showed no interference with the assay. Assay of NH₃ release from urea using the NH₃ electrode is a highly sensitive and rapid assay for C pylori urease. Bismuth subsalicylate does not inhibit urease at concentrations likely to occur in vivo.

**T44 Effect of sucralfate on human gastric bicarbonate secretion and luminal PGE₂ output**

C J SHORROCK, L GIBBONS, AND W D W REES (Department of Gastroenterology, Hope Hospital (University of Manchester School of Medicine), Salford) The mode of action...
of sucralfate in protecting gastric mucosa remains unclear. In an attempt to elucidate the mechanisms of protection we have studied the effect of sucralfate on human gastric bicarbonate secretion and luminal PGE₂ output, two important components of mucosal defense.

Gastric bicarbonate secretion was measured in six healthy volunteers using a previously published perfusion technique. Bicarbonate secretion was calculated from the pH and pCO₂ of gastric aspirates, while acid was suppressed with intravenous ranitidine. Luminal PGE₂ output was calculated from the PGE₂ concentration of gastric aspirates measured by RIA. After a basal hour, sucralfate (8 g/ml = total 1 g over one hour) was added to the perfusate and bicarbonate secretion measured for a further hour. This was followed by a final hour of perfusion with saline only.

Sucralfate significantly stimulated gastric bicarbonate secretion [463 (87) to 781 (92) μmol/hour during the second hour, means (SE), n=6, p<0.01 Mann-Whitney] with values returning towards basal secretion during the final hour [510 (96)]. Luminal PGE₂ output was significantly increased during the final hour of perfusion only [1040 (92) to 1735 (215) pm/hour, means (SE), n=6, p<0.05]. In conclusion, sucralfate stimulates human gastric bicarbonate secretion and luminal PGE₂ output and these effects may be important in mediating its action.

A comparison of ranitidine and tripotassium dicitratobismuth (TDB) in relapse rates of duodenal ulcer. The role of campylobacter pylori (CP)

A C SMITH, A B PRICE, P BORRIELLO, AND A J LEVI (Divisions of Clinical Sciences, Histopathology, and Bacteriology, MRC Clinical Research Centre, Harrow, Middlesex) It has been suggested that the treatment of duodenal ulcer with a course of TDB leads to prolonged remission. We studied relapse rates over 18 months after six weeks treatment with either ranitidine or TDB and assessed the role of CP in relapse. Sixty five patients with a duodenal ulcer were randomly allocated to receive ranitidine (34) or TDB (31) for six weeks without maintenance treatment. Endoscopy and two gastric antral biopsies for CP culture and histology were performed at diagnosis and at 6, 18, 30, 54, and 78 weeks or at symptomatic relapse. Six patients from the ranitidine group and five treated with TDB defaulted leaving 28 treated with ranitidine and 26 treated with TDB. After six weeks treatment, 22 of 28 healed on ranitidine and all remained CP positive, while 22 of 26 healed on TDB of whom 19 (86%) cleared the bacteria. By 18 weeks 13 of 22 (60%) in the ranitidine group had relapsed, compared with three of 22 (13%) treated with TDB, all three being CP positive. By 78 weeks the relapse rates for the ranitidine group were 18 of 22 (82%) compared with seven of 22 (32%) in the TDB group. In the TDB group of the 15 who remained healed, eight were consistently negative for CP. In conclusion, TDB is more effective than ranitidine in preventing duodenal ulcer relapse. We suggest that CP plays a central role in the relapse process and that permanent healing is likely when CP is eradicated.

Human gastric mucosal bleeding induced by aspirin 300 mg and its prevention by ranitidine

G K KITCHINGMAN, P J PRICHARD, T K DANESHMAND, R P WALT, AND C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) Haematemesis and melaena often follow light aspirin ingestion. Low doses are increasingly recommended for cardiovascular prophylaxis so we evaluated whether aspirin 300 mg, increases gastric mucosal bleeding in man, and the effect of ranitidine. Thirty volunteers, aged 19–23, took aspirin 300 mg daily for two separate periods, with ranitidine 150 mg or placebo. Gastric mucosal injury was quantified by bleeding into gastric washings, 90 minutes after aspirin at five and 12 days of each treatment period.

Basal bleeding rates increased six-fold after aspirin 300 mg daily from 0.5 (geometric mean, 95% confidence limits 0.3–0.8) μl/10 minutes to 2.8 (1.9–4.1) μl/10 minutes after five days and 3.4 (1.9–6.1) μl/10 minutes after 12 days, p<0.01. Ranitidine increased gastric washing pH from 2.24 (median, interquartile range 2.11–2.48) to 6.36 (4.25–6.75, p<0.01), and reduced bleeding to 1.5 (1.0–2.3) μl/10 minutes at 5 days and 1.6 (1.0–2.5) μl/10 minutes at 12 days (p<0.05 for both). We conclude that aspirin at doses used for prophylaxis of cardiovascular disease has a substantial effect on human gastric mucosal bleeding which can largely be prevented by ranitidine.

Omeprazole versus ranitidine in erosive oesophagitis: results of a French-Belgian multicentre study

P ZEITOUN AND J P ISAI (Hôpital Robert Debre, Reims and Laboratoires Astra, Nanterre, France) One hundred and fifty six patients with erosive and/or ulcerative oesophagitis were randomised to treatment with omeprazole 20 mg, once daily or ranitidine 150 mg bid. Endoscopy was carried out immediately before entry and after four and eight weeks’ treatment together with assessment of symptoms. The lesions of the oesophageal mucosa were defined as follows: grade 2 (n=112), isolated round or linear erosions; grade 3 (n=33), confluent erosions affecting the total oesophageal circumference and grade 4 (n=11), erosions as described in grade 3 plus deep ulcers, and/or columnar epithelium-lined oesophagus. Macroscopic healing of oesophagitis was defined as complete epithelialisation of all oesophageal lesions. One hundred and thirty one patients completed the first four weeks’ treatment according to the protocol and the healing rates were 81% for omeprazole and 45% for ranitidine (p<0.001). The same great differences in healing rates were seen also after eight week’s treatment; 95% and 65% for omeprazole and ranitidine, respectively (p<0.001). Omeprazole gave also a faster and a more substantial improvement in reflux symptoms. Heartburn resolved completely in 87% of the patients receiving omeprazole during the first four weeks compared with 39% of those receiving ranitidine (p<0.001).

There were no adverse events or clinically significant changes in the laboratory screen attributable to the trial medications. The present study has shown that omeprazole 20 mg once daily, is superior to ranitidine in promoting healing and relieving symptoms in patients with erosive and/or ulcerative oesophagitis.

Response surface methodology predicts duodenal ulcer healing from acid suppression data

S G CHIVERTON, D W BURGET, AND R H HUNT (McMaster Univ Med Center Hamilton, Canada. On behalf International Study Group) Duodenal ulcer healing with anti-secretory drugs depends upon the degree and duration of acid suppression, but the optimal pH and time conditions have not been determined. We studied this by meta-analysis and response surface methodology. Duodenal ulcer healing rates were obtained
from a recursive computer assisted literature search identifying 316 trials. Predetermined inclusion criteria were: blinded, randomised, endoscopic controlled trials of DU healing by drug doses for which 24 hour intragastric acidity data were available. After independent evaluation by two investigators 201 trials met the criteria. Gastric acidity data were obtained by a recursive literature search for studies of 24 hour intragastric acidity in DU patients, and seven principal investigators were contacted to obtain raw data for independent analysis. Data were obtained for eight drugs in 20 different doses or regimens representing 544 24 h studies. Acid suppression, defined as duration above a pH between 1 and 5 was studied in 0-2 unit increments. The relationship between acid suppression and weighted healing rates for each drug and dose was studied by stepwise regression analysis and used to select pH thresholds for further analysis. From these data, the effect of time spent above any target pH on healing rates was studied by a three dimensional model constructed using response surface methodology with polynomial regression. With this model the results of 24 h intragastric acidity studies can accurately predict duodenal ulcer healing rates.

**T49 Complete prevention by omeprazole of aspirin induced gastric lesions in healthy subjects**

M A Bigard and J P Isal (introduced by Dr P R Richardson) (Service d’hepatogastro-enterologie, Chu de Nancy, and Laboratoires Astra France, Nanterre, France) Low dose omeprazole (5, 10 mg) does not protect the gastric mucosa against aspirin lesions. The aim of this study is to assess the effect of high doses of omeprazole on aspirin induced gastric lesions. Fifteen healthy subjects received either omeprazole 60 mg om or placebo during four days. One hour after the last intake of the drug, 1000 mg of acetylsalicylic acid (ASA) were taken together with a glass of water. Video endoscopy (Olympus V10) with recording of the gastroduodenoscopic examination was carried out two hours after the ASA ingestion. The damage caused to the gastric mucosa were graded in a blinded fashion according to the 0-4 score of LANZA: 0=normal, 1+=single haemorrhage, 2+=2 to 10 haemorrhages, 3+=11 to 25 haemorrhages.

Utilising a score of 2+ or less as clinically significant prophyactic success, the success rates were: OME 15/15 (100%) and PLA 1/15 (6-6%). Omeprazole was statistically superior to PLA (p<0-00001). Ninety per cent confidence intervals on the difference in success rates were (75%-100%) and (0-31%).

We conclude that (1) video endoscopy with recording of the examination is a useful tool to assess protective properties of a drug by means of endoscopic studies. (2) Omeprazole 60 mg om for four days protects healthy subjects against gastric damages induced by a single dose of 1000 mg of ASA. (3) Because omeprazole 60 mg om reduces a 99% reduction of gastric acid inhibition, our study supports that complete inhibition of acid secretion is a way to protect gastric mucosa against ASA induced lesions.

**T50 Repeated high oral doses of omeprazole do not affect intrinsic factor secretion: proof of a selective mode of action**

H Festen, H Tuynman, W Hollander, and S Meuwissen (Depts of Internal Medicine and Gastroenterology, St Francisius Ziekenhuis Roosendaal, Groot Ziekenhuis St. Hertogenbosch, Free University Amsterdam, The Netherlands) Up to now all agents known to inhibit gastric acid secretion concomitantly diminish intrinsic factor secretion (IF). Omeprazole (OME) inhibits gastric acid secretion by blocking the enzyme H+ K+ ATPase in the secretory membrane of the parietal cell, therefore its effect may be very selective. We studied the effect of repeated high oral doses of OME on IF secretion.

Eight healthy volunteers were studied. To differentiate possible influences of hypochlorhydria from direct effects of OME on IF, studies were done during saline and HCl perfusion. Two control gastric secretion tests were done 48 h apart during continuous perfusion with at random 0-9 N NaCl or 0-1 M HCl. These tests were repeated after seven and nine days oral intake of 60 mg OME daily, five hours after dosing. Gastric juice was collected in 15 min samples: 4 basal and 6 during continuous pentagastrin infusion (1-5 µg/kg/h).

During saline perfusion BAO decreased by 94% (8-6±1-9→0-5±0-1 mmol H+/h) but IF secretion was unchanged: 8-9±1-4→9±1-1±2-6 µg/h. Similarly stimulated acid secretion diminished by 97% (41±5-3→1-19±0-3) but neither peak (19-0±2-1→11-1±2-6 µg/30 min) nor steady state stimulated IF secretion (10-8±1-1→10-7±2-0 µg/h) changed significantly. During HCl perfusion basal and peak IF output were unchanged: 9-2±1-1→8-7±1-5 µg/h and 17-9±2-2→12-5±2-8 µg/30 min, but steady state stimulated IF output decreased significantly: 10-5±1-2→4±1-0-7 µg/h (p<0-001).

Omeprazole acts very selective: while inhibiting gastric acid secretion by more than 90% it does not affect IF secretion.

**T51 Treatment of ultra refractory duodenal ulcer with omeprazole**

K D Bardhan, D Dhande, R F C Hincliffe, Pamela Morris, Mary Thompson, N J H Carrol, and M J Daly (District General Hospital, Rotherham, Yorks, and Astral Clinical Research Unit, Edinburgh) We assessed the effectiveness of omeprazole (Om) in treating ultra refractory duodenal ulcer (URDU), which was defined as one that fails to heal on high dose cimetidine (C) — that is, 2 g or 3 g daily, given for at least three months. Patients with URDU were randomly allocated to receive either Om 40 mg daily or to continue with the dose of C they were refractory to — that is, 2 g or 3 g, for up to two months. Endoscopy, clinical assessment and laboratory studies were done every month. Thirty patients were studied, 18 refractory to C 2 g and 12 to C 3 g. The patients assigned to Om and C were of comparable demography and had a similar length of pretial C treatment. Of 18 patients refractory to C 2 g, cumulative healing at one and two months was: on C 2 g, 10/17 and 12/17; on Om, 14/17 and 15/17. Of the five unhealed on C 2 g after crossing over, five of five healed at one month on Om. Twelve of 17 (71%) healed on C 2 g compared with 20/22 (91%) on Om. Of 16 patients refractory to C 3 g, healing at one and two months was: on C 3 g, three of seven and four of seven; on Om, eight of nine and nine of nine. After treatment crossover, healing occurred on Om in two of three resistant to C. In total, healing occurred in four of seven on C 3 g (57%) compared with 11/12 (92%) (<0.03) on Om. At four weeks, Om was more effective than C in achieving complete symptom relief. There were no serious adverse events or clinically significant changes in haematology or biochemistry.

In conclusion, Om 40 mg daily is more effective than continued cimetidine treatment in the healing of duodenal ulcers refractory to C 2 g or 3 g daily, and is significantly superior in the latter group.
T52

Effect of bile diversion of Campylobacter pylori (CP)

H J O’Connor, K M Newbold, J Drumm, I A Donovan, H Thompson, and J Alexander-Williams (Dept of Gastroenterology, Queen Elizabeth Hospital, Dept of Surgery, Dudley Road Hospital, and Dept’s of Histopathology and Surgery, General Hospital, Birmingham) To assess the effect of bile diversion on CP, 24 patients (21 male, three female; mean age 48±8 years, range 29–68) underwent gastric biopsy before and a mean 4-9 years (range 0.8–12.3) after Roux-en-Y surgery. The original partial gastrectomy (PG) specimen resected a mean 3-4 years (range 1–6.2) before Roux-en-Y was available for study in 11 patients (46%). Biopsy specimens were examined blind for CP and scored for severity of reflux gastritis (RG). Reflux gastritis has a characteristic histology comprising marked foveolar hyperplasia, oedema, and vasodilatation of the lamina propria, and a paucity of acute and chronic inflammatory cells. These five features were graded from 0 to 3 according to the prominance of each and the sum of the grades used to assign each patient a reflux score. Ten of the 11 original PG specimens (91%) were CP-positive. Only 13 of the 24 patients studied (54%) were CP-positive before Roux-en-Y falling to 21 (88%) after biliary diversion (p<0.005). Associated with these changes, median reflux score rose from 7 in the PG specimens to 11 pre-Roux-en-Y falling to 6 post-Roux-en-Y (p<0.001). The absence of CP correlated strongly (p<0.001) with high reflux scores (>10).

Our results suggest that CP may recolonise the gastric remnant after bile diversion leading to a transition from RG to CP related gastritis.

T53

Pancreas and gastric carcinogenesis in the rat

R C Mason, P R Taylor, D C Hanley, and M I Filipe (Dept of Surgery and Histopathology, Guy’s Hospital, St Thomas Street, London) We have previously shown that pancreaticoduodenal secretions, not bile, are implicated in carcinogenesis of the operated rat stomach (Mason RC et al., Gut 1988; 27: A634). This study was designed to determine whether this effect was caused by duodenal or pancreatic secretions. Male Wistar rats received a 2/3 resection of glandular stomach. Intestinal continuity was restored in such a way as to produce reflux of either duodenal secretions alone (DR) or pancreaticoduodenal secretions (PDR), or controls with no reflux of any sort (Roux diversion). After nine months all animals were killed and their stomachs examined histologically. Ten of 14 animals with PDR developed carcinoma. In contrast none of 11 animals with DR and one of 12 controls developed malignant change. The association between the presence of carcinoma and pancreatic reflux was significant (PDR v DR χ²=10.3, p<0.01, PDR v controls χ²=8.1, p<0.01), and implicates pancreatic exocrine secretions in the aetiology of gastric stump carcinoma.

T54

Can use of the Grassi test reduce the prevalence of recurrent ulceration (RU) after highly selective vagotomy (HSV) for refractory duodenal ulcer?

M Rogers, R L Blackett, J N Primrose, and D Johnston (University Department of Surgery, The General Infirmary, Leeds) Patients whose duodenal ulcer (DU) remains unhealed after three months’ therapy with H₂ receptor antagonists (H2RA’s), refractory DU’s (REFDU), have a higher incidence of RU after HSV than patients whose ulcers heal on H2RA’s (non-REFDU). Can this difference be abolished by use of the Grassi Test (GT)?

Highly selective vagotomy was performed in 27 patients (REFDU n=10, non-REFDU n=17). After HSV, the GT was performed, and the vagotomy was revised if mucosal pH was <3.0. The sequence, ‘GT-revise dissection-GT’, was repeated until mucosal pH>3.0 or, it was felt that further dissection would risk antral denervation or gastric ischaemia. The result of the ultimate GT (after the final dissection) was classified as: positive, pH<2.0; negative, pH>3.0; equivocal, 2.0<pH<3.0.

At median three year follow up four patients had developed RU (REFDU=3, non-REFDU=1). Of 12 patients with a negative GT none developed RU, but four of the other 15 patients developed RU (p<0.05). Of four patients with RU: two had positive GT’s and two equivocal GT’s. Of 23 patients without RU, the GT was negative in 12, positive in six and equivocal in five. Thus a negative Grassi Test predicts a low risk of RU after HSV in patients with REFDU or non-REFDU, yet the prevalence of RU was unchanged from our previous report. The usefulness of the Grassi Test is limited because in 15 of 27 patients it was not possible to render the stomach ‘Grassi negative’.

T55

Pathway of migration of epithelial cells in human duodenal villi

K C Liu and N A Wright (Departments of Histopathology and Medical Physics, Royal Postgraduate Medical School, London) It has long been recognised that small intestinal epithelial cells migrate upwards from crypts to villi. There has been considerable debate about the pathway of cell migration once cells move onto the villus. Scanning electron and optical observations suggest a spiral pathway, but studies in chimaeric mice show villus cells migrating in straight lines. The situation in the human small bowel is unknown.

Gastric metaplasia occurs in the human duodenum in normal subjects and in patients with duodenitis; gastric mucous cells, readily distinguished from duodenal goblet cells arise apparently in the crypts and migrate onto the villi. In serial sections of villi, we have traced the upward migration of these cells using polystyrene models and computer reconstruction. The pathway of migration is in straight lines from villus base to apex; there is more intermingling with adjacent cells than in the mouse. It is also shown that the cells emerging from one crypt can migrate onto two villi. Moreover, gastric metaplastic cells, hitherto regarded as originating from the crypts, appear from the serial section studies to arise from Brunner’s gland ducts, and share immunochemical staining for EGF with the duct cells; it is proposed that gastric metaplastic cells originate from Brunner’s glands.

T56

Exercise delays gastric emptying of liquids in man – a study using applied potential tomography (APT)

A Van der Broek-Evans, J N Lund, G L Lamont, J W Wright, and D F Evans (Dept of Surgery, Queen’s Medical Centre, Nottingham) Strenuous exercise sometimes causes nausea and vomiting which may be influenced by alterations in gastric emptying. We have measured gastric emptying of liquids during exercise in eight healthy volunteers using applied potential tomography, a technique which utilizes computed impedance imaging. Liquid emptying was measured after drinking 500 ml of 0·1 m, 0·2 m, 0·4 m, and 0·8 m glucose and four proprietary sports drinks. This was
repeated during exercise on a bicycle ergometer at 80% of predicted maximum heart rate. Gastric images were continuously monitored using APT, regions of interest and 50% liquid emptying times were calculated ($t_{50}$). $t_{50}$ was significantly lower for the 0.8 m glucose when compared with 0.1 m (median $t_{50}$ 0.1 = 5.7 minutes, median $t_{50}$ 0.8 = 8.1 minutes, p<0.05). After exercise the median $t_{50}$ was significantly slower for all the sports drinks and all but the highest concentration of glucose. (0.1–0.4 M glucose 5.2–5.7 mins ex., 7.9–23.7 mins ex., p=0.05). (sports drinks 11.4–17.0 min rest, 21.5–47.4 min ex, p=0.05–p=0.01).

Applied potential tomography is a useful non-invasive technique to measure gastric emptying during exercise and this study has shown that there is significant slowing of emptying of liquids under such conditions.

T57
Abdominal migraine – a cause of abdominal pain in adults?

D E LONG, A T R AXON, J ROTHWELL, AND N NOV (Gastroenterology Unit, The General Infirmary, Leeds) Some patients with non-organic abdominal pain do not have classical features of irritable bowel syndrome or respond to standard treatment. Abdominal migraine is recognised in children: this study provides evidence for a similar condition in adults. Seventy four patients presenting with non-organic abdominal pain were interviewed. Those with multiple pains (24) or one constant pain (16) were excluded. Three analyses were performed on the 34 patients with one intermittent pain. The following symptoms occurring in association with the abdominal pain – headache, frequent nausea, dizziness, visual disturbance or focal paraesthesiae, and radiation into the limbs – are hereafter termed ‘migraine accompaniment’ (MA). First, those with moderately severe non-colicky pain were selected (n=19). Sixty eight per cent had a family or personal history of migraine and 37% had three or more MA, compared with 33% and 13% respectively of the remainder. Second, the subgroup with a family or personal history of migraine were analysed (n=18). Seventy two per cent had moderately severe non-colicky pain and 44% had three or more MA, compared with 38% and 6% respectively of the remainder. Of the nine patients with three or more MA, 78% had moderately severe, non-colicky pain and 89% a history of migraine.

We propose that the six patients selected independently by all three analyses represent the ‘classical’ symptom complex of abdominal migraine.

T58
Long acting somatostatin in carcinoid syndrome

S LEVI, M ELLIS, E LEUNG, E ADAM, J CALAM, AND H HODGSON (Depts of Medicine and Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London) Long acting somatostatin has been advocated as treatment for carcinoid syndrome. We report results in eight patients with gastrointestinal carcinoid with hepatic metastases, resistant to conventional blocking drugs, treated with long acting somatostatin (Sandostatin) in doses of 50–250 µg tds by self-administered subcutaneous injection. In all patients there was effective and rapid symptom relief of diarrhoea, flushing, palpitations, and wheezing when present. The effect of therapy on release of serotonin from tumour was unpredictable, both increased and decreased 5 HIAA concentrations being found, suggesting that much of the action of somatostatin is peripheral. Serial observations of tumour size in this group of patients did not show convincing evidence of a direct antitumour action, with growth in tumour deposits over six months of therapy being recorded on sequential CT scans, or obvious development of extranepatic tumour masses occurring. Side effects were limited to occasional local pain at the injection site, and biochemical evidence of glucose intolerance. Currently long acting somatostatin is an effective means of preventing symptoms in carcinoid syndrome, but an effect on survival would not be predicted.

T59
Small intestinal drug absorption: influence of anatomical site and perfusate composition

S A RILEY, F A SUTCLIFFE, B KAESER-LAIRD, M ROWLAND, AND L A TURNBERG (Departments of Medicine and Pharmacy, University of Manchester, Hope Hospital, Salford and Coupland Building 3, Manchester) Lipo-philic drugs are well absorbed from the gastrointestinal tract but the absorption of hydrophilic compounds tend to be variable and incomplete. We have therefore studied the absorption of a range of such compounds using a modified triple-lumen perfusion technique.

Eighteen fasted healthy subjects were perfused with multicomponent solutions of atenolol, hydrochlorothiazide, fruseamide, salicylic acid, and cimetidine and salicylic acid. Studies were done sequentially in jejunum and ileum, at perfusion rates of 5 ml/min and 10 ml/min, with isotonic solutions of balanced electrolytes or glucose.

Steady state absorption was consistently higher in jejunum than in ileum for all drugs, except salicylic acid, which was almost completely absorbed from both sites. Absorption from jejunum and ileum increased in order hydrochlorothiazide-atenolol-fruseamide-cimetidine-salicylic acid, the same rank order as their oral bioavailabilities. Glucose in the perfusate enhanced the absorption of atenolol, hydrochlorothiazide, and fruseamide, particularly in the jejunum, and this was associated with a two fold increase in water absorption.

These studies show that absorption of a range of hydrophilic compounds is greater in jejunum than ileum and is influenced by the solvent drag suggesting absorption through a paracellular route.
clear that malnutrition per se can induce a hypersecretory state of the small intestine.

Support from the British Digestive Foundation is acknowledged.

T61 Effect of ethanol on the small intestine of the rat

VICTOR R PREDAY, KATHY TEAHON, AND TIMOTHY J PETERS (Division of Clinical Cell Biology, MRC Clinical Research Centre, Harrow, Middlesex) As well as its primary role as an absorptive organ, the small intestine is an important contributor to whole body protein turnover. Most studies on the effects of ethanol on this tissue, however, have largely been confined to the mucosal layer and to its absorptive functions. We therefore examined the chronic effects of ethanol feeding on the entire small intestine. Rats received ethanol as 36% of total calories in a nutritionally complete liquid diet; controls were fed the same diet in which ethanol was substituted by iso-caloric glucose. After six weeks there was a 21% reduction in the absolute weight of the small intestine (p<0.025). The total amounts of protein, RNA and DNA were also reduced in response to ethanol feeding by 23% (p<0.01), 16% (p<0.01), and 28% (p<0.001), respectively. In contrast, biochemical indices of the potential for the tissue to synthesis protein was increased - that is, the RNA/DNA ratio, was 1.81 (0-04) and 2.14 (0-08), mg RNA/mg DNA in control and ethanol fed rats, respectively [mean (SE) of 6 pairs, p<0.001]. Rates of protein synthesis were measured with a large 'flooding dose' of [3H] phenylalanine. Fractional rates of mixed tissue protein synthesis were slightly decreased, from 188 (12) to 170 (13)%/day (p<0.05). There was a highly significant decrease in the absolute rate of protein synthesis from 979 (87) to 722 (32) mg/day (<0.025), however, in response to ethanol. As the small intestine contributes 25% of whole body protein synthesis, chronic alcohol administration will profoundly impair protein homeostasis.

T62 Effect of moderate exercise on water and electrolyte absorption from the human jejunum in vivo

G R BARCLAY AND I A TURNBERG (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) In recent years exercise has become an increasingly popular pastime. Although its effect on cardiorespiratory and endocrine functions has been extensively investigated little is known about its effect on gastrointestinal function. This study investigated the effect of moderate exercise on jejunal absorption in seven healthy volunteers using a triple lumen perfusion technique. After a 50 minute control period subjects pedalled a bicycle ergometer at 15 km/h, for 50 minutes, against a load sufficient enough to raise their pulse rate by 40-50%.

Moderate exercise significantly reduced absorption of water from a resting value of 32±4.0 to 16.2±6.1 ml/30 cm/50 min (p<0.02), as well as sodium from 2.4±0.4 to 0.5±0.9 mEq/30 cm/50 min (<0.05), chloride from 2.0±0.4 to 0.3±0.7 (p<0.05), and potassium from 0.20±0.02 to 0.01±0.04 (p<0.01). During the 50 minutes after exercise absorption returned towards normal.

These results suggest that moderate exercise reduces human jejunal absorption. Although such changes are compatible with a parasympathetic response, changes in mucosal blood flow or neuropeptide activity could also be responsible.

T63 Parenteral utilisation of a short chain ovalbumin hydrolysate in man

G K GRIMBLE, A H RAIMUNDO, R G REES, M K HUNJAN, AND D B A SILK (Department of Gastroenterology & Nutrition, Central Middlesex Hospital, London) Substitution of peptides for free amino acids (AA) in total parenteral nutrition (TPN) solutions may offer advantages. The limited solubility or stability of some free AA's is overcome and the reduced osmolarity of the solution may make peripheral TPN possible. Dipeptidase AA pools in trauma/sepsis may also be normalised since uptake of peptides may be by routes other than free AA transport. The aim of the present study was to compare the parenteral utilisation of a highly purified, short chain length (CL) enzymatic hydrolysate of ovalbumin, with that of its equivalent free AA mixture.

In two studies, six fasted subjects were infused with a complete TPN solution (4.5 g N/l, 28% fat, and 10-5% glucose) containing either an ovalbumin hydrolysate (PEP - 9% AA, 75% CL 2-3, and 16% CL 4-5) or a free AA solution of similar composition. Infusion for six hours was at the rate of 13 g N, 1900 kcal per 24 h. Resting energy expenditure (REE) was measured and urine was collected for seven hours.

Urea-N excretion (mmol-N) was similar [243-6 (34-1) vs 228-8 (29-7); PEP vs AA; mean (SE)] whilst total-N excretion (mmol-N) was higher during peptide infusion (374-5 (61-6) vs 276-9 (28-0); NPE). Free- and bound-alpha-NH2-N (mmol) indicated peptiduria during PEP infusion (freq: 9.3 (1-4) v 2.8 (0-9); p<0.01; bound: 32.3 (3-9) v 9.9 (2-0); p<0.01) but did not account for the entire difference between total-N and urea-N excretion. Resting energy expenditure was similar during both infusion periods.

These data suggest that a significant proportion of PEP was utilised, despite some peptiduria. We conclude that highly purified short chain protein hydrolysates show promise as an effective and economical alternative to free AA's in TPN.

T64 Multiple lymphomatous polyposis of the gut

I W FELLOWS, S HART, K A MACLEAN, B HAWTHORNE, AND P J TROUGHILL (University Hospital, Nottingham) Multiple lymphomatous polyposis (MLP) is a rare form of primary gastrointestinal lymphoma in man with characteristic endoscopic and radiological features. We report the clinical, histological and immunocytochemical features of three patients. One was detected at an asymptomatic stage during faecal occult blood screening, while the other two presented with diarrhoea and rectal bleeding. All three had widespread lymphomatous involvement of the gastrointestinal tract from stomach to rectum, with multiple colonic polyps.

Light microscopy revealed a small cleaved cell lymphoma with a nodular pattern and angulated nuclei with sparse chromatin, features typical of centrocytic lymphoma.

Immunocytochemical techniques showed that two cases expressed monoclonal IgM kappa, while the other expressed IgG lambda. All three cases showed B lymphocyte markers (MB1, CD20) and two expressed the T lymphocyte marker MT1.

Two patients were treated with chemotherapy. One patient died 4-5 years after diagnosis, from carcinoma of the bronchus, with active lymphoma. The other two patients remain alive 1-5 and 2 years after diagnosis, the former asymptomatic and untreated.

The optimum type and duration of chemotherapy of MLP remains uncertain but prolonged survival is clearly possible. Recognition of the typical endoscopic and radiological features facilitates diagnosis of this rare condition.
T65
Effect of dietary fat on the small intestinal mucosa

D G MAXTON, E U CYNK, A P JENKINS, AND R P H THOMPSON (Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London) The precise roles of individual dietary constituents in promoting small intestinal mucosal growth are unknown. Dietary fat, however, may be a potent trophic factor.

Rats (n=8) were fed isocalorically for one month an elemental feed with 1% fat: Vivotex (V), or Vivotex with either 50% caloric substitution by high 84% (EFA) or low 4% (SAT) essential fatty acids. The small intestine was divided into three equal segments and their whole and mucosal weights, DNA and protein measured.

Weight gain was significantly greater in V than either EFA and SAT. Nevertheless, EFA and SAT increased gut whole and mucosal weights above V in all segments [total small intestinal weight: V 46-6 (1-3), EFA 56-6 (1-6), SAT 62-0 (0-8) mg/cm2; total mucosal weight V 16-5 (0-6), EFA 23-6 (1-3), SAT 23-6 (0-7) mg/cm2: means (SE), p<0.001]. Similarly, mucosal DNA and protein were increased by EFA and SAT especially in lower segments [total DNA: V 107-2 (7-5), EFA 152-0 (11-3), SAT 164-1 (17-6); μg/cm2, both p<0.02; total protein: V 4-71 (0-13), EFA 5-81 (0-11), SAT 6-44 (0-19); mg/cm2, both p<0.001].

We conclude that fat, regardless of EFA content, is a potent dietary stimulus to intestinal growth.

T66
Further studies on the possible role of human adenovirus 12 (Ad12) and gluten sensitivity

C J SMART, L K TREJDOSIEWICZ, J D PRIDDLE, D F JEWELL, AND P D HOWDLE (Dept of Medicine, St James's University Hospital, Leeds and Gastroenterology Unit, The Radcliffe Infirmary, Oxford) The recently described amino acid sequence homology between Ad12 and wheat gliadin has prompted a search for immunity to Ad12 in coeliac patients. In such patients there is evidence suggesting humoral immunity to Ad12 and cell mediated immunity to a synthetic peptide of the specific Ad12 homology region. It has been suggested that cross reactivity between Ad12 and gliadin may lead to gluten sensitivity developing in patients pre-exposed to Ad12. To investigate the cross reactivity further, we have attempted to stimulate murine gliadin-sensitive lymphocyte cell lines with the Ad12 synthetic peptide.

Longterm gliadin sensitive lymphocyte cell lines were established from gluten free Balb/C mice, preimmunised with purified unfraccionated gliadin. Cell lines were antigen specific after several generations of rest stimulation cycles using unfraccionated gliadin. The response to gliadin, as assessed by 3H-thymidine incorporation, was reproducible and dose (0–1000 μg/ml) dependent [peak response 73100 (12000) dpm at 250 μg/ml]. Response to Ad12 over the equivalent molar range [maximum 5000 (2300) dpm] did not exceed control values obtained with ovalbumin [maximum 9300 (7650) dpm].

We have not shown immunological cross-reactivity between the Ad12 peptide and gliadin in our murine system. The role of Ad12 in coeliac disease is still in question and further detailed investigation is necessary.

T67
Colonic hyperplasia after jejunocolic bypass for morbid obesity

G V N APPLETON, E E WHEELER, R A-MUFTI, D N CHALLACOMBE, AND R C W WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary and Somerset Childrens Research Unit, Musgrove Park Hospital, Taunton, Somerset) Over the past 20 years jejunocolic bypass (JIB) has been widely used to treat patients with morbid obesity. Jejunocolic bypass in rats causes adaptive colonic hyperplasia and enhances colorectal neoplasm. In this study crypt cell production rate (CCPR) was measured by a stathmokinetic technique in organ cultured rectal biopsies from nine patients with JIB [weighing 165 (43) kg], and from seven controls [weighing 81 (28) kg] without intestinal operations or disease. Crypt cell production rate in the group with JIB was more than double that of controls [12-80 (2-67) v 6-23 (1-49) cells/crypt/h; p<0.001]. Crypt width and crypt area were 18–29% greater in patients with JIB than in controls. Histological examination of rectal biopsies showed no evidence of proctitis nor of dysplasia. Patients with JIB have a marked and persistent increase in cell proliferation in the large intestine, and may be at increased risk of developing colon cancer.

T68
Peptide histidine methionine (PHM) increases ileostomy output

THE BRITISH SOCIETY OF GASTROENTEROLOGY

J CALAM, A MEHTA, Y YANGOU, AND S R BLOOM (Dept of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Peptide histidine methionine has sequence homology with vasoactive intestinal peptide (VIP) and both peptides are products of the same gene. Plasma concentrations of PHM are about 10 times higher than VIP concentrations in the watery diarrhoea syndrome (WDS). We have investigated the possibility that PHM, like VIP, increases ileal output in man.

Five fasted ileostomists received intravenous synthetic PHM: 23 pmol/kg/min for 90 min. Blank infusate was administered for 30 min before and 90 min after. Ileal effluent was collected every 30 min.

Plasma PHM concentrations rose from 18 (1) to 6018 (874) pmol/l [mean (SE)] during PHM infusions. The weight of ileostomy effluent rose from 17 (6) to 177 (27) g/30 min (p<0.01 by t test), the percentage of solid material, determined by desiccation, fell from 6.4 (0.8) to 2.8 (0.8) [%p<0.01] and the chloride concentration of ileostomy effluent rose from 68 (10) to 102 (6) mmol/l [p<0.01] during PHM infusions.

These effects of PHM are similar to those of VIP. Peptide histidine methionine present in ileal nerves may control ileal secretion and absorption of water and electrolytes. Mean plasma PHM concentrations during these infusions in the range seen in the WDS. Peptide histidine methionine probably contributes to diarrhoea in this condition.

T69
Polyurethane catheters as an alternative to silicone to total parenteral nutrition

G L SUTTON, M TAYLOR, AND S J KARRAN (University Surgical Unit, F Level, Centre Block, Southampton General Hospital, Southampton) The introduction of nutrition teams has so improved care of catheters for total parenteral nutrition (TPN) that mechanical and thrombotic complications have become more common than septic complications. Silicone elastomer has been regarded as the optimal material for catheters but its poor physical strength means that catheters constructed of this material are large in relation to their internal diameters and are prone to fracture. Polyurethane is much stronger and in vitro experiments have shown reduced thrombogenicity compared with silicone.

In a consecutive trial 194 silicone catheters were used to deliver over 2400 patients day of TPN. Catheter fracture...
ocurred on 12 occasions although there were no cases of catheter or air embolus. Blockage occurred on six occasions and hub fracture and disconnection in a further seven. Catheter colonisation (>20 colonies) occurred in 1-3/100 days. The next 248 catheters inserted were polyurethane incorporating an off switch in the hub. Four thousand eight hundred and eighty five days of TPN were delivered without a single case of catheter fracture, blockage or disconnection. Catheter colonisation rate was 0-35/100 days. Polyurethane is therefore a superior material to silicone elastomer and its use will reduce mechanical and thrombotic complications of TPN.

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**T70**

**Immunosuppressive effects of cultured hepatocytes**

Y Lech and H J F Hodgson (Dept of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London)

Liver cells transplanted between certain rat strains without immunosuppression are rapidly rejected. To explore this we exposed DA strain rat splenic lymphocytes to cultured August hepatocytes in vitro (a combination which in vivo results in hepatic destruction) but recorded profound inhibition of lymphocyte reactivity. Lymphocyte proliferation was inhibited by co-cultured hepatocytes, even when liver cells were present in a proportion of only one hepatocyte:1000 lymphocytes. Syngeneic and allogeneic hepatocytes were shown to exert this effect.

Inhibition, which was by >95% of 3H-thymidine incorporation, affected both non-specific mitogen mediated responses, and the specific HLA-mediated responses of mixed lymphocyte cultures, and affected rat and human lymphocytes. As a consequence, lymphocyte transformation in response to cultures of histoincompatible hepatocytes was only demonstrable at target cell ratios of 10,000:1 or greater. The immunosuppressive effect is probably because of arginase release, as had been demonstrated using cytoplasmic extracts of liver cells. Potentially, release of this immunosuppressive molecule in vivo could protect hepatocytes from rejection, or could limit intralobular extension of autoimmune damage initiated adjacent to portal tracts.

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**T71**

**Acute phase induction of alkaline phosphatase in rat hepatocytes in primary culture**

S G Parker, 1. Agius, and O F W James (Department of Medicine, University of Newcastle upon Tyne) Serum alkaline phosphatase (ALP) can be induced in patients with severe infections not involving the liver. The explanation for this is not known and we hypothesised that hepatic ALP may be induced by acute phase cytokines in a way analogous to its induction by bile acids in cholestasis. This hypothesis has been tested in rat hepatocytes in primary culture using a supernatant from activated human peripheral blood monocytes (PBMs) as the acute phase stimulus. Human PBMs were isolated by density gradient centrifugation and enriched by adherence to plastic. Adherent cells were cultured for 48 hours in RPMI 1640 with antibiotics and 5% fetal calf serum (FCS) supplemented with 5µg/ml bacterial lipopolysaccharide. The supernatant was harvested, dialysed against 0-9% saline and water, concentrated 10-fold by lyophilisation and stored. This concentrated monocyte supernatant (CMS) was used to stimulate the hepatocytes. Rat hepatocytes, prepared by a standard collagenase perfusion technique, were cultured for 24 hours in Hams F10 containing antibiotics, 5% FCS, insulin (10 M), dexamethasone (5×10−7 M) with and without CMS. Acute phase response was confirmed by measuring albumin and fibrinogen release into the culture medium (ELISA). Total protein concentration and alkaline phosphatase (ALP), and aspartate transaminase (AST) activity were assayed in cell homogenates (0-25 M sucrose/0-2% Tween 20 in phosphate buffered saline). Results are expressed as mean (SE). The five experiments each done in triplicate.

We conclude that the induction of ALP observed here in vitro offers an explanation for raised serum ALP in the absence of overt liver disease.

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**T72**

**Importance of IgA antibody to candida in diagnosis of candidiasis in fulminant hepatic failure (FHF)**

A K J Goka, N Rolando, M De La Mata, G J M Alexander, and Roger Williams (Liver Unit, King's College Hospital and School of Medicine and Dentistry, London) Bacterial infection in FHF carries a particularly high mortality; in a recent series candidiasis was also identified in 34% of patients with 100% mortality in untreated cases. Early therapy, however, was thwarted by the difficulties in making a firm diagnosis in life. A rapid ELISA for antibodies to candida was therefore developed using sonicated candida as antigen and each serum as its own control. Thirty eight cases with FHF were studied serially, 16 with proven candidiasis and 22 without any evidence of infection. There were 14 healthy controls.

There were no differences in IgG, IgM, and IgA concentrations between controls and uninfected patients, but all three antibodies were present in higher concentration in infected patients (p<0.05, p<0.001, and p<0.0001 respectively). Antibody levels exceeded the normal range, however (mean ± 2 SD) in only 25% of cases for IgG and 44% for IgM. In contrast the levels for IgA antibody exceeded the normal range in 69% of infected patients and in 82% levels rose progressively. Of five infected patients with ‘normal’ levels of IgA antibody, one died on admission, two at the time of death had levels rising from initially undetectable levels and in two positive cultures were found more than two weeks before the last available serum.

These data indicate that frequent serial estimation for high or rising levels of IgA antibodies to sonicated candida antigen provides a sensitive and rapid measure of significant candida infection, allowing early antifungal therapy.

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**T73**

**Pre-S1 and pre-S2 antigen expression in hepatitis B infection**

G M Dushieko, J D Conrade, M Bubb, and M C Kew (Introduction by N McIntyre) (Royal Free Hospital, London, UK, University of the Witwatersrand, Johannesburg, and Natal Institute of Immunology, Durban, South Africa) The S and pre-S proteins of hepatitis B virus (HBV) are structural components of the viral envelope that play a role in virus infectivity. We have correlated the presence of pre-S1 and pre-S2 antigens with the natural history of HBV infection. A total of 398 serum samples from 59 patients with acute and chronic
hepatitis B or hepatocellular carcinoma (HCC) were tested. Pre-S1 and pre-S2 antigens were tested by ELISA utilising antibodies against synthetic oligopeptides. Five patterns of pre-S antigen expression were discerned. In acute hepatitis B, pre-S1 and pre-S2 clearance preceded HBsAg. Loss of pre-S together preceded loss of HBsAg after interferon treatment. HBsAg positive carriers were invariably positive for pre-S1 and pre-S2 antigens. Carriers seroconverting to anti-HBe usually retained pre-S1 and pre-S2 when studied soon after loss of HBsAg. Thirty three per cent of long-standing carriers or HCC patient were pre-S1 and/or pre-S2 negative. Thus pre-S2 and pre-S1 antigens are a function of the duration of the carrier state, but detectable in serum for some time after seroconversion to anti-HBe. Because pre-S and S are separate translation products, the relative decline in pre-S proteins in serum may reflect progressive disruption of integrated HBV genome with longstanding disease.

T74 Evening primrose oil in chronic biliary pruritus

P J THULUVATH, M MANKU, N MORSE-FISHER, AND D R TRIGER (Department of Medicine, Royal Hallamshire Hospital, Sheffield and Efamol Research Inc, Nova Scotia, Canada)

Chronic biliary pruritus is often trouble-some and resistant to treatment. Evening primrose oil (Efamol) has been shown to relieve the itching of atopic eczema although the mechanism is uncertain. We have conducted a double blind placebo controlled crossover study in 11 patients with PBC who had pruritus for more than six months which was unresponsive to cholestyramine or Terfenadine. Efamol (1G qds)/placebo was given for three months each. Nine patients completed the study; one was withdrawn because of peptic ulcer while taking placebo and another because of poor compliance. Of the remainder, six improved significantly on Efamol, one on placebo and two experienced no improvement. All six relapsed after stopping Efamol, and improved only when Efamol was given again (after the trial). The subjective responses were confirmed by patient kept diaries of visual analogue scores. Analysis showed significant reductions in essential fatty acids (EFA) in phospholipid and triglyceric moieties with a rise in cholesterol ester before treatment, suggesting defective EFA transfer between lipid classes. Efamol appears to be of definite value in treating chronic biliary pruritus.

T75 Selenium in chronic liver disease

P J THULUVATH AND D R TRIGER (University Department of Medicine, Royal Hallamshire Hospital, Sheffield) Selenium (Se) is an essential trace element with important antioxidant properties. It has been suggested that lipid peroxidation is an important mechanism in the pathogenesis of liver disease. In alcoholic liver disease serum Se concentrations are low which is thought to be dietary in origin. We measured Se concentrations in a range of chronic liver diseases with concurrent assessment of nutritional status. Serum and liver selenium concentrations were determined by hydride generation atomic absorption spectrophotometry and nutritional status by anthropometric measurements. Serum concentrations [mean (SD) µg/l] in 45 alcoholic liver disease [63 (18)**], 43 PBC [60 (13)**], 19 auto-immune CAH [73 (20)*], eight cryptogenic cirrhosis [59 (13)*], eight viral CAH [65 (19)*], and eight hepatoma [60 (13)**] were significantly lower (** = p<0.01, * = p<0.05) than in 55 controls [88 (21)]. Se concentrations correlated with albumin (p<0.001), AST (p<0.002), ALK phos (p<0.008) but not with bilirubin. There was no difference in serum Se concentrations between Child A [64 (15) n=60], Child B [60 (17) n=29], and Child C [57 (12) n=6]. Se concentrations did not differ significantly in undernourished compared with better nourished. Selenium concentrations in liver tissue (dry weight) were lower (p<0.01) in 11 alcoholic cirrhosis [785 (391) µg/l] and three PBC [343 (303) µg/l] compared with 14 controls [1289 (285) µg/l]. Our data show that serum and liver Se concentrations are low in all liver diseases and low concentrations are not related to their nutritional status. Considerations should be given to Se supplementation in liver disease.

T76 Chemotherapy of echinococcus multilocularis

D H TAYLOR, D I MORRIS, AND K S RICHARDS (Department of Surgery, University Hospital, Nottingham and Department of Biological Sciences, University of Keele, Keele) The majority of patients infected with E multilocularis (EM) die within five years, there is also evidence that it is spreading.

E multilocularis protoscoleces were maintained in in vitro culture and exposed to albendazole sulphoxide (Alb Sx) and praziquantel (Praz). Whilst both agents showed activity prazi was active more rapidly and at lower concentrations (50 µg/l for seven days).

Eighteen infected cotton rats were studied: five control, four Alb 50 mg/kg, four Praz 50 mg/kg, and five both drugs. Drugs were administered daily by gavage for six months. Weekly weighing revealed the smallest gain in the Alb group (3 g) compared with 5 g in the combination group, 15 g in the Praz group and 40 g in controls. Similarly the mean weight of parasite tissue at necropsy was; Alb 2.1 (1.19), Alb+Praz 4.72 (3.78), Praz 6.60 (3.75), control 4.14 (12.5). Alb alone and when combined with Praz achieved significantly (p<0.01) lower weights than with Praz alone or in controls.

Electron microscopy suggested greater activity on the germinal layer in the combination therapy group. Both albendazole and praziquantel have activity for E multilocularis – combination chemotherapy may well be a useful clinical concept.
functional capacity of the liver (C-Pc). (2) Recurrent bleeding significantly decreased survival. (3) Longterm survival was not influenced by the cause but by the activity (as measured by SGOT) of the liver disease. (4) All efforts should be directed towards preventing variceal rebleeding and inactivating the liver disease.

T78
What is the response of the mediastinum to variceal sclerotherapy?

S W Hosking, R Nakielny, G Jacob, and A G Johnson (Departments of Surgery and Radiology, Royal Hallamshire Hospital, Sheffield) Computed tomography scanning is used to diagnose occasional severe complications of injection sclerotherapy such as perforation and mediastinitis. This may be misleading because there is virtually no information on the reaction to uncomplicated sclerotherapy for comparison.

Eight patients with newly diagnosed varices underwent CT before, and one week after intravariceal sclerotherapy – the time when most complications occur. Scans commenced at the carina and extended to mid-stomach by 1 cm intervals. Endoscopy was performed immediately after the second scan.

Preinjection CT showed thickened oesophagus in all patients extending for 70–100% of the endoscopically visible length of the varices. Sclerotherapy caused a further thickening of the oesophageal wall and increase in cross sectional area of >25% in five patients, and <25% in three. Small pleural effusions occurred in two patients, one of whom developed mediastinal oedema and a further patient developed oedema alone. Of these latter three patients, two had normal endoscopies. Endoscopy showed superficial injection slough in three patients – CT scanning was unchanged in two and showed oesophageal thickening >25% and a small pleural effusion in the other.

We conclude that after sclerotherapy (1) CT changes are unrelated to injection slough; (2) oesophageal thickening, mediastinal oedema and small pleural effusions do not necessarily signify a serious complication. Postsclerotherapy CT scanning must be interpreted only with reference to the clinical picture.

T81
Effect of portal venous flow on the washout of a regionally injected marker from the liver

D M Noott, J Yates, J S Grime, D Chang, T C Cooke, and S A Jenkins (University Department of Surgery and Nuclear Medicine, Royal Liverpool Hospital, Liverpool) The treatment of overt hepatic metastases by systemic administration of chemotherapeutic agents does not improve prognosis. Similarly administration of cytotoxics via the hepatic artery has only a marginal beneficial effect. Starch degradable microspheres (DSM) when injected via the hepatic artery have been shown to increase the tumour concentration of cytotoxics given concomitantly, although the beneficial effect of this treatment has not been fully established. Therefore, the aim of this study was to evaluate the effects of portal venous flow on the washout of 51Cr labelled methylene diphosphonate (51CrMDP) and DSM injected simultaneously into the hepatic artery in normal Fisher rats using a scintillation counter placed over the lungs. Complete hepatic blockade assessed visually occurred with an hepatic arterial injection of 4 mg DSM (n=20). Although complete hepatic arterial blockade was
achieved, 68 (3.67)% of the marker passed through the liver. If the portal vein was clamped immediately prior to the injection of DSM and Tc-MDP (n=10) only 19 (2.14)% of the marker passed from the liver into the systemic circulation. Restoration of portal venous flow resulted in the washout of 67 (3.04)% of the marker from the liver. These results indicate that portal venous flow has a substantial effect on the clearance of substances injected via the hepatic artery and may explain why this mode of administration of cytotoxics only produces a marginal beneficial effect in the treatment of hepatic metastases.

T82
Effects of somatostatin and SMS 201-995 on hepatic and systemic haemodynamics in patients with cirrhosis and portal hypertension
S A JENKINS, J N BAXTER, S ELLENBOGEN, S SNOWDON, G WHITEHOUSE, AND R SHIELDS (University Department of Surgery, Anaesthesia, and Radiodiagnosis, Royal Liverpool Hospital, Liverpool) There is conflicting evidence on the effects of somatostatin (SRIF) and its long acting analogue SMS 201-995 on hepatic haemodynamics in cirrhotic patients with portal hypertension. To date 13 such patients both compounds were given by a bolus administration and the effects upon corrected wedged hepatic venous pressure (WHVP) and systemic haemodynamics were determined. Each patient received randomly a bolus administration of 50 and 250 µg SRIF and 50 µg SMS 201-995. Wedged hepatic venous pressure was measured using a balloon catheter inserted into a hepatic vein. Mean systemic arterial blood pressure (ABP) was measured directly via a cannula placed in the femoral artery and heart rate recorded using a digital ECG. Administration of 50 µg SRIF significantly decreased (p<0.01 Student’s t test) WHVP [23.04 (1.9) to 17.92 (1.8) mmHg] and heart rate [77.2 (2) to 59.3 (3) beats/min] but significantly increased ABP [106.3 (4) to 119.5 (5.0) mmHg]. Similar changes were observed following the administration of 250 µg SRIF and 50 µg SMS 201-995. There were no significant differences between the two doses of SRIF and the one dose of SMS 201-995 (ANOVA) in the fall in WHVP, rise in ABP and slowing of heart rate. These studies indicate that (1) both SRIF and SMS 201-995 given as a bolus reduce WHVP but have a systemic haemodynamic effect (2) SMS 201-995 like somatostatin may be a valuable therapeutic agent for treating bleeding oesophageal varices.

T83
Portal and parenchymal macrophage populations in alcoholic liver disease (ALD)
INCI KARAKUCUK, SUSAN DILLY, AND J D MAXWELL (St George’s Hospital Medical School, London) Previous studies indicated increased numbers and depressed clearance function of hepatic macrophages (HM) in ALD. We examined HM in 45 liver biopsies from patients with a spectrum of ALD (13 fatty change; 11 cirrhosis; nine cirrhosis + hepatitis) and compared them with 20 normal biopsies from non-alcoholics. Indirect immunoperoxidase and PAP methods were used to stain formalin fixed paraffin embedded tissues for monoclonal (MAC-400) and polyclonal (lysozyme, α 1-antitrypsin) antisera. Hepatic macrophages were assessed separately in parenchyma and portal tracts. Portal tract HM increased in fatty change with all three markers (p<0.05) and, with MAC-400, in all histological groups (p<0.01). In parenchyma MAC-400 staining HM increased in cirrhosis + hepatitis (p<0.01). Other markers were unchanged in parenchyma except in livers with cirrhotic and/or hepatic damage where decrease in lysozyme +ve HM was confirmed (p<0.01).

Use of three markers revealed heterogeneity of HM phenotype, and indicated increased numbers of HM in ALD, even in fatty change, in contrast with previous reports. As HM can release cytotoxic mediators, this new observation may indicate a role for HM in the pathogenesis of tissue damage in ALD.

T85
Oxidant stress, antioxidant supply and recurrent pancreatitis
SUDEN, B SALH, P GUYAN, P KAY, P MILLER, J P HUNT, J P DAY, AND J M BRAGANZA (Department of Gastroenterology and Computation, Royal Infirmary, Department of Inorganic Chemistry, The University, Manchester) Pancreatic oxidant stress has been implicated in the pathogenesis of experimental pancreatitis. If this holds true for human pancreatitis, it implies that antioxidant demand outstrips supply. We have tested this deduction by analysing sera from 21 patients with recurrent pancreatitis (acute three, chronic 18) and 20 healthy controls. The per cent molar ratio of octadeca 9,11 dienoic acid to linoleic acid in serum was used as an index of free radical activity, whilst serum selenium concentrations were used as a measure of antioxidant status. The molar ratios in the patients significantly exceeded the values in controls [mean (SE), 3.78 (0.32%) v 2.24 (0.18) p<0.001] whilst their selenium concentrations were significantly lower [85 (3.26) µg/l v 118 (3.92) p<0.001]. The overlap between data from patients and controls was virtually eliminated when the two parameters were analysed in conjunction, using discriminant analysis. These results are compatible with the notion that oxidant stress may be involved in human pancreatitis, and
the faster theophylline clearance by the patients compared with 15 controls [94 (7-78) ml/kg/h v 74 (4-11) p<0.001] suggests that P450 induction may contribute to the problem. The corollary that selenium containing supplements should curtail attacks is supported by observations in three further patients (acute two, chronic one) over a mean of 12 months during which a rise in serum selenium was recorded [113 (14) μg/l v 78 (7-9) p<0.05] but no change in molar ratio [3:37 (0-39)% v 4:78 (0-83)].

T88 Experience with a combined percutaneous and endoscopic approach to stent insertion in malignant obstructive jaundice

D A NICHOLSON, D F MARTIN, D E TWEEDLE, AND P N RAO (The Gastrointestinal Unit and Dept of Urology, University Hospital South Manchester, Withington, Manchester) Endoscopic treatment of common duct stones (CDS) fails when stones are too large to pass the sphincterotomy. We are assessing the role of extracorporeal shockwave lithotripsy (ESWL) in patients where endoscopic stone extraction has failed after sphincterotomy. Twelve patients (aged 69–87) with CDS (diameter 10–36 mm) have been treated. Five patients had multiple stones. Stone density measured by computed tomography (CT) varied from 44–110 Hounsfield units. Before ESWL, a nasobiliary catheter was inserted to enable stone localisation. Liver function tests, amylase, urinalysis, bile cultures and upper abdominal CT were performed before and after ESWL to assess safety and complications. Under local anaesthetic and antibiotic cover a maximum of 6000 discharges at 19 KV (max) were administered per session, using a Siemens Lithostar. Six patients required two ESWL sessions.

Fragmentation of stones was seen in nine of 12 patients, and at ERCP, complete duct clearance was achieved in four. One patient developed transient haematuria; otherwise, except for petechiae and haematoma, no complication was seen. All biochemical tests remained normal.

We conclude that ESWL can disintegrate CDS, however subsequent ERCP seems necessary to achieve early duct clearance.

T87 Chronic pancreatitis: influence of surgical pathology of the choice of operative procedure

M LAVELLE-JONES, M P HOLLEY, AND A CUSCHIERI (Departments of Surgery and Pathology, Ninewells Hospital and Medical School, Dundee) The optimum surgical procedure in the treatment of chronic pancreatitis (CP) remains controversial. We have analysed the perioperative findings in 32 consecutive laparotomies for CP to determine the influence of surgical pathology on the procedure of choice. Fourteen patients underwent total pancreatectomy (four with segmental pancreatic autotransplantation). The remainder had various lesser resections, none underwent ductal drainage. Twenty-five patients (61%) had severe extrapancreatic fibrosis (EPF). In 15/25, the lesser sac was completely obliterated. Portal hypertension and cirrhosis coexisted only in two individuals. In contrast, 10 had segmental (left sided) portal hypertension with splenomegaly (9/10) and splenic vein thrombosis (6/10). Pancreatic calcification, sectoral portal hypertension, and pancreatic duct abnormalities only existed in patients with EPF. Seven ducts were strictured and three had a chain of lakes appearance. The remainder were normal. None had generalised duct dilatation. The common bile duct was dilated in seven of 32. Two of these had pancreatic cancer. Overall, three of 32 had ductal adenocarcinoma and one of 32 a cystadenocarcinoma.

In conclusion, EPF and the absence of major duct dilatation frequently renders pancreatic resection the only surgical option in CP. Extrapancreatic fibrosis often presents segmental pancreatic autotransplantations in CP.

T89 Second generation shockwave lithotripsy in the management of retained common duct stones after endoscopic sphincterotomy

D A ROBERTSON, R AYRES, C N HACKING, H SHEPHERD, S BIRCH, AND R WRIGHT (Departments of Medicine and Radiology, Southampton General Hospital, Tremona Road, Southampton, Hampshire) Surgical treatment of malignant obstructive jaundice is rarely curative and carries a high mortality. Endoscopic insertion of a biliary stent is established as a valuable alternative to surgery with reduced mortality and morbidity, but endoscopic stent insertion may fail in up to one of three of cases. We report our experience with a combined endoscopic and percutaneous approach to stent insertion in 14 patients in whom endoscopic stent insertion had failed. During an eight month period 25 patients had successful endoscopic stenting and 11 (31%) failed. Reasons for failure were: Polyga gastronomy two; ampulla in diverticulum one; inability to pass a guide wire across a tight biliary stricture eight. In addition, three patients with external biliary drains were referred for conversion to an internal stent. The average age was 75 years and all had advanced malignant disease not amenable to surgery.

Failure of endoscopic stenting was followed directly by percutaneous transhepatic cholangiography. A guide wire was manipulated across the biliary stricture by this route and retrieved through an endoscope. A wide bore stent was then fed through the endoscope, over the guidewire and across the biliary stricture. The procedure was technically successful in 12 with effective palliation in 10, mean survival 12 weeks. There were no early complications and the introduction of this technique has improved the success rate for endoscopic stent insertion in our Unit from 69% to 97%.

T90 Piezoelectric shockwaves – gall stone lithotripsy and tissue interactions

CH ELL, W KERZEL, E FOERSTER, P HERMANEK, U MISCHKE, AND W DOMSCHKE (Depts of Medicine, Pathology, and Surgical Pathology, Univ Erlangen-Nuremberg, Erlangen/ West-Germany) A new extracorporeal lithotripter of the piezoelectric type (Piezolith, Wolf Inc, FR Germany) was tested for its gall stone disintegration properties and in short and longterm animal experiments for possible tissue interactions.

A total of 211 surgically removed gall bladder stones were investigated. Before shockwave application, the diameter, weight, volume, CT density and MRT signal intensity were determined. 1000–4000 shockwave discharges were applied to 10 surgically removed, stone containing human gall bladders. In six acute and six chronic experiments on mongrel dogs, between 500 and 3000 shockwaves were applied to the gall bladder, liver, spleen, lung, and bowel. Before and after treatment CT, MRT, and laboratory tests were performed.

All 211 stones (max diameter 7–37 mm) were successfully fragmented. Stone volume, weight and diameter are the most important factors involved in the fragmentation process. Fragmentation appears to be independent of chemical composition or calcium content of the stone. Shockwave application to the human gall bladders resulted in disintegration of the stones with no macroscopically or microscopically detectable tissue changes. In acute animal
experiments, small haematomas were observed at surfaces—for example, capsule of the liver, bed of the gall bladder, but also inside the organs.

After four weeks, haematomas have been reabsorbed and only residual lesions are to be seen microscopically.

BASIC SCIENCE
T91–96

T91
Pathogenic potential of anti-α-gliadin antibodies in coeliac disease
R B GALLAGHER, P CERVI, JACINTA KELLY, CLARE DOLAN, D G WEIR, AND C FEIGHERY (Departments of Immunology and Clinical Medicine, Trinity College Medical School, St James’ Hospital, Dublin) The possible pathogenic capabilities of IgG antibodies to α-gliadin in coeliac disease were examined by measuring the subclass profile of these antibodies and their ability to activate complement. In a randomly selected group of coeliac patients, α-gliadin antibodies (AGA) of subclasses IgG1 and IgG3 were significantly raised (p<0.01) in comparison with control groups. This result was, however, influenced by increased total AGA concentrations in the coeliac patients. When a group of coeliac patients and normal controls matched for total IgG AGA were compared, it was found that IgG3 AGA concentrations were higher in the coeliac group (p=0.006) while IgG4 titres were higher in the control group (p=0.005). Because of the marked differences between the ability of IgG3 and IgG4 to activate complement, α-gliadin-specific complement activation was measured. Using randomly selected coeliac and normal sera, the patient group activated higher quantities of complement than controls, p<0.01. Furthermore, when groups were matched for total IgG AGA, sera from coeliac patients again activated greater amounts of complement than controls (p=0.02). Thus AGA in coeliac patients are structurally and functionally distinguishable from AGA in normal controls and have the potential to contribute to the disease process.

T92
Mode of action of 5 amino salicylic acid in inflammatory bowel disease—scavenging of toxic oxygen metabolites?
J G WILLIAMS AND M B HALLETT (INTRODUCED BY PROF L E HUGHES) (Department of Surgery, University of Wales College of Medicine, Cardiff, South Glamorgan) Phagocytic cells, prominent in inflammatory bowel disease, produce toxic oxygen metabolites including superoxide and hypochlorite. These are thought to play an important role in the pathogenesis of tissue damage in inflammation. We have previously shown that 5 amino salicylic acid (5ASA) markedly inhibits neutrophil luminol dependent chemiluminescence (a sensitive indicator of oxygen metabolite production). In attempting to explain this inhibition, we have investigated the possibility that 5ASA acts as a free radical scavenger, by assessing the effect of 5ASA on cell-free oxygen metabolite producing systems.

Superoxide ions were generated in solution by the action of xanthine oxidase on hypoxanthine, and detected by reduction of cytochrome C, measured by absorbance at 550 nm. One hundred micromoles 5ASA produced 14% inhibition of superoxide production. Hypochlorite ions (detected by luminol dependent chemiluminescence) were generated by hydrogen peroxide and peroxidase or by adding 0.005% sodium hypochlorite. Fifty micromoles 5ASA produced 100% inhibition of control responses. The dose of 5ASA producing 50% inhibition (K50) was 0.75 μM. Fifty micromoles sulphalaprazine produced 70% inhibition (K50, 10 μM) and sulphapyridine in doses up to 250 μM had no effect on chemiluminescence.

These results show that 5ASA acts as a specific scavenger of toxic oxygen metabolites, especially hypochlorite, a property which may be important in its mode of action.

T93
Visualisation of somatic mutation provides an inducible clonal marker system that shows that colonic crypts are maintained by a single stem cell
D F R GRIFFITHS, G T WILLIAMS, S DAVIES, D WILLIAMS, AND E D WILLIAMS (Department of Pathology, University of Wales College of Medicine, Heath Park, Cardiff) Glucose-6-phosphate dehydrogenase (G6PD) is an X-linked enzyme which is easily demonstrable histochemically throughout mouse colonic epithelium. In normal mice given weekly subcutaneous injections (20 mg/kg) of the colon specific carcinogen dimethylhydrazine (DMH) we have observed focal enzyme loss in small numbers of individual crypts, randomly scattered throughout the colonic mucosa. The affected crypts show uniform enzyme loss throughout, ceasing abruptly on the surface epithelium adjacent to the crypt opening. No crypts showing partial enzyme loss were seen. The change was not observed in age and sex matched untreated animals. Two of 141 mucosal tumours (adenomas) induced after 18–27 weekly injections of DMH also showed a similar uniform loss of G6PD. The results suggest a sporadic heritable carcinogen-induced mutation of the G6PD gene in a single long life stem cell which gives rise to all of the cells of the affected crypt. They also support the suggestion that DMH-induced colonic tumours are of monocrypt origin. This histochemically detectable X-linked enzyme loss provides a valuable inducible clonal marker system which may be used for further study of normal and abnormal crypt cell kinetics and organisation, and potentially in studies of human colonic carcinogenesis.

T94
Giardia lamblia cloned genomic DNA probes: uses in faecal diagnosis and genetic analysis of clinical isolates
P D BUTCHER, C CLARK, AND M J G FARTHING (Department of Gastroenterology, St Bartholomew’s Hospital, West Smithfield, London) The varied clinical forms of infection with Giardia lamblia from asymptomatic to severe chronic diarrhoea with malabsorption may be caused by strain differences or host immune responses. Faecal microscopy is labour intensive and immunodiagnosis by detection of faecal antigen is not widely available. The potential sensitivity and specificity of cloned DNA probes for G lamblia would provide powerful diagnostic and molecular epidemiological reagents to study these problems. Giardia species specific DNA probes have been derived from a plasmid library of G lamblia strain Portland 1 genomic DNA by in situ colony hybridisation with DNA blotted from three strains of Giardia and other closely related protozoa. DNA from a minimum of 105 cysts in 0.1 g faeces was detected by a dot blot DNA hybridisation assay. Mechanical and enzymatic methods of cyst DNA extraction are being tested to increase the sensitivity of detection. Restriction fragment length polymorphisms of Giardia strains Portland 1, WB and a local isolate Bart’s 1 were analysed using three probes. No differences have been observed after digestion with four restriction endonucleases indicating a high degree of homology between these.
strains. Probe/enzyme combinations that differentiate clinical isolates are being sought so that strain type may be correlated with clinical severity, geographic location and reinfection rates. Using this approach the effect of strain variation on the immunopathology of giardiasis may be explored.

**T95**

**Effects of dietary fibre on intestinal epithelial cell proliferation in conventional and germfree rats**

R A Goodlad, B Ratcliffe, J P Fordham, W Lenton, and N A Wright (Royal Postgraduate Medical School, Cancer Research Campaign Cell Proliferation Unit, Department of Histopathology, Hammersmith Hospital, London, Polytechnic of North London, Holloway Road, London, and AFRC Institute of Food Research, Reading, Berkshire) It has been previously shown that feeding starved rats with an elemental diet supplemented with dietary fibre (but not inert bulk), is capable of stimulating intestinal epithelial cell proliferation throughout the gastrointestinal tract (Goodlad et al, Gut 1987; 28: 171–80). The aim of the present experiment was to investigate the role of hind gut fermentation and short chain fatty acid release in this.

Three groups of 10 germ free rats and three groups of 10 conventional rats, were used. All groups were starved for three days and then refed for two days with either an elemental diet (Flexical); or Flexical plus 30% kaolin; or Flexical plus 30% of a fibre mixture (1 part Ispaghula gel to 9 parts Trifyba). Cell production was measured by counting the rate of entry of vincristine arrested metaphases in microdissected crypts.

In conventional rats the fibre mixture was associated with a significant (p<0.01) increase in intestinal crypt cell production rate in the small intestine when compared with the elemental diet only group (from 11.56±2.00 to 21.60±2.5) and in the colon (from 2.17±1.21 to 13.94±3.24). Kaolin had no effect. The addition of fermentable fibre to the germ-free rats had no influence on cell proliferation, thus it can be concluded that it is the products of hind gut fermentation, not fibre per se that stimulate intestinal epithelial cell proliferation.

**T96**

**Molecular cloning and expression of Clostridium difficile toxin A and macrolide resistance determinants in Escherichia coli**

Brendan W Wren, Peter P Mullany, Christopher L Claydon, and Soad Tabaqchali (Department of Medical Microbiology, St Bartholomew's Hospital Medical College, West Smithfield, London) Clostridium difficile is recognised as the major cause of pseudomembranous colitis (PMC) and antibiotic associated diarrhoea, its pathogenicity being related to the production of an enterotoxin, toxin A. The use of antibiotics, in particular the macrolide, clindamycin, has also been shown to be important in the development of C difficile related disease, and, at the genetic level, antibiotics may play a direct role in the regulation of potential virulence factors such as toxin A. In this study, two different cloning strategies were used to clone the toxin A and macrolide resistance genes, to investigate the genetic basis of toxin production and antibiotic resistance in C difficile. Two gene libraries were obtained from a toxigenic, multiresistant isolate of C difficile from a patient with PMC. Toxin A was cloned into the bacteriophage vector LambdaL3. The toxin A positive clone, lambda5, expressed a 235 kDa protein which retained the cytotoxic and haemagglutinating properties characteristic of toxin A. The macrolide resistance determinant was cloned into the cosmid vector pHC79 where the clone pER3 exhibited high levels of resistance to erythromycin. The 14.3 kb toxin A insert hybridised positively to various regions of the 31 kb cosmid clone containing the C difficile derived macrolide resistance determinant, suggesting that the two genes are linked on the C difficile chromosome.

**T97**

**Dysphagia in AIDS: symptoms, causes and value of investigations and treatment**

G M Connolly and B G Gazzard (St Stephen’s Hospital, London) One hundred and forty consecutive patients who were human immunodeficiency virus (HIV) antibody positive and developed AIDS were studied prospectively. Forty patients had oesophageal disease, the commonest cause being candidiasis. Ten patients had discrete oesophageal ulceration caused by cytomegalovirus (CMV), herpes simplex or associated with aphthous ulceration of the mouth. The endoscopic appearances of the ulcers were distinct, enabling a macroscopic diagnosis to be made, but repeated biopsies were required in half the patients to confirm the cause of the ulceration histologically. Non-specific inflammation of the oesophagus was seen in all 40 patients. The likely cause of dysphagia was obvious from inspection of the mouth in all but seven patients. Barium swallow examination only revealed an abnormality in half the patients with dysphagia, however, and was unable to predict its aetiology.

All the patients had dysphagia which was painful and equally severe for solids and liquids, yet in only two cases did severe weight loss result. There was only one patient who developed an oesophageal stricture. All eight patients with CMV or herpes induced ulcers responded well symptomatically to phosphonoformate or intravenous Acyclovir. One aphthous ulcer of the oesophagus responded dramatically to thalidomide. The median survival from the development of dysphagia was only five months.

**T98**

**Reproducibility of 24 hour ambulatory oesophageal pH monitoring**

C S Ball, I R Jenkinson, and A Watson (Royal Lancaster Infirmary, Lancaster) Twenty four hour ambulatory pH monitoring has proved a useful diagnostic and research tool in the study of patients with gastro-oesophageal reflux. Its validity has been questioned, however, on the grounds that it may not provide reproducible data. Eighteen patients with endoscopic oesophagitis, recruited into an approved therapeutic trial, underwent 24 h ambulatory pH monitoring on two occasions, eight weeks apart, before the administration of anti-reflux medication. Eight parameters obtained from each pH profile by computer analysis were compared, using Spearman’s Rank Correlation Test, with the corresponding parameters obtained eight weeks later. Percentage time spent at pH<4 for upright and supine periods and number of reflux episodes >5 mins were all highly reproducible parameters (p<0.001). Fair correlation was found with number of supine episodes >5 mins, longest upright episode (p<0.02) and longest supine episode (p<0.05). The number of upright reflux episodes was the least reproducible parameter (p<0.1). This study has confirmed that highly reproducible data can be obtained by 24 h ambulatory pH monitoring. It is recommended that attention be directed towards the most reproducible
parameters of the pH profile when evaluating sequential studies in clinical trials.

T99

Ten year study of cimetidine or surgery for severe ulcer dyspepsia

D T HANSELL, M MCGUSHIN, R N MEDDINGS, I S SMITH, G R GRAY, AND G GILCREASE (Division of Surgery, Victoria Infirmary, Glasgow) In 1977, 55 patients with severe longstanding dyspepsia originally selected as candidates for elective duodenal ulcer surgery were instead offered maintenance cimetidine. Forty six patients have been reviewed at 10 years by personal interview and examination, or by interview with a relative. Twenty one required surgery in the first three years but since then no further patient has undergone surgery. Four of these patients have had endoscopically proven recurrent ulcer, while two others have had significant dyspepsia which responded to cimetidine. Of the 25 patients who have avoided surgery, 17 have remained on continuous cimetidine, 400 mg nocte while eight have used full dose cimetidine intermittently. Of the 17 on continuous cimetidine, six admitted to episodes of recurrent symptoms controlled by a temporary increase in cimetidine dosage. Three of these patients had endoscopy during an acute episode and each had duodenal ulceration. All eight patients on intermittent cimetidine relapsed within 8–12 weeks of drug withdrawal. Two of these patients ended up during an acute episode had duodenal ulceration, but those asymptomatic at review endoscopy had no ulceration.

By using cimetidine, over 50% of patients selected for surgery avoided operation over this 10 year period, although none has had drug free remission.

T100

Acupuncture inhibits the response to sham feeding

Y Y LI, S G CHIVERTON, G TOUGAS, AND R H HUNT (McMaster University Medical Center, Hamilton, Ontario, Canada) Acupuncture has been used empirically in China for the treatment of gastrointestinal disorders, and in unanaesthetised dogs has been shown to decrease intragastric acidity. A randomised placebo controlled study of the effect of electroacupuncture (EA) on basal acid output (BAO) and maximal stimulated acid output after sham feeding (SMAO) was performed in healthy male volunteers. On two different days, in random order, BAO was measured in eight subjects for one hour before and after 15 mins EA which was assigned to (1) the Zusanli points of the stomach meridians or (2) placebo EA (PEA) not applied to any known active point. Subsequently 10 subjects were randomised after one hour for BAO to receive either 15 mins EA or PEA synchronously with a sham feed, and the gastric juice collected for a further hour.

Electro acupuncture resulted in a decrease in BAO from 3.43±1.43 mmol/l to 2.42±1.52 mmol/l (p<0.01) compared with PEA, 3.17±1.48 mmol/l to 3.40±1.63 (NS). The difference in response between PEA and EA was significant p<0.03. SMAO after PEA 21±3.27 mmol/l (p<0.001); compared to SMAO after EA 3.62±3.05 mmol/l (p<0.01). The difference in response between EA and control was significant p<0.001.

Electroacupuncture results in a decrease in both basal and maximal sham fed acid output of 30% and 80% respectively. We conclude that acupuncture reduces basal and vagally mediated acid secretion, presumably by a central mechanism.

T101

Treatment of refractory peptic ulcer with omeprazole

K D BARDHAN, J NAESDAL, G BIANCHI-PORRO, M LAZZARONI, R F C HINCHLIFE, MARY THOMPSON, PAMELA MORRIS, M J DALY, N J H CARROLL, AND A WALAN (District General Hospital, Rotherham, Dept of Gastroenterology, Regionsjukhuset, Linkoping, Sweden, Ospedale L. Sacco, Milan, Italy, and Astra Clinical Research Unit, Edinburgh) We assessed the effectiveness of omeprazole (Om) in treating refractory peptic ulcer (RPU), which is one that fails to heal after at least eight weeks treatment with H2-RA (cimetidine 0.8–1 g or ranitidine 0.3 g daily). Patients with RPU were randomly allocated to treatment with either Om 40 mg daily or continued H2-RA for up to eight weeks. Treatment was double blind. Endoscopy, clinical assessment and laboratory studies were done every four weeks. If the ulcer(s) persisted at eight weeks in patients who had been assigned to H2-RA, then open treatment with Om was given for a further four weeks. Patients in the two treatment groups (Om n=54, H2-RA n=53) were of comparable age, sex ratio, smoking and drinking habits, and in the duration of pre-trial H2-RA treatment. Cumulative healing rates (per protocol analysis) were: at four weeks Om 87%, H2-RA 39% (p<0.001, 95% CI for difference 31% to 65%); at eight weeks Om 98%, H2-RA 60% (p<0.001; 95% CI for difference 23% to 53%). Om healed the ulcer in 21/22 (95%) patients with ulcers unhealed after H2-RA therapy. Daytime epigastric pain was significantly (p=0.01) less frequent in the omeprazole group after four weeks. Treatment was well tolerated and there were no withdrawals for adverse events.

In conclusion, omeprazole 40 mg is significantly more effective than continued H2-RA treatment in the healing of refractory peptic ulcer.

T102

The British Society of Gastroenterology. A further report

F T DE DOMBAL, H THOMPSON, G T WILLIAMS, A B PRICE, A G MORGAN, A SOFTLEY, S E CLAMP, AND B J UNWIN (Clinical Information Science Unit, University of Leeds, Leeds) This presentation reviews the status of the BSG Early Gastric Cancer Survey as of January 1988. The survey comprised 319 cases from 41 hospitals; 132 (41%) were agreed to have early gastric cancer (EGC), and 63 (19.7%) dysplasia.

There was good agreement between the original ‘centre’ diagnosis and a panel of pathologists as regards EGC v dysplasia (159 cases of 170, 93.5%). Agreement was less good on the extent of gastric cancer (76.2%).

Most EGC cases (84.3%) were only diagnosed firmly on biopsy. In 33 EGC cases coming to barium meal, cancer was only suspected in nine (36.4%); in seven cases (21%) the stomach was said to be normal. In 114 EGC cases coming to endoscopy, gastric ulceration was the commonest finding; though this was said to be of ‘benign appearance’ in 46 cases (40.4%).

Symptoms of cases with EGC and dysplasia were subjected to computer analysis. The computer correctly identified 76% of EGC cases, and placed over 90% into a high risk group – that is, warranting urgent endoscopy.

On preliminary (actuarial) follow up the overall five year survival for all cases sent as EGC was 87%. In cases agreed by the panel to have early gastric cancer, the five year survival rate was over 90%. Amongst cases agreed by the panel to have advanced gastric cancer, however, the four year survival was only 70%. Almost one third of 65 patients with ‘dysplasia’ on entry to the survey came within four years to surgery for ‘EGC’.
LIVER
T103–108

T103 Differential expression of the transferrin receptor in liver and gut in hereditary haemochromatosis (HH)

M LOMBARD, A BOMFORD, R POLON, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital and School of Medicine and Dentistry, London) The metabolic abnormality in hereditary haemochromatosis (HH) remains uncharacterised despite the inappropriate absorption of iron. Examination of transferrin receptor (TfR) expression in the liver of patients with HH has shown an appropriate and reversible reciprocal relationship with cellular iron stores. To assess whether such regulation occurred at the site of iron absorption, we examined TfR expression by immunohistochemical technique in small bowel biopsies from control subjects and patients with primary and secondary iron overload.
Five patients with untreated HH showed expression of the receptor in the subnuclear region of duodenal epithelial cells indistinguishable from control biopsies. All patients had shown downregulation of TfR in their liver biopsies. In contrast, three patients with secondary iron overload due to β-thalassaemia showed an absence of TfR in duodenal epithelial cells. While the role of TfR in iron absorption is unclear, its persistence in the presence of a marked increase in body iron in HH is inappropriate. Normal regulation of TfR in the liver and other cells suggested that a generalised defect of cellular iron metabolism does not operate in HH. The present study supports the concept of a tissue specific failure of cellular iron homeostasis localised to the specialised iron absorbing cells of the duodenal mucosa.

T104 Prognosis and survival in primary biliary cirrhosis (PBC): does colchicine help?

C BABBWS, A SMITH, B P ROWAN, L HUNT, N Y HABOUB, AND T W WARNES (University Department of Gastroenterology and Computation, Manchester Royal Infirmary, Department of Pathology, University Hospital of South Manchester, Manchester) New tests to predict survival would be valuable in PBC. Although treatment remains unsatisfactory, colchicine improves biochemistry and may be of benefit. The AIMS of this study were to compare the prognostic importance of serum procollagen III peptide (P3NP) with other known prognostic variables in PBC and to assess the influence of colchicine on survival.
Sixty five patients with PBC were studied (59 women; mean age 57/8 years). Twenty nine were symptomatic and 36 asymptomatic. Mean follow up was 37 months (0–87). P3NP was measured by RIA (Hoechst, FRG).

Variables with a significant influence on survival (log rank test) were serum P3NP (p<0.001), serum bilirubin (p<0.001), prothrombin index (p<0.001), histological cholestasis (p<0.001), symptom status (p<0.001), age (p<0.001) and serum AST (p=0.02). Cox proportional hazards model was used to establish independent variables and to assess the influence of colchicine treatment. Raised serum P3NP (p<0.001), raised serum bilirubin (p<0.001), cirrhosis (p=0.001), presentation with symptoms (p=0.012), and increasing age (p=0.03) all had an adverse effect on survival. Colchicine treatment improved survival (p=0.005).

We conclude that (1) Serum P3NP is an important new prognostic indicator in PBC. (2) Colchicine treatment improves survival in PBC when other prognostic factors are adjusted for.

T105 Reduced sympathetic reactivity in cirrhosis: evidence for a postreceptor, vascular defect

A J MACGILCHRIST, N DEIGHTON, D SUMNER, AND I L REID (University Dept of Materia Medica, Stobhill Hospital, Glasgow) In cirrhosis, peripheral vasodilatation persists despite sympathetic overactivity. We have attempted to identify the site of the defect in sympathetic vascular reactivity by studying alpha adrenoreceptor status and selective sympathetic agonists in 10 cirrhotics and 10 matched controls. Number (Bmax) and affinity (Kd) of alpha2 adrenoceptors on platelets were calculated by Scatchard analysis of specific binding to [3H]yohimbine. Bmax and Kd were unchanged in cirrhotics and controls (Bmax 24-9 v 22-1 fmol/1012 platelets; Kd 4-6 v 5-5 nmol 1). There is thus no down regulation of alpha receptors, nor any evidence of interference at the receptor site by false neurotransmitters. Phenylephrine (PHE), alpha-methyl noradrenaline (AMN), and isoprenaline (ISO), selective agonists to alpha1, alpha2, and beta receptors respectively, were infused intravenously and the doses required to raise BP by 20 mmHg (PD20) or heart rate by 20 bpm (CD20) were calculated from quadratic dose-response curves. The mean PD20 was higher in cirrhotics than controls for both PHE (2-34 v 1-51 μg/kg/min, p<0.05) and AMN (0-59 v 0-36 μg/kg/min, p<0.01), but the mean CD20 for ISO was similar in the two groups (17-6 v 20-6 ng/kg/min, p=0.49). This reduced responsiveness to alpha but not beta-receptor mediated stimulation suggests a local, vascular defect rather than generalised sympathetic desensitisation. These studies provide indirect evidence that reduced sympathetic reactivity in cirrhosis is due to a post-receptor defect within vascular smooth muscle. This localisation may assist the search for the underlying cause of the peripheral vasodilatation which in turn may be important in the initiation of ascites.

T106 Measurement of liver blood flow using a new, non-invasive radioisotopic technique

H L SMART, WENDY TINDALE, D C BARBER, AND D R TRIGER (University of Sheffield, Department of Medicine and Medical Physics, Royal Hallamshire Hospital, Sheffield) A triple tracer radioisotopic technique has been used to study liver blood flow in 36 subjects (20 cirrhotics, 16 non-cirrhotics). The method utilises dynamic gamma camera scanning and peripheral venous blood sampling after injection of 99mTC sulphur colloid and 99mTC human serum albumin (day 1) and 123I-methylnoradrenaline (day 3). Computer analysis of the data yields values for total liver blood flow (TLBF) and arterial to total flow ration (A:T) from which portal vein blood flow (PVBF) can be derived. Extraction efficiency (EE), half time of hepatic uptake (t1/2) and hepatocellular clearance rate (HCR) can also be calculated. Although TLBF and PVBF did not differ significantly between groups [values expressed as mean (SD)] cirrhotics, TLBF 2951 (1038) ml/min, PVBF 1390 (508) ml/min; non-cirrhotics, TLBF 2185 (649) ml/min, PVBF 1383 (358) ml/min], cirrhotics had a significantly (p=0.0001) higher proportion of arterial flow [53 (10)%] than non-cirrhotics [36 (8)%]. EE was significantly (p<0.02) reduced and t1/2 significantly (p<0.0001) prolonged in cirrhotics compared to non-cirrhotics. [EE 20 (9)% v 31 (13)%; t1/2 5-1 (1-9) min v 2-4 (0-4) min respectively] with no significant difference in HCR between groups. This technique offers considerable potential in studying
liver blood flow and its therapeutic manipulation in patients with portal hypertension.

**T107**

**Effects of nalmefene in cirrhosis**

**J R THORNTON AND M S LOSOWSKY** (Department of Medicine, St James’s University Hospital, Leeds) We found that plasma methionine and leucine enkephalins are markedly raised in liver disease. Therefore we gave nalmefene, a pure opioid antagonist, orally to 11 patients with cirrhosis (nine primary biliary (PBC), one alcoholic, one cryptogenic). In a dose one-sixtieth of that devoid of subjective effects in health, nalmefene produced a florid reaction, manifest by nausea, abdominal pain, constipation, bradycardia, raised arterial pressure and unpleasant cerebral disturbances, sometimes including hallucinations. To minimise withdrawal, patients were hospitalised, given clonidine for the first week and a gradually increasing dose of nalmefene to 20–60 mg tds. Most withdrawal symptoms settled within a few days. Eight patients continued nalmefene for six months or more. Pruritus and fatigue were assessed by visual analogue scales, 0–10, for two weeks period before and at 1, 3, and 6 months. Both were rapidly and considerably alleviated: Pruritus (baseline) median 7.4, range 6.4–9.8; at one month 0.2, 0–2.4 (p<0.001); at three months 0.2, 0–1.3 (p<0.001); at six months 0–3, 0–1.8 (p<0.001). Fatigue (baseline) 6.7, 1.3–9.6; at one month 2.6, 1.0–6.9 (p<0.01); at three months 2.0, 0.6–6.8 (p<0.01); at six months 2.3, 0.8–4.6 (p<0.01). Plasma bilirubin (µmol/l) which had risen from 58, 8–122 to 71, 11–173 (p<0.05) in the six months preceding nalmefene, fell to 53, 11–162 at 1 month (p<0.01), 54, 11–143 at three months (p<0.02), and 48, 14–138 at six months (p<0.02).

Thus, nalmefene produces opioid withdrawal in cirrhosis. In patients with PBC, it relieves pruritus (perhaps by blocking opioid-mediated histamine release) and fatigue. The fall it produces in plasma bilirubin may indicate that there is a functional component to the cholestasis of PBC which is mediated by increased opioid peptide activity.

**T108**

**Longterm follow up of patients with chronic active hepatitis maintained in remission on azathioprine alone**

**P J JOHNSON, J G McFARLANE, AND ROGER WILLS** (Liver Unit, King’s College Hospital, London) In a short term controlled trial we have reported that, once patients with autoimmune chronic active hepatitis (CAH) have entered remission, corticosteroid therapy can usually be withdrawn and remission maintained with azathioprine 2 mg/kg. We now report on the subsequent progress of patients in this trial and that of 40 further patients treated in a similar manner, for up to 36 months (mean follow up=22 months) from the time prednisolone was withdrawn completely. To date 10 of the 67 patients (15%) have required reintroduction of corticosteroid therapy: four had biochemical and clinical relapse, in four azathioprine had to be withdrawn because of severe myelosuppression, and in two severe arthralgia could not be otherwise controlled. Haematological appearances in those 37 patients who have so far undergone liver biopsy showed no deterioration, and at most mild activity in 35 and moderate activity in two. Apart from occasional severe myelosuppression, the only major side effect was arthralgia which occurred in 70% and in four this remains severe at more than one year. Three patients have developed malignant disease, the primary sites being pharynx, lung, and liver. Maintenance of remission on high dose azathioprine is a useful therapeutic option in CAH patients particularly where steroid side effects are prominent. If biochemical remission is induced before withdrawal 85% may be expected to remain in remission long term.

**ENDOSCOPY/oesophago/gastro/duodenal POSTERS 2 T109–126**

**T109**

**Endoprosthesis for malignant liver hilum stricture: report of 171 cases**

**A POLYDOROU, S R CAIRNS, J DOWSEST, D VAIRA, P R COTTON, AND P R SALMON** (Department of Gastroenterology, Middlesex Hospital, London) Relief of jaundice in patients with malignant obstruction of the biliary tree may be achieved by bypass surgery or insertion of a prosthesis endoscopically. The first method has a high mortality in poor risk patients. We present our data concerning palliation of jaundiced patients with insertion of a prosthesis endoscopically. One hundred and seventy one patients (M/F 66/105, mean age 71 years) who had a primary or secondary tumor involving the biliary tree and were judged to be poor surgical candidates were treated endoscopically. Patients were divided into three groups according to the type of stricture (type I, 51; type II, 66; type III). The prosthesis was successfully inserted endoscopically in 128 (75%) at the first attempt and in 25 (15%) at the second. EST was done in 97 (57%). Combined procedure was done in the remaining 18 (10%) with only one failure in a patient with type III stricture. Bilirubin decrease of more than 30% was achieved in 92% of the patients with type I stricture, in 85% with type II and in 78% with type III. Thirty day mortality was 7.4%, 15.7%, and 28.8% for type I, II, and III strictures respectively. There were significantly more complications in patients with type III hilar strictures (23%) compared with the other two groups (13% and 5.5% for II and I strictures). The mean survival was 35.7, 29, and 26.5 weeks for I, II, and III strictures respectively. We conclude that endoprosthesis is a safe and effective palliative treatment for unresectable malignant liver hilum strictures.
ment in all and lower Bil levels in all but one cirrhotic patient. Temporary stenting was followed by stable liver function for up to 11 months after stent removal.

Endoscopic stent placement produced symptomatic and biochemical improvement in patients unfit for surgery and perhaps should be considered as the initial therapy for most patients with postoperative biliary strictures.

T111 Role of general practitioner education in affecting referral to an open access gastroscopy service

J D HARRISON AND D L MORRIS (Department of Surgery, Queen’s Medical Centre, Nottingham) To investigate the effect of education on the referral practice of GPs to an open access gastroscopy service we have randomly selected two local group practices of equivalent size and socio-economic status to participate in the study. One practice was educated by means of an audiovisual presentation and printed material on the advantages of diagnosing gastric cancer in its ‘early’ stage, whilst the other was sent a letter offering the service without including any education material. Over a nine month period the educated (E) group referred 125 patients for gastroscopy, whilst the non-educated (NE) group referred eight patients. There were no significant differences between the groups for H2 blocker or simple antacid therapy, family history of peptic ulcer or gastric cancer, previous gastric surgery or smoking history. Endoscopic findings in the E group include two carcinomas, four Barrett’s oesophagus, three oesophageal candidiasis, one achalasia, seven gastric ulcers, nine duodenal ulcers, and a group of gastric ‘pre-malignant’ conditions including 12 patients with intestinal metaplasia and six with dysplasia. By comparison the NE group yielded six patients with mild oesophagitis, five of whom also had mild antral inflammation. We conclude that GP education favourably affects the rate of referral to an open access gastroscopy service.

T112 Endoscopic sphincterotomy for common bile duct stones in patients with intact gall bladders

D T HANSELL, M A MILLAR, W R MURRAY, G R GRAY, AND G GILLESPIE (Divisions of Surgery and Radiology, Victoria Infirmary, Glasgow, and University Department of Surgery, Western Infirmary, Glasgow) Endoscopic sphincterotomy was performed in 121 patients (age range 34–92 years; median 80 years) with intact gall bladders and common bile duct (CBD) stones. Clearance of the CBD by basket extraction at the time of sphincterotomy was attempted in 97 patients and was accomplished at the first attempt in 57 patients. In the remaining patients the CBD was cleared by spontaneous emptying, repeat endoscopy with basket retrieval, or by surgery. Immediate complications occurred in five patients (two haemorrhage, two perforation, one haemorrhage/perforation). One of the patients with haemorrhage required surgery and subsequently died. Three patients required surgical clearance of the CBD within two weeks of sphincterotomy. Of the 101 patients reviewed 12–72 months (median 24 months) after sphincterotomy, 18 required cholecystectomy for recurring biliary symptoms one to 24 months after sphincterotomy. A further seven had recurrent biliary colic or cholangitis necessitating further sphincterotomy and stone retrieval in three of these patients. The remaining 76 patients have been free of all biliary symptoms since sphincterotomy.

Endoscopic sphincterotomy is an effective treatment for CBD stones in high risk patients, but subsequent cholecystectomy is required in a significant number of patients because of continuing biliary symptoms.

T113 Comparison of the value of mesenteric angiography and on table colonoscopy in massive acute large bowel haemorrhage

P D CUSSONS, E W L FLETCHER, AND A BERRY (John Radcliffe Hospital, Oxford) Emergency investigation of large bowel haemorrhage has routinely included mesenteric angiography to identify the site of bleeding in preparation for surgery. Nine cases over 18 months were identified from the angiography register and reviewed retrospectively. Angiography showed the bleeding point in only one case, rendering colonoscopy unnecessary. That patient became shocked, however, requiring six units of blood during angiography. A second patient suffered cardio pulmonary arrest during angiography. The mean time taken was one hour 30 minutes, a delay of over two hours before proceeding to surgery.

Table colonoscopy with antegrade lavage showed the bleeding site in seven of nine cases. The mean time for operation was three hours.

In one patient a rectal tear seen sigmoidoscopically was oversewn, and one patient stopped bleeding spontaneously. There was one postoperative death from an unrelated cause.

We conclude that there is no place for emergency mesenteric angiography in massive acute large bowel haemorrhage and that early surgery with antegrade lavage and on table colonoscopy is the treatment of choice.

T114 Is duodenal diverticulum a risk factor for sphincterotomy?

D VAIRA, S R CAINRS, J F DOWSETT, AND P R SALMON (Department of Gastroenterology, The Middlesex Hospital, London) The aim of this study was to assess the (1) Failure rate of diagnostic ERCP (2) Failure rate of sphincterotomy (EST) (3) Complication rate of EST in patients with and without duodenal diverticulum (DD). During a four year period to November 1987, ERCP was attempted in 2458 consecutive patients; DD were found in 271 (11%) - M/F 117/154. The prevalence of DD increased with age. The indication for EST in patients with DD was: stones 85%, pancreatic carcinoma 5-4%, papillary carcinoma 5-4%, hilar stricture 1-6%, pancreatitis 2-1%, sump syndrome 0-5%.

The failure rate of diagnostic ERCP in patients with and without DD was 4-4% (12/271) and 2-9% (72/2458) respectively. EST failure rate in patients when cholangiography was successful with and without DD was 1-1% (2/186) and 0-2% (3/1274) respectively. EST failure rate when cholangiography was not obtained and EST was intended in patients with and without DD was 5-9% (11/186) and 2-3% (30/1274) respectively. The immediate complication rate in patients with and without DD was similar (2%). Haemorrhage 1-8% and pancreatitis 0-2% in patients with DD.

We conclude that (1) DD makes cannulation of the papilla more difficult; (2) EST fails more frequently (2-5 fold) in patients with DD; (3) Complication rate of EST with or without DD is similar.

T115 Comparison of bursting pressures of human colon and intraluminal pressures reached during colonoscopy

D S BURKITT AND I DONOVAN (Department of Surgery, Dudley Road Hospital, Birmingham) Perforation occurs at about 0-25% of
diagnostic colonoscopies. Perforation has been attributed to overdistension and intraluminal pressures during colonoscopy measured by perfused tube have been reported exceeding 130 mmHg.

Bursting wall tension was determined in 12 freshly excised segments of sigmoid colon by rapidly infusing saline until rupture. Diameter, length, pressure, and volume infused at bursting were noted. Values are expressed as mean (SD). Mean bursting pressure was 133 mmHg (25) at mean diameter of 4.1 cm (0.36); calculated bursting wall tension was therefore 3.6×10⁶ dynes cm⁻² (0.8×10⁶). From these figures a sustained intraluminal pressure of, for example, 70 mmHg at radius of 4 cm or 46 mmHg at 6 cm may be sufficient to cause rupture.

Intraluminal pressure was monitored during 14 colonoscopies for a total of 6-2 hours by both perfused and non-perfused open ended fine bore tubes. With the former maximum recorded pressure was 140 mmHg whereas with the latter it was only 58 mmHg. For 61% of the time pressures were less than 20 mmHg and exceeded 30 mmHg for only 4% of the time. Previous data based on a perfused tube are misleading as peak pressures arise from tube blockage giving high spike pressures. With avoidance of excessive gas insufflation there is a wide margin of safety from pneumatoic injury.

T116
Use of omeprazole in the management of chronic oesophageal ulceration after injection sclerotherapy

A GIMSON, R POLSON, D WESTABY, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital and Medical School, London) Transient oesophageal ulceration is a common finding after sclerotherapy of varices. In a small proportion these become chronic and resistant to conventional therapy. Such chronic ulcers have been associated with pain, stricture formation and recurrent haemorrhage. We have examined the use of omeprazole, a proton pump inhibitor, in the treatment of nine patients (six women, three men, age range 27-86 years) with cirrhosis (PBC four, sclerosing cholangitis two, alcohol one, crypogenic two) who developed an oesophageal ulcer after a mean of 13 (range 8-21) sessions of sclerotherapy. The ulcers had been present for three to 54 months despite prolonged treatment with high dose H₂-receptor antagonists and sucralfate. In each case one or more complications had occurred – severe pain in three, stricture formation in four, and recurrent haemorrhage in seven cases. After an eight week course of omeprazole 20 mg bd endoscopy confirmed complete healing of the ulceration in all nine cases with symptom resolution. In two cases the ulcer recurred, with associated bleeding within six weeks of discontinuing the treatment. Both responded to repeat therapy.

These results confirm the efficacy of omeprazole for postsclerotherapy ulceration and imply that acid-pepsin has a role in perpetuating such ulcers.

T117
Measurement of reflux episodes during intra-oesophageal pH monitoring

L R JENKINSON, T L NORRIS, AND A WATSON (Department of Surgery, Royal Lancaster Infirmary) Recent recommendations suggest that pH 4 be used as the cutoff point for intraoesophageal pH monitoring and that a reflux episode is the interval below this value. Previous workers have used a fall below pH 4 and return to pH 5 as the end points to account for the effects of repetitive episodes. Which definition correlates better with the severity of oesophagitis is at present unknown.

Thirty three patients with oesophagitis (grade I-IV) and 16 healthy asymptomatic subjects were evaluated using 24 hour ambulatory intraoesophageal pH monitoring. Data from each subject were analysed first using pH 4-4 as the definition of a reflux episode and subsequently pH 4-5. Spearman’s Rank correlation coefficient was calculated for each parameter (no episodes, longest episode, number exceeding 5 min) during a 16 hour upright and an eight hour supine period to establish which definition was more appropriate.

Using pH 4-4 as the definition, only the number of episodes in the upright period (pH 4.4=0.74; pH 4.5=0.66) and surprisingly the number of supine episodes exceeding five minutes (pH 4.4=0.71; pH 4.5=0.69) showed a greater correlation than the pH 4.5 parameters. The remaining six parameters correlated better using pH 4.5.

This study has shown that overall pH 4.5 provides a better definition for a reflux episode although the number of daytime episodes are more accurately assessed using pH 4-4 as the cutoff points.

T118
Acid sensitivity in reflux oesophagitis with and without complications

C S BALL AND A WATSON (Royal Lancaster Infirmary, Lancaster) The observation that many patients with reflux stricture and Barrett’s oesophagus have little or no antecedent history of reflux symptoms led us to investigate the sensitivity of the oesophageal mucosa to acid perfusion in these patients and, for comparison, in others with uncomplicated reflux oesophagitis. Twenty patients with uncomplicated endoscopic oesophagitis (group A) and 20 with reflux stricture, seven of whom had associated Barrett’s oesophagus (group B) were studied. The distal oesophagus was perfused sequentially with 30 ml isotonic saline and 30 ml 0·1 N HCl at a rate of 6 ml/min. Subjective sensitivity to acid perfusion was scored on a scale of 0–6, higher scores reflecting a rapid onset of severe symptoms. All group A patients scored 3 or over, and 14 (70%) scored the maximum of 6. In Group B, eight (40%) experienced no symptoms during acid perfusion and only three (15%) scored the maximum of 6. There was no significant difference in sensitivity between stricture patients with or without Barrett’s oesophagus. This study suggests that impairment of subjective sensitivity to acid in the distal oesophagus may explain the late presentation with complications of some patients with reflux oesophagitis. Symptomatic assessment will be an unreliable guide to therapeutic response in such patients.

T119
The pH and concentration of bile in the oesophagus

D L STOKER, J G WILLIAMS, J F DEWAR, AND D G COLIN-JONES (Queen Alexandra Hospital, Portsmouth, Hants) Bile salts can damage the oesophagus in concentrations as low as 200 μmol/l, especially when mixed with acid. There are, however, little data available on bile salt concentrations in oesophageal refluxate. When bile reflux occurs it is assumed to be alkaline. The study aims to examine the relationship between oesophageal total bile salt concentration and pH in reflux. During routine endoscopy lists, bile stained fluid was aspirated from the oesophagus when seen on initial intubation. The Olympus Q10 endoscope was used, with a clean, air dried suction channel. Exclusions were difficult intubation or retching, pH of each specimen was measured. Samples were then centrifuged to remove debris, and frozen at −20°C before assay using the 3α-hydroxy-steroid dehydrogenase colourimetric method. Thirty eight patients were found to have bile
pooling in the oesophagus. Five patients had undergone gastric surgery, and were excluded (bile concentrations 680–7450 \( \mu \)mol/l). Twenty three of the remainder (70%) had oesophagitis. Bile concentrations varied from 15–230 \( \mu \)mol/l (mean 336 \( \mu \)mol/l). pH ranged from 1.5–7.8 (mean 4.2). There was a positive correlation between the concentration of bile salts and rising \( \text{pH} \) \((r=+0.526, p<0.005)\). These results show gastro-oesophageal reflux of bile may be present at acid or neutral \( \text{pH} \), and suggests that a significant amount of potentially damaging bile reflux will be missed on standard standard \( \text{pH} \) monitoring.

T120

**Aetiology of mid oesophageal diverticula**

R M Charnley (introduced by MR T W Balfour), K R Knowles, and F D Salama (Department of Thoracic Surgery, City Hospital, Nottingham) It has been shown that midoepithelial diverticula are usually associated with an abnormality of oesophageal motility. Of over 400 patients referred for investigation of dysphagia and acid regurgitation between 1981 and 1986, 21 midoepithelial diverticula were diagnosed in 19 patients. In each case the patients were investigated to determine the aetiology of the diverticula (two cases occurred at the site of previous oesophageal surgery). All diverticula were of the pulsion variety. They varied in size and shape, the larger and more dependent diverticula causing more severe symptoms, including dysphagia.

Oesophageal \( \text{pH} \) monitoring showed significant gastro-oesophageal reflux in 10 of 12 patients tested but oesophageal manometry failed to show the presence of a primary motility disorder in any of the patients. Twelve patients were treated with antireflux medication and seven patients underwent surgery for large symptomatic diverticula or for gastro-oesophageal reflux resistant to medical therapy. Surgery was successful in five of seven cases.

We conclude that primary oesophageal motility disorders are not common causes of mid oesophageal diverticula. The majority of cases are associated with gastro-oesophageal reflux and respond well to standard antireflux therapy.

T121

Is it possible to control bleeding from gastro-oesophageal cancer using endoscopic laser therapy?

T122

**Clinical spectrum of Barrett’s oesophagus: surveillance for all?**

B J Collins, M Abbott, G Morstyn, R Thomas, and D J R St John (The Royal Melbourne Hospital and Ludwig Institute for Cancer Research, Melbourne, Australia) A retrospective survey identified 81 patients (48 men) with Barrett’s oesophagus, diagnosed in the Royal Melbourne Hospital between 1978 and 1986. The age at presentation varied from 20–93 years and 44% were >70 years. Only 27% smoked cigarettes and 63% drank alcohol (14% >80 g alcohol daily). Heartburn was a presenting symptom in 69%, regurgitation in 54%, dysphagia in 35%, and haematemesis or melaena in 28%. At endoscopy, the length of Barrett’s epithelium ranged from 3 cm to 15 cm. Macroscopic oesophagitis was observed in 69%, oesophageal strictures in 16%, and a coexistent adenocarcinoma of the lower oesophagus in 14% of patients. Oesophageal symptoms, oesophagitis, stricture or carcinoma were not more frequently encountered in patients who smoked cigarettes and/or drank alcohol (Fisher’s exact probability test). If patients with cancer, the elderly (age >70 years) and those with a chronic alcohol problem are excluded from endoscopic cancer surveillance, only 38% of the patients described in this survey would be suitable for enrolment in such a programme. This represents a recruitment of approximately four new patients yearly for endoscopic cancer surveillance.

T123

**Use of endoscopy and blood measurement to show dose dependent protection of human gastric mucosa by famotidine against aspirin**

P J Prichard, T K Daneshmand, P J Millins, T J Edwards, N K Bhaskar, and C J Hawkey (Dept of Therapeutics, University Hospital, Nottingham) We devised an ultrathin endoscope (3.5 mm diameter) to assess aspirin induced gastric mucosal injury in unsedated subjects. Eighteen subjects took aspirin 900 mg, five times over 48 hours, with and without famotidine, 2 mg or 20 mg, before endoscopic grading of antral petechiae (from 0–4) and measurement of bleeding into gastric washings, using the orthotolidine reaction.

Aspirin significantly (p<0.05) increased antral damage from grade 1 (median, interquartile range 0–1), to 3.5 (2–4), and bleeding from 1·8 (1·1–6·3) \( \mu \)l/12 minutes to 10·7 (5·4–14·8) \( \mu \)l/10 minutes. Famotidine 20 mg significantly (p<0.05) raised the \( \text{pH} \) of gastric washings, from 2·4 (2·21–2·53) to 6·55 (5·77–6·68), reduced antral damage to grade 1·5 (1–3), and reduced bleeding to 2·9 (1·5–6·0) \( \mu \)l/12 minutes. After famotidine, 2 mg, washings \( \text{pH} \) was only 2·83 (2·50–6·05) and there was no significant mucosal protection. There was a good correlation between endoscopy and bleeding (10·7 (5·9–19·4) \( \mu \)l/12 minutes with grades 3–4 versus 2·0 (1·2–3·5) \( \mu \)l/12 minutes with grades 0–1).

We conclude that endoscopy and bleeding data correlate in showing aspirin injury and protection by famotidine, 20 mg. These data do not support previous suggestions that lower doses of \( \text{H}_{2} \) antagonists are protective.

T124

**High grade dysplasia of the gastric epithelium: an indication for radical gastrectomy?**

M Lansdown, P Quirke, D C Ward, M F
DIXON, A T R AXON, AND D JOHNSTON (University Departments of Surgery and Pathology and The Department of Gastroenterology, The General Infirmary, Leeds) The natural history of high grade dysplasia (HGD) of the stomach and its relationship to gastric carcinoma (CA) are ill defined. Between 1984 and 1987, 11 patients were found to have HGD on endoscopic biopsy. Carcinoma was identified in further biopsies from four patients after follow up of four to 14 months: three underwent gastrectomy with Radical (R2) lymph node dissection and each was found to have intramucosal CA in the resected specimen. The other patient, being unfit was treated by laser photocoagulation.

In the remaining seven patients, further endoscopies with biopsy over a two to 12 month period confirmed the continuing presence of HGD. Five have undergone R2 gastrectomy: invasive CA was found in one, intramucosal CA in three and multifocal areas of HGD in one. Thus, among eight patients with HGD who underwent R2 gastrectomy (four total, four subtotal), six were found to have intramucosal CA, one had invasive CA and one had HGD. None of the eight had metastases in lymph nodes, and their progress should therefore be good.

The finding of HGD in serial endoscopic biopsies in an indication for radical R2 gastrectomy, if the patient is "fit". Because the extent of gastric resection depends on the distribution of HGD in the gastric mucosa, multiple pre-operative biopsies must be taken.

T125
Early results of a population based screening programme for gastric cancer
J D HARRISON AND D L MORRIS (Department of Surgery, Queen's Medical Centre, Nottingham) We have used a simple self-administered postal questionnaire to define symptomatic subjects in a group of 914 people aged 50–75 from gp records of whom 834 (91.2%) replied. Two hundred and fifty two (29.1%) were positive for symptoms of dyspepsia. Of the patients with dyspepsia 52.3% have not consulted their gp with the complaint, and of those who had, only 13% had done so in the last six months. 19.3% had a family history (FH) of peptic ulcer and 5.4% had a FH of gastric cancer; 26.5% of patients were smokers and 37.7% were ex-smokers. In the 161 patients who have gastroscoped, pathology was diagnosed in the majority of cases (95%). A gastric carcinoma has been detected and a group of patients with 'premalignant' lesions such as gastric intestinal metaplasia or dysplasia (11), Barrett's oesophagus (five), and gastric polyps (four) have been identified. We have also diagnosed three gastric ulcers and four duodenal ulcers. Other patients had oesophagitis or antral gastritis.

We conclude that a good response rate can be achieved with a simple self-administered symptom questionnaire, that the majority of dyspeptic patients manage their own symptoms, and that it is possible to identify a group of approximately 10% of symptomatic subjects who may comprise a high risk group for endoscopic follow up.

T126
Educational value of the BDF/BSG patient information leaflet
G M HAWKEY, M EDMUNDS, B G POULSON, AND C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) A series of 12 information leaflets about gastrointestinal disease was written by members of the BSG. They were 1518–3012 words long, with reading ease scores of 46–74 (mean 62) – that is, accessible to individuals with an IQ of 90. They were assessed by postal questionnaire in 1150 patients attending 24 medical and surgical gastroenterology outpatient clinics in teaching and non-teaching hospitals throughout the UK. Half the patients received an information leaflet and all subsequently received a disease related questionnaire. Seven hundred (61%) completed questionnaires without prompting. Twenty factual questions were scored +5 (correct) or −5 (incorrect) – maximum possible score 100, score for random response 0.

There was a significant increase in the knowledge score in recipients of each leaflet (Heartburn from 19.2 to 49.3, n=111; peptic ulcer 0.2 to 34.6, n=77; diarrhoea and constipation 10.5 to 30.2, n=35; inflammatory bowel disease 15.2 to 36.22, n=285; diverticular disease 28.4 to 51.7, n=30; irritable bowel syndrome 22.3 to 47.4, n=99; liver disease 23.4 to 54.6, n=77; gall stones −4.9 to 29.6, n=43). Patterns of misconception, common in control patients, were less in leafleted patients.

We conclude that the BSG/BDF Patient Information Leaflets improve patient knowledge.

T127
Experience with peroperative colonoscopy in patients with primary colorectal cancer
P J FINAN, D R DONALDSON, T ALLEN-MERSH, J NORTHOVER, P R HAWLEY, AND C B WILLIAMS (Leeds General Infirmary and St Mark's Hospital, London) Assessment of the entire colon in patients presenting with primary colorectal cancer is mandatory. This allows synchronous lesions to be detected and appropriate surgery planned. Several studies have noted increased sensitivity of colonoscopy over routine barium radiology. It has been claimed that peroperative colonoscopy should be the procedure of choice and we wish to report our initial experience with this technique.

Twenty three patients were studied (rectum n=9, left colon n=6, right colon n=8). Conoscopy, performed after laparotomy and assessment of the primary tumour, took, on average, 16 minutes to perform (range 7–30 minutes) and reached the caecum or proposed line of resection in 78% of cases. Synchronous polyps were noted in nine patients (39%) and one synchronous carcinoma was confirmed. Preparation of the bowel was considered good in only 43% of cases. Colonoscopy has been repeated in eight patients (35%) six months after surgery (CBW). Previously undetected polyps were noted in five (size ranging from 0.3 cm–2.0 cm).

It is concluded that peroperative colonoscopy may have a role in stenosing left sided lesions were limited views of the colon have been obtained preoperatively. This technique, however, is no substitute for a careful preoperative colonoscopic examination.

T128
Prognosis in carcinoma of the caecum: the effect of appendicectomy
C P ARMSTRONG, Z AHSAH, AND G HINCHLEY (Bristol Royal Infirmary, Bristol) Carcinoma of the caecum is often advanced at presentation and this may relate to the relative paucity of symptoms until late in the disease process. Another reason for these tumours being advanced might relate to peroperative surgery such as appendicectomy (APX).

A consecutive group of 519 patients with adenocarcinoma of the caecum who were presented in Plymouth between 1975–87 was studied. Of these 133 (25.6%) had a history of APX and this was similar to 120 (23.1%) of 519 matched controls. APX patients had significantly (p<0.001, χ²) more Duke's D and less Duke's B tumours than patients
without previous APX and these tumours were also less differentiated (p<0.01). Synchronous carcinomas and adenomas were equally common in both groups at 7-5%; 5-2% and 22-6%; 19-2% respectively. Local invasion was more common in APX patients (39-8% v 5-7%; p<0-001) and the resection rate was considerably less (75-2% v 93-3%; p<0-001). The age adjusted five year survival rate was lower for APX patients (29-1% v 42-9%; p<0-001) and this was most marked for Duke's C and moderately differentiated tumours. Local recurrence was higher for APX patients (32-1% v 13-1%; p<0-01). Appendicectomy does not increase the risk of carcinogenesis in the caecum. Previous appendicectomy does have a major influence on outcome, however, and reduces survival in patients who subsequently develop carcinoma of the caecum.

T129
Importance of unsuspected colorectal cancer
C P ARMSTRONG (Bristol Royal Infirmary, Bristol) The prognosis of colorectal cancer (CRC) has not changed over the last two decades although screening for asymptomatic disease has shown encouraging results. This study has addressed the phenomenon of patients who die at home with unsuspected CRC in an attempt to determine the incidence of asymptomatic disease.

All 33 000 deaths at home in Plymouth (pop 412 000) between 1977–86 were analysed. Five thousand seven hundred and eighty two coroners autopsies were carried out on these patients (autopsy rate 17.5%). Only patients with unsuspected CRC who had no investigations were studied. Sixty one patients with 62 tumours were found and this compares with 1490 patients who died from CRC in Plymouth in the same period. Fourteen patients were under 70 years. The site of the tumours was caecum/ascending colon 14, transverse seven, descending five, sigmoid colon 16, rectum 20. Ten tumours could have been felt on PR examination. Rigid and flexible sigmoidoscopy might have diagnosed 24 and 41 tumours respectively. In 57 patients CRC was the cause of death and in 27 patients curative surgery would have been possible as there was no evidence of metastatic spread.

A significant number of colorectal cancers are undetected until after death and extrapolation to the United Kingdom population would give 800 cases per year. These figures support the use of screening programmes for CRC in asymptomatic individuals over 50 years.

T130
Peroperative scanning of 111In labelled anti-CEA monoclonal antibody to detect the extent of colorectal carcinoma
S D BLAIR, S RIGGS, E R V LLOYD-DAVIES, N A THEODOROU, O SOUTHL, G BOXER, R BEGENT, AND P GREGORY (Departments of Surgery and Cancer Research Campaign Laboratories, Charing Cross Hospital, London) Peroperative clinical assessment of colorectal carcinoma spread may be difficult. We have studied whether complete excision can be improved by peroperative intraindividural scanning of lesions with a hand held gamma detecting probe. Twelve patients with colorectal carcinoma were injected with 111In labelled anti-CEA monoclonal antibody (5B7) four to eight days preoperatively. At laparotomy, the probe was placed directly onto tumour, surrounding tissues and background areas and gamma emissions counted. Counting was repeated on the resected specimen and results were correlated with histology.

In 11 patients there was increased radioactivity over the tumour compared with normal colon with a mean (SE) of 3-2 (0-4) for cases. Scanning of the resected specimen showed lower counts but still with a mean ratio 3-5 times background. The uptake of antibody was independent of the serum CEA concentration.

There were five Duke's C carcinomas of which three showed high counts over lymph nodes. High counts were also obtained over one invaded distal resection margin and one active duodenal ulcer. Low counts were recorded over histologically normal small bowel adherent to a tumour.

Peroperative anti-CEA scanning helps to define the extent of colorectal carcinoma and there is scope to improve results by reducing background.

T131
Use of blood in patients with large bowel cancer
R S KIFF AND R D KINGSTON (Department of Clinical Studies, Park Hospital, Davyhulme, Manchester) Blood transfusion has an adverse effect on recurrence and survival in patients with malignant disease. This may be related to the number of units transfused. Normovolaemic anaemia can be of benefit to patients perioperatively. The use of blood transfusions in 476 patients who underwent potentially curative surgery for large bowel cancer was examined.

Transfusion was only considered necessary if the haemoglobin was less than 10 g/dl. A post transfusion haemoglobin of 11–12 g/dl represented an excess transfusion of one unit, 12–13 g/dl an excess of two units etc. Of 128 patients not transfused only four were discharged with a haemoglobin <10 g/dl. Three hundred and forty eight transfused patients received a total of 1164 units of blood and again only four were discharged with a Hb <10 g/dl.

Most patients were over transfused. Transfusion could have been avoided altogether in 146 patients (42%), including 89% transfused one unit, 64% given two units, 44% given three units, and 24% given four units.

We accept that rigid transfusion rules cannot be applied and haemoglobin measurements are dependent on several factors. On the criteria used in this study, however, more than half of all blood transfusions were unnecessary. The risks of blood transfusion could have been avoided for many patients. Perioperative transfusion practices should be reviewed.

T132
Enhanced prostaglandin E2 production by tissue fixed macrophages from colonic tumour
W J MAXWELL, J KEATING, F P HOGAN, G S A MACDONALD, AND P W N KELING (Department of Clinical Medicine, TCD Medical School, St James's Hospital, Dublin) Recent studies have shown that the prostanooid content (PGE2, F2 alpha and 6 keto F1 alpha) of homogenates of colonic cancer is increased. This work did not examine production by individual cell populations, however, nor did it examine the production by the cells from colonic polyps. The aim of this study was to compare PGE2 and LTD4 production by freshly isolated colonic tissue fixed macrophage and epithelial cells from normal colon, colonic polyps and tumours. Prostaglandin E2 production by zyosman stimulated tissue fixed macrophages, from colonic tumours, was significantly greater than that found in colonic polyps or normal colonic mucosa [values expressed as mean (SE)] [15.4 (3), n=24 v 2.0 (0.5), n=7 v 7.1 (2.8), n=20, p<0.0025, tumour tissue v colonic polyp v control tissue]. This was also observed when cells were stimulated in the presence of arachidonic acid, the substrate for eicosanoid biosynthesis [29 (4-4), n=20 v 28 (7), n=6 v 59 (6) ng, n=19 PGE2/106 monocytes,
p<0.0025, control tissue v colonic polyps v tumour tissue]. Monocyte LTB₄ production was lower than PGE₂ biosynthesis and was similar in all tissues. Epithelial cell eicosanoid production was similar in all groups. These results demonstrate that mononuclear cells isolated from colonic tumours produce greater amounts of PGE₂ compared with colonic polyps or those taken from control tissue. Because PGE₂ is immuno-suppressive, this increase may explain the local immunoparesis found in colonic neoplasia.

T133

Influence of tumour cell DNA in colorectal cancer

N C ARMITAGE, J WRIGHT, D F EVANS, K C BALLANTYNE, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Tumour cell DNA content (ploidy) has been shown to be an independent factor in determining prognosis in colorectal cancer. To further investigate ploidy, we measured tumour cell DNA content, from paraffin embedded material, by flow cytometry in 410 patients who underwent resection for colorectal cancer between 1970 and 1977.

Overall 211 (51%) tumours had abnormal DNA (aneuploid). Patients with aneuploid tumours had a poorer five year survival – 68/211 (32%) than those with diploid tumours – 87/199 (44%) (mantel-Cox 5.5, p<0.02). The five year survival for patients without distant metastases with diploid tumours was 84/172 (49%) and 65/172 (38%) for those with aneuploid tumours (χ²=3.84, p<0.05). For each pathological stage there was a survival advantage to patients with diploid tumours, which was significant for stage B (Mantel-Cox 4.2, p=0.01). More patients having curative resections with diploid tumours survived – 66/105 (63%) than with aneuploid tumours – 53/103 (51%) (mantel-Cox 2.8, p=0.09).

For rectal tumours the survival was; diploid – 34/74 (46%), aneuploid – 22/71 (31%).

By multivariate analysis ploidy (χ²=5.1, p=0.02) was shown to be an independent factor with pathological stage (χ²=95.8, p<0.001).

Abnormal DNA content is associated with a poorer overall survival and may indicate patients who may most benefit from adjuvant therapy.

T134

Fewer anastomotic tumours in defunctioned colon: a further link between adaptation and carcinogenesis?

G V N APPLETON, PW DAVIES, AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) An intestinal suture line potentiates experimental carcinogenesis in its vicinity. By contrast, a defunctioning colostomy causes distal hypoplasia and fewer tumours develop. Male Sprague-Dawley rats (n=160) were used to study adaptation and azoxymethane induced carcinogenesis at an end-to-end anastomosis that was raised in either functioning or defunctioned left colon. Controls had no procedure and other rats had proximal colostomy alone. Defunction had a profound antitropic effect on the colon, reducing crypt cell production rate (CCPR) by 22–56% (p<0.02). Aneu-

stomotic CCPR was increased by a factor of 2.5 over controls (12.7±2.85 v 4.87±0.41 cells/crypt/h: p<0.02), but defunction reduced this by 74% to a value (3.00±0.52 cells/crypt/h: p<0.0001) below that in the intact colon. Compared with controls there were 71% fewer tumours in defunctioned colon (1.18±4.09 tumours/rat: p<0.0001). Rats with a defunctioned anastomosis had 84% fewer suture-line tumours than those with a functioning anastomosis (0.48±2.95 tumours/rat: p<0.0001). Anastomosis and defunction have powerful but contrasting effects on colonic adaptation and carcinogenesis. The relative lack of anastomotic tumours in defunctioned colon suggests that the rate of cell proliferation is an important determinant of risk.

T135

Adaptation of the defunctioned rectum

G V N APPLETON and R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Colonic defunction is commonly performed in surgical patients either to protect an anastomosis or to ‘rest’ the colon in inflammatory bowel disease. After defunction by withdrawal of food, substitution of elemental diets or isolation from the luminal stream, rat colon undergoes marked hypoplasia and has a reduced propensity to experimental carcinogenesis. In this study mucosal biopsies were taken from the upper rectum of 11 patients with a defunctioned large bowel (of between two months – five years standing) and from 14 controls without abdominal operations or disease. Samples were established in organ culture and after 16 h crypt cell production rate (CCPR) was determined by a stathokinetick technique. Crypt morphometry was also studied. Rectal CCPR among the patients with a defunctioned large bowel was less than half that of controls (1.96±0.68 v 4.65±0.54 cells/crypt/h: p<0.0001). In patients with a stoma, crypt length was 24% less than controls (0.336±0.051 v 0.444±0.041 mm: p<0.0001) and crypt width was 38% less (0.445±0.007 v 0.701±0.066 mm: p<0.0001). Rectal defunction causes profound and persistent hypoplasia in man. The high incidence of diarrhoea after colostomy closure may be due partly to functional impairment which accompanies hypoplasia.

T136

Conservative treatment of appendicitis

T GLEDHILL, S SHEEHAN, H KASHI, S KENDALL, D WALLER, AND T G BRENNAN (St James’s University Hospital, Leeds) Thirty per cent of patients with a clinical diagnosis of appendicitis have histologically normal appendices. To await the onset of clinical signs without treatment, however, may increase morbidity. Antibiotic therapy during observation might be a safer alternative.

Appendicitis without peritonitis was diagnosed using a scoring system based on clinical findings. Patients were then prospectively randomised to receive either immediate surgery or iv cefotaxime 1 g tds and metronidazole 500 mg tds. In the conservative treatment group increase in pulse, temperature, abdominal signs or failure to improve in 48 h constituted failed medical treatment. If surgery was performed, severity of appendicitis was graded 0 (normal), 1 (inflamed), or 2 (perforated or gangrenous).

Treatment groups were matched for age, sex, and diagnostic score. Of 50 patients treated conservatively, 38 (76%) made an uneventful recovery and 12 (24%) required surgery – one with perforated diverticular disease (with grade 0 appendicitis), five with grade 1 appendicitis, and six with grade 2. Of 50 patients treated by surgery, nine, 32, and nine had appendicitis grades 0, 1, and 2 respectively.

Initial antibiotic treatment is a safe holding practice and does not increase perforation rate or morbidity. Conservative treatment may be an alternative to surgery in selected patients.

T137

Prolonged ileo-caecal motor activity in ambulant subjects
D KUMAR AND D L. WINGATE (GI Science Research Unit, London Hospital Medical College, London) Measurement of ileocaecal motility by perfused tube manometry does not allow prolonged monitoring under physiological conditions. We have recorded ileocaecal motility in six healthy subjects who were freely mobile during the study period and were able to sleep at home. Motility was measured from a pressure sensitive probe (3 m long and od 3 mm) with three sensors spaced at 15 cm intervals from the tip which carried an inflatable balloon. The probe was positioned under x-ray control so that the distal sensor was in the caecum. Data were continuously recorded on magnetic tape. During the study, subjects consumed three normal meals. The distal ileum exhibited two types of activity (i) MMCs with 8/min contractions (cycle length 110±20 min) and (ii) discrete clusters of 8/min contractions (DDCs) with a mean cluster duration of 2 min (fasted) and 1.5 min (fed). Postprandial activity (mean duration -310±60 min) consisted of irregular contractions and DCCs. Phasic caecal contractions (6/min) followed 10% of ileal phase III episodes, and DCCs with a similar frequency (6/min) were associated with 10% of ileal DCCs. However, spontaneous caecal DCCs were also seen. Isolated contraction waves were seen prior to defaecation and in the morning. Our data show that ileal phasic activity is more regular at night and that a proportion of this activity is propagated to the caecum. This technique will allow assessment of ileocaecal motor dysfunction in gut disorders.

T138
Effect of the menstrual cycle on bowel habit and whole gut transit

M A KAMM, M J G. FARTHING, AND J E. LENNARD-JONES (St Mark’s Hospital, City Road, London) Sex hormones are thought to influence gut motility. We have accurately measured whole gut transit time and stool output during the follicular and luteal phases, and recorded bowel frequency throughout the menstrual cycle, to determine the effect of a changing hormonal profile.

Twenty healthy women (ages 22–47, mean 32) swallowed three different lots of 20 radio-opaque PVC shapes on each of days 5, 6, and 7 and 19, 20, and 21 of the menstrual cycle. Stools were collected, weighed and x-rayed from days 5 and 19 until all shapes were recovered. Transit time for each half cycle was determined by taking the mean of the transit time taken for each of the 60 shapes (hence 3 day average). Blood samples on days 5, 19, 21, and 23 to confirm ovulation. A diary card for the entire cycle recorded bowel frequency.

Eightteen women ovulated (progesterone (P) >18 nmol/l), and form the basis of the comparison. There was no significant difference between the follicular and luteal transit rate [45 (3) v 51 (4) mean (SE), P=0.1]. Bowel frequency per five days [5:6 (0.5) v 5:2 (0.4), P=0.4] or stool weight (132 (7) v 123 (10), P=0.4). Bowel frequency was also unchanged during menstruation. A positive correlation existed between transit rate and peak serum P (r=0.59, p=0.01) and oestradiol (E2) (r=0.61, p=0.007) in the follicular but not luteal phase. (*transit in hours; tstool wt in g/day).

Cyclical hormonal changes did not affect the whole gut transit rate, bowel frequency or stool weight. P and E2 concentrations correlated with transit rate in the follicular but not luteal phase. Either higher hormone concentrations would be needed to influence motility, receptor saturation occurs, or other factors play a greater role in influencing transit.

T139
Postoperative intraluminal pressures in the left and right colon after anterior resection

D S BURKITT AND I A DONOVAN (Department of Surgery, Dudley Road Hospital, Birmingham) Some surgeons still use caecostomy as a vent to protect left colonic anastomoses; however, its effect on left colonic pressures has not been documented. Using perfused fine bore tubes intracæcal pressures were measured in 10 patients following left colonic resections and compared with pressure changes recorded synchronously 2-5 cm distal to the anastomosis.

In the absence of colonic activity intraluminal pressure remained within 5 mmHg of atmospheric pressure throughout the postoperative period. Activity recovered on a median of day three, that in the caecum consisting of simple waves with mean of 5 mmHg (peak 25 mmHg) occupying 5% of recording time. Mean amplitude of waves distally was 19 mmHg (peak 90 mmHg). No coincident or peristaltic waves were recorded. Four patients had sustained tonic contractions distal to the anastomosis lasting for periods up to one hour with mean pressure of 30 mmHg and peak of 45 mmHg. These raised distal pressures were not in association with a rise in intracæcal pressure.

In conclusion intracæcal pressure was not raised during the postoperative period even when pressure at the anastomosis was raised. These data suggest that a caecostomy does not affect the pressure at a left colonic anastomosis.

T140
Differences in anal sensation in continent and incontinent patients with perineal descent

R MILLER, D C C BARTOLO, F CEVERO, AND N J M MORTENSEN (Bristol Royal Infirmary, Bristol) Neuropathic damage to the pelvic floor secondary to perineal descent (PD) is considered to be an important aetiological factor in idiopathic faecal incontinence. Perineal descent, however, does not necessarily result in a loss of motor function or incontinence. To elucidate the role of anal sensation in the continence mechanism we measured anal mucosal electrosensitivity and thermal sensitivity in normal controls and in continent and incontinent patients with PD. There were 20 patients in each group, which were matched for age and sex. A catheter carrying two platinum electrodes connected to a constant current generator was used to assess mucosal electrosensitivity and a water perfused thermode, 1 cm long to measure thermal sensory thresholds. In addition, routine anal manometry was performed using a water filled micro-balloon system. Perineal descent was assessed radiographically.

The results show that despite a greater degree of perineal descent in the continent patients, anal sensation is largely preserved and that it was severely impaired in incontinent patients. Loss of anal sensation may therefore be an important factor leading to incontinence in patients with PD.

T141
Physiological parameters which will predict the outcome of postanal repair

K YOSHOKA, M PINHO, AND M R B KEEGHLEY (General Hospital, Birmingham) A prospective study was carried out in 16 patients having postanal repair for faecal incontinence of whom 12 were improved by operation. Preoperative anal pressures were significantly lower than in age and sex matched controls at rest (R), during maximum pelvic floor contraction (Sq) and attempted defaecation (St). (R: P<0.005, Sq: P<0.005, St: P<0.005). First leakage of saline and total tolerable volume were significantly lower in patients than controls (first leak: P<0.005, tolerable volume:
Proctograms showed that pelvic floor descent and perineal descent were greater in patients than controls (R: p<0.05 and p<0.05). Anal canal length was significantly shorter incontinent patients compared with controls at rest and during maximum pelvic floor contraction (R: p<0.05, Sq: p<0.05). None of these parameters, however, changed significantly after postanal repair.

Preoperative parameters which significantly predicted clinical improvement after post anal repair included: maximal squeeze pressure (129 ± 79 cmH2O; p=0.025) and maximum anal pressure during attempted defection (121 ± 71 cmH2O; p<0.05). Pelvic floor descent was significantly less in patients who were improved (R: 4.66 7.2 cm; p=0.01) as was perineal descent (R: 7.9 9.9 cm; p<0.05). Anal canal length was significantly greater in those who were improved (R: 4.3 2.9 cm; p<0.05).

These results indicate that the outcome of postanal repair can be predicted by preoperative anal manometry and proctography.

Use of the dorsal genital nerve pudendoanal reflex for the treatment of neurogenic faecal incontinence

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The dorsal genital nerve pudendoanal reflex is constituted by the afferent dorsal genital nerve (DGN), the conus medullaris and pudendal nerve efferents (S2, 3, 4) to the pelvic floor and external anal sphincter. Acute stimulation of the DGN produces a measurable latency response, an integrated EMG external anal sphincter response and a rise in the maximum resting anal canal pressure, establishing the presence of an incomplete denervation – for example, a neuropathy.

This was then followed by chronic stimulation of the DGN in five women with neurogenic faecal incontinence. Stimulation of the DGN was carried out with 1 Hz square wave stimuli 120–150 volts for five minutes three times a day for two months. This produced an increase in the physiological canal length (from 2.4 cm ± 0.5 cm to 3.2 cm ± 0.4 cm), the maximum voluntary contraction of the external anal sphincter (from 112±37 cm water to 162 cm water) and the maximum resting anal canal pressure (from 57±17 cm water to 94±21 cm water). All subjects regained full continence apart from one with poor control of flatus. It is suggested that this technique reinforces the activity of the pelvic floor, is applicable only if the pathways of the reflex are intact, and may correct incontinence of neurogenic causation.

Prolonged anorectal mechanical and electrical activity in ambulant human subjects

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Assessment of anorectal function, usually a brief laboratory procedure, is not optimal for physiological acts – for example, micturition, passage of flatus, etc, that require privacy. We have, for the first time, developed a technique for combined prolonged anorectal manometry and EMG of the external sphincter (ES) in ambulant subjects. We studied 11 healthy subjects for 210 hours (mean 19.1 h/subject). Manometry was performed using a 2 sensor pressure sensitive probe (OD 2.2 mm). One sensor was located in the rectum and the other in mid-anal canal. EMG was recorded by Ag–AgCl surface electrodes positioned 0.75 cm from the anus, on either side. Data were recorded on magnetic tape. The ES showed significantly (p<0.05) more action potentials (APs) during the day (12 APs/10 min) than at night (1.5 APs/10 min). During sleep, bursts of APs lasting 3–4 minutes occurred every 30–45 minutes. We recorded 41 flatus episodes. In 34, anal canal pressure increased (20 mmHg) in association with an AP in the ES. Transient relaxation followed by anal canal and ES contraction was seen in five, and in the remaining two, neither anal canal pressure or ES activity changed. Powerful ES contractions with a rise in anal canal pressure (mean 15 mmHg) were seen during micturition. Our data show periodic activity in the ES during sleep, and contractile activity both in the anal canal and ES during micturition and the passage of flatus; this may account for faecal continence during sleep and while voiding flatus or urine.

Intramural innervation of the internal sphincter is normal in severe idiopathic constipation

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Internal sphincter myectomy may be helpful in patients with severe constipation suggesting possible abnormal internal sphincter function. Assessment of internal sphincter function relies on resting anal canal pressure, or the response to balloon distension in the rectum. The latter may be influenced by rectal volume and compliance and is difficult to standardise. We have therefore assessed the response of the sphincter to a rectal mucosal electrical stimulus as a test of intramural innervation.

Ten healthy women (mean age 31) and 17 women with severe idiopathic constipation (mean age 32, bowel frequency range 1–4 weeks) were studied. A bipolar electrode was placed in the rectum 6 cm above the internal sphincter, and a microballoon connected to a pressure transducer placed in the anal canal at the point of maximum pressure. Constant current stimuli of 20 Hz and 1 ms were applied from 0 to 40 mamp.

Outlet obstruction constipation (obstructed defecation) – a failure of the posterior pelvic floor?

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Outlet obstruction constipation (OOC) has been attributed to puborectalis paradox. We reported that unobstructed defeation requires lifting of the posterior pelvic floor (PPF) before puborectalis relaxation. Using videoproctography we studied 21 female patients with OOC (group 1) and 17 controls (group 2) at rest and during attempted expulsion of 120 ml liquid barium.

The anorectal angle (ARA) at rest was 119° (3° [mean (SE)]) in group 1 and 109° (4°) in group 2. The corresponding increase in ARA on straining was 1° (3°) in group 1 and 13° (2°) in group 2, p<0.001. Perineal descent was measured at (a) the anorectal angle, and (b) the posterior pelvic floor at the midpoint between ARA and the coccyx. The mean descent at rest of the ARA was 2.0 (0.3) cm in group 1 and 1.9 (0.2) cm in group 2, p=NS. In contrast, PPF descent was 3.5 (0.3) cm in group 1 and 1.5 (0.2) cm in group 2, p<0.001. These results show that in patients with OOC the posterior pelvic floor falls below the ARA on straining at stool. These appearances suggest that the primary abnormality occurs in the posterior pelvic floor rather than the puborectalis.
T146 Randomised trial of infrared photocoeagulation (IRPC) and bipolar diathermy (BD) for the outpatient treatment of haemorrhoids

A R DENNISON, M J S DENNIS, G L LAMONT, AND D L MORRIS (Department of Surgery, University Hospital, Nottingham) Infrared photocoeagulation (IRPC) is a commonly used treatment for haemorrhoids. More recently BD has also been shown to be effective, inexpensive and well tolerated. We have compared these two techniques in 118 patients with symptomatic 1st and 2nd degree haemorrhoids (49 IRPC/59 BD) who have been entered into a randomised trial. Patients were reviewed monthly after the initial treatment until asymptomatic or treatment was considered to have failed.

Using a specially designed disposable probe and an ACM-BICAP 50 watt generator, BD is applied to the base of the haemorrhoids in 2s pulses. IRPC is similarly applied but using a MBB-AT probe and an Ohio Medical 50 watt power module. Multiple applications, in each case, are used to produce a visible eschar. There were no significant differences between the two groups in respect of number of treatments needed or in treatment related discomfort. Similar numbers of patients were also asymptomatic after one (BD 33-9%, IRPC 26-7%), or two (BD 50-8%, IRPC 51-0%), treatments. Significantly more patients experienced pain (IRPC 16-3%, BD 5-1%), or a transient worsening of symptoms, however, in the week post-treatment (bleeding in two patients), after IRPC than BD.

Bipolar diathermy is as effective as IRPC in the outpatient management of haemorrhoids. As it is also likely to be less expensive it is to be recommended.

T147 Admission abdominal CT scan and prediction of severity of acute pancreatitis

N J M LONDON, J P NEOPTOLEMOS, JANET LAVELLE, I BAILEY, AND D JAMES (Departments of Surgery and Radiology, Leicester Royal Infirmary, Leicester) One hundred and twenty six patients with acute pancreatitis had enhanced abdominal CT scans within 24 hours of admission. Ninety two attacks were clinically mild, 34 clinically severe. Pancreatic enhancement was defined as decreased, increased or normal. The maximum anterioposterior measurement (cm) of the head and body were multiplied together to produce a ‘pancreatic size index’.

Significantly more patients with severe attacks had decreased pancreatic enhancement (27/34 v 53/92, p=0.02, \( \chi^2 \)) and loss of peripancreatic tissue planes (28/34 v 50/92, p=0.006, \( \chi^2 \)). The median (range) pancreatic size index for severe attacks was 12.8 cm\(^2\) (3.0-52.0), for mild attacks 6.0 cm\(^2\) (1.1-23.4), p<0.0001 Mann-Whitney U Test. Modified Glasgow criteria had a sensitivity of 85% and specificity of 79% for severe attacks. A pancreatic size index of \( \geq 10 \) cm\(^2\) had a sensitivity of 71% and a specificity of 77% for severe attacks. In patients less than 50 years of age a pancreatic size index of \( \geq 10 \) cm\(^2\) had a sensitivity of 82% for severe attacks compared with 64% for modified Glasgow criteria.

Patients with severe attacks had significantly greater admission pancreatic size indices, and in patients less than 50 years of age a CT pancreatic size index of \( \geq 10 \) cm\(^2\) had a greater sensitivity than modified Glasgow criteria for a severe outcome.

T148 \(^{14} \text{CO}_2\) breath test for the study of starch digestion in normal subjects and patients with pancreatic disease

M HIELE, Y GHOOS, P RUTGERTS, AND G VANTRAPPEN (Department of Internal Medicine – Division of Gastroenterology University Hospital Gasthuisberg, Leuven, Belgium) The hydrolysis of starch was studied by measuring the \(^{14} \text{CO}_2\) excretion after ingestion of 50 g of \(^{13} \)C-starch and 50 g \(^{13} \)C-glucose in 10 healthy volunteers and 14 patients with pancreatic disease.

The hourly rate of \(^{14} \text{CO}_2\) excretion in % dose per hour, three hours after ingestion of carbohydrate by normal subjects, was 6.89 (1.55) [mean (SD)] for glucose, and 4.21 (1.27) for starch. In patients with pancreatic disease the \(^{14} \text{CO}_2\) excretion rate after three hours, was 4.41 (2.14) for glucose and 1.32 (0.72) for starch. These differences are statistically significant (p<0.01). Comparable differences were found for the cumulative \(^{14} \text{CO}_2\) excretion in a six hour period. To eliminate the effect of impaired glucose metabolism on the difference in \(^{14} \text{CO}_2\) excretion between normal subjects and patients with pancreatic disease, the ratio of 6 h % cumulative \(^{14} \text{CO}_2\) after starch intake to 6 h % cumulative \(^{14} \text{CO}_2\) excretion after glucose intake was calculated. In the patients this value was 0.44 (0.16), whereas in normal subjects it amounted to 0.81 (0.21) (p=0.001).

We conclude (1) starch hydrolysis and not monosaccharide absorption is the rate limiting step in starch digestion, (2) The marked difference in starch hydrolysis between normal subjects and patients with pancreatic disease warrants the study of this test as a pancreatic function test.

T149 Comparison of sodium diclofenac and pethidine in suspected biliary colic

T GLEDDHILL, S SHEEHAN, S KENDAL, B FOZARD, D WALLER, AND T G BRENNAN (St James’s University Hospital, Leeds) Sodium diclofenac (Voltarol) is as effective as pethidine in relieving renal colic without producing opiate related side effects. We have compared the effect of these two agents in patients with suspected biliary colic in a prospective randomised double blind study.

Patients with acute, severe, upper abdominal pain were given a single intramuscular dose of Voltarol 75 mg or pethidine 100 mg. Pain was scored hourly for six hours on a five point severity scale. Analgesia was defined as a two point decrease in pain score.

The twenty five patients in each group were comparable for age, sex, and duration of pain. Of those receiving Voltarol, three failed to obtain analgesia, and three requested further opiates within six hours. Of those receiving pethidine, seven failed to achieve analgesia, four requiring further opiates. Eight patients in the pethidine group complained of nausea and vomiting compared with one receiving Voltarol (\( \chi^2 = 4.9, p<0.05 \)). Subsequent ultrasound examination demonstrated gall stones in 16 patients receiving Voltarol and eight in the pethidine group.
We conclude that sodium diclofenac is as effective as pethidine at relieving acute severe upper abdominal pain but has fewer side effects.

T150
Combined percutaneous endoscopic intubation of inoperable biliary strictures

R I Hall, M E Denyer, and A H Chapman
(Departments of Surgery, Radiology and Medicine, St James’s University Hospital and Seacroft Hospital, Leeds) Some inoperable biliary strictures are difficult to palliate endoscopically because the stricture is narrow or the ampulla is inaccessible. Passage of a percutaneous transhepatic guidewire into the duodenum enables an endoprosthesis to be passed endoscopically along the wire and through the stricture. This avoids passing large endoprostheses through the liver. This technique has been applied to 28 patients with strictures of the distal (11) or proximal bile duct (17).

Endoprostheses were successfully placed in 26 patients (93%). Both hepatic ducts were drained in 13 patients, individual or segmental ducts were drained in 13. This required a single procedure in four patients, two procedures in 19, and three procedures in three. Serum bilirubin decreased by more than 20% in the first week in all patients where both ducts drained and nine (69%) with unilateral drainage. Two patients with bilateral duct drainage (15%) and four patients with unilateral drainage (31%) developed transient cholangitis. Overall 30 day mortality rate was 25%. Two patients survived for more than six months, both had unilateral duct drainage.

The combined percutaneous endoscopic approach enables difficult biliary strictures to be intubated. Although bilateral duct drainage is preferable the palliation is often worthwhile even when segmental ducts alone are drained.

T151
Cholecystectomy via the cystic duct

M J S Dennis, D L Morris, and D C Wherry
(Department of Surgery, University Hospital, Nottingham) We have previously described the use of a 2-5 mm Olympus cholecystoscope via the cystic duct in 10 patients. We have now evaluated a new instrument – a disposable, semiflexible, semimicro, 2 mm scope (Microvasive).

The diameters of the cystic duct (CD) and common bile duct (CBD) were measured in 25 post mortem specimens by passing semiflexible rods of decreasing diameter. The scope was then introduced via the CD and passed into the duodenum through the CBD in 23 of the 25 cases. The two failures were caused by inability to cannulate the cystic duct. Mean CD and CBD diameters were 2.4 (SD 0.5) and 4.2 (SD 0.7) mm.

We evaluated the Microvasive cholecystoscope in 11 patients undergoing cholecystectomy. The instrument was passed through the CD via the CBD and into the duodenum. A clear view of the distal biliary system was obtained in nine, the two clinical failures were caused by inability to cannulate and instrument failure.

Recent advances in instrument technology allows inspection of the distal biliary tree via the cystic duct. The clinical role for this is undefined, but it may prove an alternative or adjunct to peroperative cholangiography, and reduce the number of negative common bile duct explorations.

T152
Indications and outcome of choledochoduodenostomy in 96 cases

A Polydorou, P Peveretos, and B Golemati
(Department of Surgery, Hippokration Hospital, Athens University, Athens, Greece) The clinical features, indications, operative and long-term results in a consecutive series of 96 patients who underwent choledochoduodenostomy (CBD) over a period of eight years (1979–1986) were reviewed. They were 43 men and 53 women with mean age 63.5 years (range 33–93). Twenty-nine (30.2%) patients had not undergone a previous operation upon the biliary tree. 48 (50%) had undergone one previous operation, and 19 (19.8%) had undergone two previous procedures. Seventy-six (79.2%) patients had CDD as an elective procedure and the remaining 20 (20.8%) as an emergency because of jaundice or cholangitis. The indications for CDD were: multiple CBD stones or sludge 39 (40.6%), retained or recurrent CBD stones 13 (13.5%), papillary stenosis 15 (15.6%), intrahepatic stones five (5.2%), CBD strictures 4 (4.2%), cholangitis 10 (10.4%), impacted ampullary stone 2 (2.1%), obstructive jaundice due to ruptured hydatid cyst of the liver 8 (8.4%). There were two immediate postoperative deaths, both after emergency operations. Major postoperative complications occurred in 9 (9.3%) patients and minor complications occurred in 15 (15.6%) patients. Follow up was available in 85 (88.5%) patients for a period of one to nine years. Long-term complications were seen in 5 (5.2%) patients (recurrent cholangitis in 3 and Sump syndrome in 2).

We conclude that CDD is an effective procedure for permanent biliary drainage but carries an appreciable (9–26%) rate of complication especially after emergency operations.

T153
Gall bladder function and bile reflux and the effect of cholecystectomy

D S Burkitt, I A Donovan, I K Harding, and W H Thomson
(Departments of Surgery and Nuclear Medicine, Dudley Road Hospital, Birmingham) We have measured duration and amount of duodenogastric bile reflux in 28 patients with cholecystitis before and after cholecystectomy and in 10 controls. Each patient had a 45 minute Tc99m diethyl HIDA bile reflux study two weeks before and six weeks after cholecystectomy. A liquid fatty meal was used to stimulate gall bladder contraction. Thirteen patients had functioning gall bladders (FG) and 15 non-functioning gall bladders (NFG). Reflux was considered to occur if more than 1% of the injected dose was detected in the stomach. There was no significant difference between FG group and controls with respect to duration (mean 12 minutes and 5 minutes respectively) or amount of reflux (0.58% and 0.24% respectively). Non-functioning gall bladders refluxed significantly more (2.5%) (Wilcoxon’s rank sum p<0.05) than FG group and for significantly longer (24 minutes, p<0.05). In the NFG group there was no significant alteration in amount or duration of reflux after cholecystectomy (mean 2.5%, mean duration 29 minutes). The FG group, however, had a significant increase in both percentage of dose refluxed (2.2%, p<0.01) and duration of reflux (28 minutes, p<0.05) after surgery.

In patients with FG, non-operative therapy for cholecystitis should be encouraged to avoid iatrogenic bile reflux.

T154
Resection for hilar cholangiocarcinoma: does clearance matter?

R H Gompertz, I S Benjamin, and L H Blumgart
(Department of Surgery, St Hammersmith Hospital, DuCane Road, London) Since 1977 a policy of resection for cure of cholangiocarcinoma either by local resection or by liver resection has been pursued. Twenty six patients have undergone resection between 1977 and 1985.
Three patients died in hospital (11.5%), all of whom had liver resection; there were no deaths among the group undergoing local resection. There was microscopic involvement of the resection margin in seven of 12 patients (58%) who had local resection and four of 14 (29%) who underwent liver resection. Follow up is complete. Three patients are still alive between 108 and 124 weeks and two have died of unrelated causes at 37 and 267 weeks. Median time to death in the local resection group was 78 (22–267) weeks, and in the liver resection group 115 (35–348) weeks. Although all three surviving patients had clear resection margins microscopic clearance did not affect actuarial survival prediction (p>0.1). Resection gave good palliation and avoided the inevitable morbidity associated with indwelling prostheses. These data do not suggest that microscopic involvement of the resection margin adversely influences survival.

T156
Mucosal lymphocyte isolation using recombinant interleukin 2: a preliminary study
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The standard method of isolating mononuclear cells from intestinal mucosa is enzymatic. This is associated with release of cytotoxic and immunomodulatory factors which may influence in vitro findings and cast doubt on their relationship with in vivo function. Interleukin 2 is a non-mitogenic T cell derived lymphokine which is stimulatory for activated T cells and has been used to isolate synovial T cells. The aim of this study was to assess whether Interleukin-2 could be used to isolate lymphocytes from colorectal mucosa. Mucosal biopsies were incubated with culture medium and recombinant Interleukin-2 (10–12 v/ml) in 5% CO2 for six days. Emitter lymphocytes were separated and subcultured, grown continuously for one month and cryopreserved at −70°C. The yield of mucosal lymphocytes was approximately 1×107/g wet weight, similar to the 2×107/g produced enzymatically. Single labelling of lymphocyte subsets with monoclonal antibody produced results similar to enzymatic separation (OKT3, 81±5, OKT4, 62±10, OKT8, 21±2, anti-IFR 34±16, anti-D19, 38±16%). This method has the advantage that cells are maintained in their in vivo medium and do not undergo enzymatic degradation. This technique is currently being used to generate continuous T cell lines for functional studies in Crohn’s disease.

T157
Comparison between the effects of enprostil and proglumide on a human gastric cancer cell line grown both in vitro and as a xenograft
D L Morris, S A Watson, J Harrison, and L G Durrant (Department of Surgery, University Hospital, Nottingham and Cancer Research Campaign Laboratories, Nottingham University, Nottingham)
The prostanoglandin, enprostil, reduces serum gastrin concentrations in man. Proglumide is a relatively weak gastrin receptor antagonist.

Enprostil (10 µg/ml) inhibited the stimulatory effects of gastrin-17 (G17) (135% of control) on the in vitro growth of the human gastric carcinoma cell line MKN45. Proglumide failed to affect the response. Enprostil administered orally (10 µg/kg) transiently reduced postprandial serum gastrin levels in nude mice to below 15 pg/ml compared with 200 pg/ml in untreated animals.

For in vivo studies, nude mice received xenotransplants of MKN45 and were treated either with enprostil (administered via osmotic mini-pumps, 10 µg/kg/day) or proglumide (250 mg/kg tid). Respective control mice were treated with saline. Tumour diameter was measured daily for 23 days.

In enprostil treated mice, the mean tumour area at day 23 was 3.58 cm2 compared to 5.48 cm2 in the controls and the tumour growth rate was slower (p=0.022). Proglumide had no effect on tumour growth.

The inhibitory effects of enprostil on tumour cell growth may not be entirely related to gastrin but it indicates that hormonal control of gut tumours may be a useful clinical concept.
healthy volunteers (HV), 12 patients with duodenal ulceration (DU), and 23 patients with rapid GE following TV + D – nine being asymptomatic and 14 with dumping and/or diarrhoea. An immediate estimation of GE at 30 min was made and an equivalent volume of labelled dextrose re-fed. Gastric activity (%) at 15 min was compared with that at 45 min, paired y' test. As expected, refeeding did not significantly alter GE in vagally intact subjects [HV 90 (2-6) v 91 (2-8), mean (SE) DU 75 (2-5) v 76 (2-6)] and resulted in slower initial GE in asymptomatic patients with TV + D [36 (4-2) v 58 (7-7), p<0.005]. Symptomatic subjects with TV + D, however, exhibited partial or complete return to a phase of rapid initial GE [17 (2-8) v 25 (4-1), NS]. These results provide further insight into the pathophysiology of postvagotomy dumping and diarrhoea.

T159  
Prostaglandins and the gastric epithelium: trophic effects of misoprostol on gastric epithelial cell proliferation in the dog

R A GOODLAD, A J A MADGWICK, M R MOFFATT, S LEVIN, J L ALLEN, AND N A WRIGHT (Royal Postgraduate Medical School, Cancer Research Campaign Cell Proliferation Unit, Department of Histopathology, Hammersmith Hospital, London and Searle Research and Development, G D Searle & Co, Skokie, Illinois, USA) Treatment with prostaglandins and their stable analogues, such as the methyl ester of prostaglandin E1, misoprostol, is associated with gastric hypertrophy. Some investigators have suggested that this is because of decreased cell loss rather than increased cell production, as they were unable to demonstrate any differences in labelling index. Twelve male Beagle dogs were labelled with 3H-Thymidine and killed one hour later, six of these had been given 300 mg/kg/day of misoprostol orally for 11 weeks, which resulted in a 36% increase in stomach wet weight when compared with the control animals (p<0.05). There was also a significant (p<0.01) increase in fundic gastric gland length (cell column count), predominantly in the foveolar region. While there was a significant increase in mitotic index in the misoprostol treated group, the changes in labelling index were not significant, nevertheless if the same data were expressed as labelled cells per gland, or as the gland cell production rate, a significant increase (25-9±5-9 to 44-7±4-0 cells per gland per day) was observed (p<0.05). Thus the hyperplastic changes in the gastric mucosa associated with prostaglandins are caused by increased epithelial cell production, and previous reports that this was not so are probably because of a failure to realise the limitations inherent in simple state measures.

T160  
Gastrin dependence of human colorectal and gastric tumours

S A WATSON, I G DURRANT, AND D L MORRIS (Cancer Research Campaign Laboratories, Nottingham University and Department of Surgery, University Hospital, Nottingham) The aim of this study was to determine the proportion of gastric and colorectal carcinomas in man which respond to gastrin. Seventeen fresh primary human colorectal and gastric tumours were disaggregated, cultured in vitro with gastrin-17 (G-17) and their growth was assessed by 3H-sele-no-methionine incorporation. It was found that four tumours achieved a response greater than 200% of control. In addition, moderate responses were observed in seven of the tumours (113 to 158% of control) while only six tumours showed no response to G-17 concentrations ranging from 10-4 to 10-11 mol/l.

To study the ability of such tumour cells to produce gastrin, the culture medium from nine colorectal and gastric tumour cell cultures grown in vitro for two to four weeks was assayed for gastrin by a radioimmune assay. Gastrin (20–280 pg/ml) was secreted by eight tumours.

It is concluded that 65% of gastric and colorectal tumours respond in vitro to gastrin and that many such tumours are capable of secreting gastrin. This may have clinical therapeutic implications.

T161  
Eicosanoid biosynthesis by peripheral blood leucocytes (PBL) from alcoholic patients and the in vitro response of PBMC to alcohol

J KEATING, W J MAXWELL, F P HOGAN, AND P W N KEELING (St James’s Hospital, Trinity College, Dublin) Alcohol inhibits phospholipase A2 (PLA2) activity. This enzyme liberates arachidonic acid (AA) from membrane phospholipids for subsequent metabolism to eicosanoids. Consequently, it has been suggested that ethanol inhibits prostaglandin production which may in part explain the acute inflammatory response so often found in alcoholic hepatitis. In this study, osponised zymosan stimulated peripheral blood mononuclear cells (PBMCs) and ionophore stimulated neutrophils from 44 patients who abuse alcohol (ALC) and 24 control subjects (CS) were incubated in the presence (PLA2 independent) and the absence (PLA2 dependent) of added AA. PBMCs from alcoholics produced less cytoprotective prostaglandin E2 (PGE2) [20-5 (3-2) v 40-0 (5-1) ng PGE2/106 monocytes, ALC v CS mean (SE), p<0.01], and also neutrophils from patients with ALC produced lower amounts of leukotriene B4 than the control group. Furthermore, in patients with inactive cirrhosis, the production of PGE2 by PBMCs of ALC was increased by incubating these cells with arachidonic acid [120 (118) v 585 (55) ng PGE2 ALC v CS, p<0.005]. Decreased eicosanoid production was more marked in those with alcoholic hepatitis compared with those produced by the cells from patients with inactive cirrhosis (p<0.01). However, PBMCs from 10 CS and 10 ALC incubated with 50 mmol ethanol for two hours produced similar amounts of PGE2. These results support the observation that chronic alcohol inhibits membrane bound PLA2 activity rather than the cyclooxygenase system, whilst acute exposure to ethanol does not alter PGE2 biosynthesis.

T162  
Segmental variability of aldosterone induced sodium transport in human colon

G I SANDLE (University Department of Medicine, Hope Hospital, Salford) Mammalian distal colonic epithelia generate electrical currents which are inhibited by the sodium channel blocker amiloride, enhanced by aldosterone and sulphate ions, and are generally taken to reflect electrogenic sodium transport. Recent studies in human colon indicate that amiloride-sensitive current (I_{mili}) is higher distally (sigmoid/rectum) than proximally (ascending colon), suggesting a segmental variability in mucosal responsiveness to circulating aldosterone. To investigate this further, mucosa from resected proximal and distal colon was mounted in Ussing chambers and I_{mili} (mucosal amiloride 10^{-4} M) measured under basal (pseudoluminal) and aldosterone (10^{-4} M) Bathed in NaCl Ringer, pseudoluminal I_{mili} {mean (SE)} was higher in distal [64 (19) µA/cm²; n=4] than in proximal colon [26 (12) µA/cm²; n=8; p<0.025], and did not change post-aldosterone [89 (31) µA/cm² and 11 (4) µA/cm² respectively]. Bathed in Na sulphate-Ringer, pseudoluminal I_{mili} was again higher in distal [113 (36) µA/cm²; n=4] than in proximal colon.
in proximal colon [30 (11) μA/cm²; n=8; p<0.015]. Moreover, in the presence of sulphate, aldosterone increased $I_{\text{max}}$ in distal colon from 82 (30) μA/cm² to 140 (29) μA/cm² (p<0.05; n=6), but had no effect in proximal colon [30 (11) μA/cm² v 23 (8) μA/cm²; n=8]. These results indicate that short term exposure to aldosterone stimulates amiloride-sensitive electrogenic sodium transport in human distal colon but not in human proximal colon, and this difference is accentuated by the presence of sulphate ions.

T163

Secretory activity of peptide histidine methionine and neurotensin in rat small intestine closely match their distribution

R A SPOKES, Y C LEE, Y YIANGOU, AND S R BLOOM (Dept of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Peptide histidine methionine (PHM) and neurotensin (NT) concentrations are similar throughout the small intestine of the rat while neurotensin (NT) is absent in the duodenum but present in increasing quantities along the jejunum and ileum. Neurotensin, PHM and its human equivalent, peptide histidine methionine (PHM) all cause net fluid secretion in the small intestine of the anaesthetised rat but their relative activity in different regions is not known. This has now been tested. Segments of the small bowel, 5 cm long, were tied off, one in the duodenum, three in the jejunum and one in the ileum. Each segment was injected with 0.5 ml of Krebs solution and the rat infused with PHM, NT or saline. After 40 min the rat was killed, the loops removed and weighed, before and after being opened and emptied. Fluid absorption in the control rats decreased along the gut. Peptide histidine methionine caused net fluid secretion in all areas. Neurotensin had no significant effect in the duodenum but had similar activity to PHM in the proximal jejunum and significantly more effect in the remaining gut sections. Thus, the ability of these two peptides to cause net fluid secretion into the gut closely matches their distribution.

F1

T cell immunoregulation of mucosal immunoglobulin secretion in coeliac disease

J E CRABTREE, R V HEATLEY, J M FINDLAY, AND M S LOSOWSKY (Dept of Medicine, St James’s University Hospital, Leeds and Gastroenterology Dept, Bradford Royal Infirmary, Bradford) Abnormalities of humoral immune responses occur in the intestinal mucosa in coeliac disease. In this study, the regulatory role of T lymphocytes in controlling intestinal immunoglobulin secretion has been investigated.

Intestinal mononuclear cells (IMC) were isolated from jejunal biopsies of 22 patients with normal mucosa and 22 patients with coeliac disease (10 untreated and 12 treated) by enzymatic digestion with collagenase (126 IU/ml) and density gradient centrifugation. Isolated IMC were cultured in vitro for six days, with or without autologous peripheral blood T-cells (PBT), and secreted immunoglobulins were measured by ELISA. Mean values (μg/10⁶ cells) for IgM and IgA in control patients were 1.1±0.24 and 4.82±1.56 respectively. In untreated coeliac patients significantly higher amounts of both IgM (8.82±2.65, p<0.001) and IgA (11.69±4.75, p<0.05) were secreted. IgM and IgA secretion in treated coeliac patients was comparable with control values.

Coculture of autologous PBT of untreated coeliac patients with mucosal lymphocytes at a ratio of 5:1 resulted in significant increases (p<0.05) in both IgM (129%) and IgA (281%) secretion by jejunal lymphocytes. No significant increases were evident in treated coeliac or control patients.

These results show that jejunal lymphocytes from untreated coeliac mucosa show major differences in their capacity to secrete IgM and IgA in vitro, and the enhanced secretion may result from changes in T-cell immunoregulatory function.

F2

Randomised trial of emergency endoscopic sclerotherapy versus oesophageal staple transection for acute variceal bleeding. Final report

A K BURROUGHS, P A MCCORMICK, G MEXANOTTE, G HAMILTON, K E HOBBS, AND N MCINTYRE (Academic Departments of Medicine, Surgery and Clinical Epidemiology, Royal Free Hospital and School of Medicine, London) Oesophageal staple transection (OST) is reported to be 100% effective in controlling variceal bleeding but many consider that it has too high a mortality. Thus endoscopic sclerotherapy (ES) is used widely, although its efficacy when drug therapy has failed is poorly evaluated. Few randomised trials are published comparing operative and non-operative treatment. Cirrhotics were randomised to either OST (EEA stapler) or sclerosis (intravascular 5% ethanolamine) if variceal bleeding was not controlled with transfusion and vasoactive drugs during the first five days after admission. During 336 consecutive admissions (192 patients) bleeding was controlled in 193 (3% mortality at six weeks); of the remaining 143, 23 were not eligible leaving 120 (101 patients) randomised to ES (59) or OST (61) – Pugh’s grade A 15, B 45, C 50. Mortality at six weeks was 31% OST and 37% ES by an intention to treat analysis. No differences in prognostic variables were detected using Cox’s regression models. There were four exclusions (three died) from ES and 13 from OST (seven died); five died without alternative treatment being performed. Failure to achieve a five day variceal bleed free interval (elective treatment on sixth day) occurred in 17% (11 of 65) ES (up to three injection sessions), and 0% in 50 OST patients. Another two ES and five OST patients, however, relbled from other sources. In this study the decision to treat variceal bleeding by OST or ES resulted in similar mortality, with OST being more haemostatically effective. Prediction of ES failure and/or earlier transition to other therapies may improve survival. Staple transection remains a gold standard for control of acute variceal bleeding.

F3

Effect of somatostatin compared with codeine and loperamide on calorie absorption, intestinal fluid loss and transit rate in the short bowel syndrome

C A RODRIGUEZ, J E LENNARD-JONES, D G THOMPSON, AND M J G FARTHING (St Mark’s Hospital, London) The effect of somatostatin analogue SMS 201-995 on intestinal absorption and transit after a liquid test meal was compared with two standard anti-diarrhoeal drugs in five short bowel patients (median small bowel length 60 cm, range 30–120 cm). After an overnight fast, 300 ml Ensure (Abbott) containing 5 μCi (3H)-PEG was taken orally and stoma/stool output collected for six hours. After a control study, the protocol was repeated on separate days with the following drugs: somatostatin analogue SMS 201-995 50 mcg sc 30 min before the study, codeine phosphate 60 mg orally 60 min before the study...
Thirty-two patients were included in the study, 15 of whom were men and 17 women. The mean age was 67.2±12.9 years (range: 40-83 years). The median time from start of therapy to last follow-up was 6-7±2.2 and 134±14 respectively. The mean score excluding the last two weeks of the patient’s life was also significantly improved to 6-3±2 and 125±12 (p<0.01).

F6 Extrapercorporeal shock wave lithotripsy (ESWL) for gall bladder stones (GS): initial experience in 20 patients

K A HOOD, A KEIGHTLEY, J DICK, S RAJAGOPAL, J C FORGACS, R H DOWLING, AND C N MALLINSON (Gastroenterology Unit, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals, Dulwich Hospital, and Lewisham General District Hospital, Lewisham) Extracorporeal shock wave lithotripsy using an underwater spark discharge system has recently been applied to the treatment of GS but there is little experience with piezo-ceramic systems. We therefore assessed fragmentation efficacy, safety and side-effects in 20 patients (six men, 14 women) aged 50 SD (13) y. All had radiolucent GS in opacifying gall bladders (oral cholecystography: OCG). Computed tomography scanning of the gall bladder in 11 showed CT-lucent GS in 10 and a CT-dense stone in 1. Thirteen had single and seven multiple GS, max diameter 2-1 (0.5) cm (1.5-3.0). A total of 38 treatments was given, none of which required sedation, analgesia or anaesthesia (1-4 per patient) with 4070 (717) (200-5000) shocks per session. CDCA 7.5±UDCA 5 mg/kg/day was started before or on the treatment day.

Extracorporeal shock wave lithotripsy was painless and well tolerated in all patients. Gall bladder stones fragmentation was achieved in 15. The CT-dense stone did not fragment despite four treatments. Two patients had transient microscopic haematuria and one abnormal LFTs for 24-48 h. OCG, performed 24 h after ESWL on 15 occasions, showed a poor or non-opacifying gall bladder in seven cases. No patient had biliary pain or pancreatitis post-treatment. One had a transient episode of cholestasis two months after treatment.

We conclude that ESWL using the Wolf Piezolith 2200 is an effective, safe, and well-tolerated method for GS fragmentation in selected patients.