The British Society of Gastroenterology

The 1986 Autumn Meeting of the British Society of Gastroenterology was held in Cardiff on 24–26 September 1986 under the presidency of Dr G P Crean. Below are printed the abstracts of the oral and poster communications selected by the BSG Programme Committee for presentation at the meeting.

**W1**

**Success and failure in the medical treatment of gall stones**

L O’DONNELL AND K W HEATON (University Department of Medicine, Bristol Royal Infirmary, Bristol) Since 1975 we have treated 95 patients with radiolucent gall stones ≤1.5 cm in functioning gall bladders with chenodeoxycholic acid (CDCA) 15 mg/kg (n = 74) or ursodeoxycholic acid (UDCA) 10 mg/kg alone (n = 8) or CDCA 8 mg/kg plus UDCA 5 mg/kg (n = 13). Obese patients were asked to lose weight. Three patients have started treatment within the last six months and three were lost to follow up.

Of 97 instances of gall stones in the remaining 89 patients there were 46 complete dissolutions in 39 patients. Thus the intention to treat dissolution rate of 47% case and 43% patient. Partial dissolution has occurred in six patients still on treatment. Failures were because of no radiological response after 12 months’ treatment (25), drug side effects (six), occurrence of cancers (bowel and breast) preventing further treatment (two), failure of compliance (three), inappropriate selection (three) and development of symptoms requiring surgery (five).

By life table analysis the cumulative recurrence rate±SE were 13±5% at one year, 22±7% at two years, 33±8% at three years and 48±10% at four years. Thereafter recurrence rate levelled out, being 56±11% at nine years. Redissolution was achieved in all seven patients who had a second course of therapy but the recurrence rate was 73±19% at two years.

We conclude that (i) about 50% of dissolutions remain stone free in the long term. (ii) Redissolution of recurrent stones is highly successful but rerecurrence is usual.

**W2**

**Trophic effects of cholecystokinin on the guinea pig gall bladder in vivo and on human gall bladder epithelial culture**

A N SHEPHERD, C GALLACHER, P E ROSS, AND I A D BOUCHIER (Department of Medicine, Ninewells Hospital and Medical School, Dundee) The trophic effect of cholecystokinin was investigated in vivo on epithelial cell proliferation in the guinea pig gall bladder and on human gall bladder epithelial tissue culture. The acute effects on deoxyribonucleic acid synthesis activity was explored with [3H] thymidine pulse labelling and autoradiography after a supramaximal subcutaneous injection of cholecystokinin (50 Ivy Dog Units/kg×2 two hours apart) in the guinea pig. Groups of 10 animals were killed at 6, 12, 24, and 48 hours after injection, 10 sham injected animals acted as controls. [3H] thymidine pulse labelling and autoradiography were undertaken in human gall bladder epithelial culture after the addition of cholecystokinin (0.5 Ivy Dog Units/ml of culture medium). The administration of supramaximal doses of cholecystokinin induced a significant increase in the cellular uptake of [3H] thymidine by the guinea pig gall bladder epithelial cells. 2234±205 to 3011±370 (mean±SE) (p<0.01) DPM/µg DNA six hours after subcutaneous cholecystokinin.

The significant growth promoting effect seen at six hours after injection of cholecystokinin was maintained up to 48 hours. Similarly the labelling index rose significantly throughout the study period from 0.67±0.24% to 4.01±1.24% (mean±SE) (p<0.01) at 48 hours post cholecystokinin.

Nuclear uptake of [3H] thymidine significantly increased in the cholecystokinin supplemented human gall bladder epithelial culture when added on initial day of culture (p<0.05) or after three days of culture (p<0.05). We conclude that cholecystokinin in pharmacological doses has a trophic effect on the guinea pig gall bladder epithelium in vivo and on human gall bladder epithelial cells in culture.

**W3**

**Predictive value of different symptom complexes for diagnosis of gall stones**

R JAZRAWI, G GALATOLA, R M KUPER, D P MAUDGAL, A LANZINI, A E A JOSEPH AND T C NORTHEFIELD (Departments of Medicine and of Diagnostic Imaging, St. George’s Hospital Medical School, London) It is widely believed that biliary colic is the only symptom complex of specific value in the clinical diagnosis of gall stones. In order to test this hypothesis we have studied 220 consecutive patients referred to a gastro-enterology clinic complaining of abdominal pain. At the first visit, a proforma was completed, recording whether or not the patient had a range of 11 different additional symptoms of potential relevance. An abdominal ultrasound examination was arranged plus any other investigations that were clinically indicated. Gall stone disease was diagnosed in 26 patients (12% of the population studied). Other diagnoses included peptic ulcer (n=46), gastro-oesophageal reflux (n=49), irritable bowel syndrome (n=61) and other diseases (n=38). The only symptom which, in association with upper abdominal pain, significantly increased sensitivity (SS) and specificity (SP) in the diagnosis of gall stones was radiation of the pain to the back (20/26 patients, SS=77%, SP=74%, p<0.005).

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*Because of the time lag between acceptance of abstracts and the meeting, the data presented at the scientific sessions may not correspond exactly to the information contained in the abstracts.*
Only six of 26 patients had classical biliary colic (SS=23%, SP=98%).

We conclude that radiation of upper abdominal pain to the back is a more sensitive, though less specific, characteristic of gall stones than is classical biliary colic; that this symptom complex is present in about 75% of such patients; and that it should therefore be regarded as an indication for abdominal ultrasound examination.

W4

Effect of gastric distension on gall bladder emptying in man

S ELLENBOGEN, J S GRIME, M CRITCHLEY, C R MACKIE, S A JENKINS AND J N BAXTER (University Department of Surgery, Royal Liverpool Hospital, Department of Nuclear Medicine, Royal Liverpool Hospital) We have investigated a 'gastric' phase to gall bladder emptying (GBE) in man using 99mTc-EHIDA cholecintigraphy and balloon distension of the stomach.

The gastric stimulus was achieved by distension of a nasogastric balloon tube with 500 ml water at 37°C over a 20 minute period. The study was done on nine fasted healthy volunteers (group I), and repeated in six healthy volunteers with prior administration of atropine, 0.6 mg iv and 0.9 mg sc (group II). Blood samples were taken for gastrin radioimmunoassay. Comparison has been made with a group of 11 healthy volunteers observed for a variable period (134–298 minutes) with a nasogastric tube in place and without any form of stimulation (group III).

In a 10 minute period, the probability of spontaneous GBE in group III was 0.09. Gall bladder emptying occurred in six of nine (67%) group I volunteers (p<0.001, group I vs group III, Poisson Test) and none of six (0%) group II volunteers (p=0.03, group II vs group I, Fisher’s exact test). In group I, GBE started 8.2±1.9 minutes from the start of gastric distension, and from the start of GBE the 20 minute gall bladder ejection fraction was 41±6.9%. Serum gastrin was significantly raised after gastric distension (basal=19±9.2±3.3 ng/l, post gastric distension=25.2±4.2 ng/l) (0.02<p<0.05, Wilcoxon’s Test).

These results suggest that a gastric phase of GBE exists in man, which is inhibited by atropine.

W5

Terminal ileal bile acid absorption after truncal vagotomy and cholecystectomy

D DURRRANS, T V TAYLOR, H B TORRANCE AND H J TESTA (Departments of Surgical Gastroenterology and Nuclear Medicine, Manchester Royal Infirmary, Manchester) Diarrhoea is a recognised complication of both truncal vagotomy and cholecystectomy. The underlying mechanism is unclear but may relate to the deposition of excessive quantities of bile acids on the colonic mucosa. In this study the SeHCAT retention test, which examines the active terminal ileal absorption of cholic acid, was used to compare bile acid absorption in the following six groups, each with 10 subjects: normal controls, patients with and without diarrhoea after truncal vagotomy, patients with and without diarrhoea after cholecystectomy, patients after vagotomy and cholecystectomy. Statistical analysis was by the Mann Whitney U test. No significant difference was found in cholic acid retention between the control group and those following either vagotomy or cholecystectomy without diarrhoea. Bile acid malabsorption of a degree sufficient to cause bile acid induced diarrhoea was seen in all other groups when compared with both controls and the uncomplicated operation groups (p<0.001 all groups).

These results support the idea that bile acids are of importance in the aetiology of postvagotomy and postcholecystectomy diarrhoea. The specificity of the test in examining terminal ileal absorption of bile acids indicates an abnormality of small bowel function or motility rather than a colonic motility problem.

W6

Are bile acids gastrotoxic in duodenogastric reflux? Dose response and structure activity studies using an ex vivo rat gastric chamber model

D ARMSTRONG, M FARRELL, G M MURPHY AND R H DOWLING (Gastroenterology Unit, Div. Medicine, UMDS of Guy's and St. Thomas' Hospitals, London) The toxic components of duodenogastric reflux (DGR) have not been defined. Many studies demonstrating bile acid (BA) gastro-toxicity have used a single BA in unphysiological concentrations. We, therefore, carried out systematic structure-activity and dose response studies, using an ex vivo rat gastric chamber model, on the effect of BA's±HCl, on gastric mucosal histology, PD and the 'release' of nucleic acids (NA) and acid phosphatase (AP) into the gastric chamber. The sodium salts of the prototypic BA, deoxycholic acid (DCA) (0.2, 0.5, 1.0, 2.0 and 5.0 mM) and its glycine conjugate (GDCA) (0.5–5.0 mM) were studied in groups of six rats, with 9±10 min study periods (two equilibration, one baseline, one BA challenge and five postchallenge). The results show that 5 mM DCA induced prompt (5–7 min) loss of transmucosal PD from −30±SEM 4.0 mV (baseline) to −3.6±2.3 mV, followed by recovery over 40–50 min. The ΔPD values with 5 mM DCA were 26±3 mV, 23±1 mV with 2 mM 23±2 mV with 1 mM, 16±2 mV with 0.5 mM, 3.6±0.9 mV with 0.2 mM, and 1.1±0.7 mV with saline. A dose dependent increase in NA and AP loss was seen, 5 mM GDCA produced a loss of PD similar to that produced by DCA:ΔPD 22±0.7 mV with 5 mM GDCA, 14±1.6 mV with 2 mM, 3.5±1.3 mV with 1 mM and 2.0±1.4 mV with 0.5 mM.

We conclude that studies with this model (i) show its suitability for systematic studies of the gastrotoxicity of duodenal contents, and (ii) indicate the gastric mucosal toxicity of DCA and GDCA.

W7

Expression of C-terminal flanking peptide of human progastrin in human gastroduodenal mucosa, G cell hyperplasia and islet cell tumours producing gastrin

M HARA, I M VARNDELL, A E BISHOP, J RODE, S R BLOOM AND J M POLAK (Departments of Histochemistry and Medicine, RPMS, Ducane Road, London, and The Bland-Sutton Institute of Pathology, The Middlesex Hospital Medical School, London) Recently, the structure of human progastrin was deduced from the nucleotide sequence of mRNA cloned from human pancreatic gastrin producing tumours. In this study, an antisera to synthetic C-terminal peptide of human progastrin, Ser-Ala-Glu Asp-Glu-Asn (peptide serine, asparagine, asparagine, PSN), was used on human gastroduodenal mucosa (n=5), G cell hyperplasia (n=10) and islet cell tumours producing gastrin (n=6). The results were compared with those obtained with antisera to the C-terminal of gastrin and to the N-terminal of
G34. In the gastric antrum, PSN-immunoreactivity was colocalised with gastrin in antral G cells. At the EM level, PSN-immunoreactivity was associated with each granule type in the antral G cells – that is, both electron-lucent and electron-dense granules. Hyperplastic G cells, in endoscopic biopsies from pernicious anaemia patients, also showed PSN-immunoreactivity. In the duodenum, PSN- and G34-immunoreactive cells were scattered, in contrast with the large number of gastrin immunoreactive cells detected by a C-terminal reacting gastrin anti-serum. In the pancreatic tumours, the antisera to PSN, C-terminal gastrin and G34 revealed a similar, variable pattern of localisation. Thus, we report the existence of C-terminal flanking peptide of human progastrin in normal gastroduodenal mucosa, G cell hyperplasia and islet cell tumours producing gastrin.

W8
Light microscopic and ultrastructural evaluation of rat gastric mucosa protection by De-Nol

D W R Hall and W E Van den Hoven (introduced by P R Salmon) (Gist-Brocades NV, Postbox 1, 2600 MA Delft, The Netherlands) Visually De-Nol protects rats gastric mucosa against ethanol damage (cytoprotection), though light microscopic and ultrastructural features of this protection have yet to be documented. Consequently, the morphological changes in the mucosa after De-Nol and ethanol administration were examined. Groups of 10 Wistar rats (130-150 g) received De-Nol (120 mg/kg po) or vehicle, and one hour later 1 ml absolute ethanol (ig). At one and six hours after ethanol the rats were killed and the stomachs excised. These were then filled with buffered formalin and ligated. After 0-5 hour the stomachs were dissected along the greater curvature and the mucosa assessed visually, and by light and scanning electron microscopy (SEM). Macroscopically almost complete protection was noted in the De-Nol groups at both times, while the control groups showed severe necrotic, haemorrhagic lesions. Although light microscopy and SEM at one hour after ethanol revealed disruption and desquamation of the epithelium extending into the gastric pits of both groups, De-Nol protected deep pit surface mucus cells and gastric gland cells against injury. Necrotic lesions were virtually absent after De-Nol, in contrast with mucosa treated with ethanol alone. By six hours surface epithelium was mostly restituted in the De-Nol group, but not in the ethanol treated controls. We conclude that De-Nol, like probastandins, protects the gastric mucosa by preventing ethanol induced deep mucosal necrosis and by promotion of mucosal restitution. This is in accordance with the postulated role of prostaglandins in the cytoprotective activity of De-Nol.

W9
Different mechanisms for gastric mucosal injury by aspirin and sodium salicylate

P H Rowe and W Silen (introduced by J McColl) (Department of Surgery, UMDS, Guy's Hospital and Harvard Medical School, Beth Israel Hospital, Boston, USA) Aspirin (ASA) is rapidly hydrolysed to salicylate (SA) in vivo, but both intravenous ASA and SA cause haemorrhagic lesions in the rat gastric mucosa. The effect of a vascular injury in the development of the haemorrhagic lesions in the gastric mucosa by ASA and SA has been investigated using the extravasation of Evans Blue (EB) as an indicator of vascular permeability, and Monoastral Blue (MB) to label damaged vascular endothelium. Anaesthetised pyloric ligated rats were given a bolus of 100 mM HCl via a nasogastric tube. Autopsy was carried out 20 minutes after an intravenous bolus of ASA, SA or saline (control). An intravenous bolus of EB or MB was given before autopsy. Salicylate but not ASA caused an increase in EB concentration in the gastric mucosa compared with control (p<0.05). Salicylate but not ASA or control produced monastral stained blood vessels and this area of the gastric mucosa correlated with histological surface injury. Haemorrhagic lesions in the gastric mucosa caused by SA, but not ASA are associated with vascular permeability with morphological evidence of an endothelial injury. This implies different mechanisms for the haemorrhagic lesions caused by ASA and SA.

W10
Omeprazole is less potent against acid secretion stimulated by insulin

B H Hirst, E Arilla, B Shaw and J C Williams (Department of Physiological Sciences, University of Newcastle upon Tyne, Medical School, Newcastle upon Tyne) The effects of acute, intravenous injections of omeprazole, a substituted benzimidazole, were investigated against gastric acid and pepsin secretions in conscious, gastric fistula cats. Gastric acid secretion was stimulated by equimolar, approximately half maximal doses of pentagastrin, histamine and insulin. (Omeprazole, 0.1-2.0 mg/kg, was a potent, dose dependent, inhibitor of acid secretion in the cat. The effects of omeprazole were sustained; significant inhibition was still evident 2-5 hours after a single injection. Omeprazole was equipotent against acid secretion stimulated by pentagastrin and histamine (ID50-10-2 mg/kg=0.58 μmol/kg). Insulin-stimulated acid secretion required five times the omeprazole dose for equivalent inhibition (ID50~1.0 mg/kg). Pepsin output stimulated by pentagastrin, and to a lesser extent insulin, was reduced by omeprazole, probably indirectly as a result of inhibition of acid secretion.

The hypokalaemic activity of insulin, increasing intracellular K+ concentration, or omeprazole stimulation of K+ secretion, may explain the reduced responsiveness of insulin to inhibition by omeprazole.

W11
Gastric mucosal damage by pepsin

A Leonard and A Allen (Department of Physiological Sciences, Medical School, University of Newcastle upon Tyne, Framlington Place, Newcastle upon Tyne) Anaesthetised rat stomachs, after oesophageal cannulation and pyloric ligation, were instilled with 1 ml buffer pH 2-2 for five successive 30 minute periods. Infusion of pepsin (0.5-2 mg/ml) in periods two to five resulted in a dose dependent increased mucous glycoprotein release (maximal mean 1-26 mg) compared with buffer control pH 2-2 (mean 0-44 mg) over two hours (n=6 all experiments). The adherent mucus layer on unfixed mucosal sections was continuous and unchanged by exposure to buffer at pH 2-2 but severely disrupted and discontinuous after 60 minutes exposure to pepsin (2 mg/ml). Mucosal damage by pepsin (after two hours), visible as lesions, was quantified by mean luminal iron content 0.05 μmol/ml to 0.12 μmol/ml in periods two and five respectively; no iron was detectable in pH 2-2 controls. Pepsin 2 mg/ml for 30 minutes released means of 320 μg and 146 μg mucus glycoprotein from perfused stomach and duodenum respectively, in vitro. Smectite, (aluminium: magnesium:silicate) an anti-ulcer agent administered in vivo two hours previously,
significantly reduced this degradation of gastric mucus by pepsin by 46%.

These results show: (i) mucosal damage by excess luminal pepsin; (ii) digestion of the adherent mucus barrier by pepsin in vivo (normally balanced by mucus secretion); (iii) an animal model for studying mucosal protection against damage by pepsin.

GASTRODUODENAL
W12–21

W12
A new potent cholecystokinin (CCK) antagonist
A. MCDONALD, J. C. BOJARSKI, AND J. CALAM
(Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane, Road, London) Cholecystokinin antagonists could be valuable in pancreatic and biliary disease but proglumide, which has been the best available drug, is not sufficiently potent for clinical use. We have assessed the specificity and potency of CR1392 (Rotta, Milan) – a new CCK antagonist.

CR1392 (100 μM) inhibited responses of dispersed rat pancreatic acini to CCK octapeptide (CCK8). ED50 values were; control (C) 15±8 PM, and with drug (D) 683±290 PM (mean±SE, n=6, p<0.05, Student’s t test). CR1392 (100 μM), however, had no effect on responses to carbachol (C: 190±40, D: 300±100 nM), bombesin (C: 230±80, D: 340±150 PM) and vaso-active intestinal peptide (C: 9.6±4.2, D: 12.6±3 nM). Proglumide (100 μM) had no significant effect on responses to CCK8 (C: 16±7, D: 19±5 PM).

CR1392 (10 μM) also inhibited the direct effect of CCK8 on guinea pig gall bladder muscle (C: 5±2, D: 42±26 nM, n=10, p<0.001) and its nerve mediated effect on longitudinal muscle of guinea pig ileum (C: 0.9±0.3, D: 21±14 nM, n=6, p<0.05). Proglumide had no significant effect at concentrations less than 1 mM. Responses to these tissues of carbachol were unaffected by CR1392 (10 μM).

We conclude that CR1392 is >100 times more potent than proglumide and selectively inhibits the responses of pancreatic acini, gall bladder muscle and myenteric nerves to CCK.

W13
Gastritis associated with campylobacter-like organisms in patients with rheumatoid arthritis taking non-steroidal anti-inflammatory drugs
(Department of Gastroenterology and Pathology, Royal Infirmary, Glasgow) Forty four patients with rheumatoid arthritis were questioned about upper gastrointestinal symptoms (and scored). All underwent endoscopy at which the macroscopic appearance of stomach and duodenum was recorded and two antral biopsy specimens obtained. The presence and severity of gastritis and of campylobacter-like organisms (CLO) (using Cresyl Violet Stain) were recorded using a scoring system.

Campylobacter-like were present in 23 of 44 (52.2%) patients. Fifteen of these patients (65.2%) had significant (score five or more) gastrointestinal symptoms as compared with six or 21 (28.5%) patients without CLO (p<0.05). There was no correlation between the presence of organisms and the macroscopic appearances at endoscopy, or with ingestion of any particular non-steroidal anti-inflammatory drug (NSAID). Histological evidence of gastritis was present in 36 patients (81.8%). All CLO positive patients had acute gastritis (polymorph response) in addition to chronic gastritis. Only two patients with acute gastritis were not associated with CLOs.

The results show two subgroups of gastritis (in patients with rheumatoid arthritis taking NSAID) – either positive or negative for CLOs. These cannot be differentiated by appearances at endoscopy, and thus biopsy and staining for CLO is required. Gastrointestinal symptoms are strongly associated with CLO positive patients and this may have therapeutic implications.

W15
Effect of duodenal ulcer surgery on campylobacter-like organisms (CLO) – the role of enterogastric reflux (EGR)
(Gastroenterology Unit and University Departments of Pathology and Surgery, General Infirmary at Leeds, Leeds) The effect of duodenal ulcer surgery on gastric CLO has not been previously assessed. In this study 35 DU patients and 54 who had undergone surgery underwent gastric biopsy and measurement of total bile acid concentration (BAC) in their fasting gastric aspirate. Biopsies were blindly assessed for the presence of CLO and also scored for severity of reflux gastritis (RG). We have previously shown that RG has a characteristic histology comprising marked foveolar hyperplasia, oedema, and vacuolation of the lamina propria, and a paucity of acute and chronic inflammatory cells. These five histological features were each graded from 0 (normal or absent) to 3 (severe) and the sum of the grades used to assign each patient a ‘reflux score’ (0–15). Thirty four of 35 DU patients and 15 of 16 after highly selective vagotomy (HSV) were CLO-positive compared with only two of nine after Billroth I partial gastrectomy (BIPG), eight of 17 after Billroth II PG (BIPG) and six of 12 after truncal vagotomy and gastroenterostomy (TV&GE). Absence of CLO correlated (p<0.001) with high reflux scores (>10) and increased BAC’s (>1 mmol/l). Reflux scores and BAC’s were higher...
(p<0.01) after BIPG, BIIPG and TV&GE compared with both DU and HSV.

We conclude that DU patients may revert from being CLO-positive to CLO-negative and undergo a transition from CLO-related chronic gastritis to RG after operations that increase EGR. HSV may protect against these changes in the gastric mucosa.

W16
Campylobacter-like organisms in ‘non-ulcer dyspepsia’

T ROIKAS, C PURSEY, N A SIMMONS, M J FILIPE, AND G E SLADEN (Gastroenterology Unit, Division of Medicine, Departments Clinical Bacteriology and Histopathology, UMDS Guy’s Hospital, London) Gastric campylobacter-like organisms (CLO) have recently been identified as a possible cause of gastroduodenal pathology. The purpose of this study was to determine the prevalence of CLO in non-ulcer dyspepsia (NUD) and to relate this to histological abnormalities. Forty consecutive patients (23 men 17 women, mean age 40 yr, range 18–65) with upper GI dyspeptic symptoms and no recent history of NSAID consumption were studied. All had normal abdominal ultrasound and in all upper GI endoscopy revealed no significant GI pathology. Antral biopsies were taken for bacteriological and histological examination. CLO was cultured in 16 (40%) of the patients. Sixteen (100%) of CLO positive patients had gastritis in contrast with only five (20.8%) of the CLO negative patients (p<0.001). Positive culture was also associated with sex (60.9% of men were CLO positive compared with 11.7% of women, p<0.01). Positive cultures were not associated with smoking, alcohol consumption or endoscopic evidence of gastritis. We conclude that there is a strong association between antral CLO and gastritis in patients with NUD, and a male preponderance among the CLO positive patients. The relevance of these findings to symptoms and to treatment is being explored.

W17
Preparation of monoclonal antibodies to Campylobacter pyloridis

B J RATHBONE, R V HEATLEY, M S LOSOWSKY, AND L K TREDJOSIEWICZ (Department of Medicine, St. James’s University Hospital, Leeds) Campylobacter pyloridis has been isolated world wide from gastric biopsies of patients with chronic gastritis. No highly selective media are available and attempts to isolate the organism from sites other than the gastric mucosa have proved unsuccessful. A monoclonal antibody specific for C pyloridis would provide an invaluable means for further study of this organism. To raise monoclonal antibodies eight strains of whole C pyloridis were inoculated into 10 male Balb/c mice together with B pertussis vaccine. Sonicated organisms were used for subsequent booster immunisations. Splenocytes from two mice with high serum antibody responses by ELISA were used for the generation of hybridomas. Subsequent screening for C pyloridis and C jejuni reacting antibodies was carried out by ELISA and immunofluorescence on bacterial smears. Antibodies from the hybridomas reacting with C pyloridis antigen were predominantly non-reactive with C jejuni antigens. It is likely that the specific antibodies produced will be a useful tool in identifying the environmental reservoir and mode of transmission of C pyloridis.

W18
Limitations of the Vagoroc electromotortest in the assessment of proximal gastric vagotomy (PGV)

J DRUMM, I A DONOVAN, J ALEXANDER-WILLIAMS, P LASARIDES, D BURKETT, N T DORRICOTT, AND J G TEMPLE (Dudley Road Hospital, Birmingham and The General Hospital, Steelhouse Lane, Birmingham) The incidence of recurrent ulceration reported after PGV varies considerably from one centre to another and consequently intra-positive tests for completeness of vagotomy are being advocated. We have been evaluating the Vagoroc electromotor test of the proximal and distal stomach. All operations were carried out by consultants experienced at PGV and no further dissection was done irrespective of the test result. Fifty patients were studied and follow up (including endoscopy) has been for a median of 27 months (range 13–32). There are six patients with recurrent duodenal ulceration, three from 21 patients with incomplete vagotomy on testing and three from 10 patients who apparently had a totally denervated stomach. There are no recurrences in 19 patients with confirmed PGV. In our hands the Vagoroc test has shown a high incidence of incomplete vagotomy (42%). Only half the recurrent ulcers occurred in this group, however. The misleading responses in amongst the 20% of patients whose Vagoroc test suggested total gastric denervation could be because of failure of the stimulus or failure to detect the intragastric pressure rise. We are currently investigating modifications of the test as until it has been made more reliable it cannot be recommended for wider usage in surgical training.

W19
Late complications of partial gastrectomy

R MAZZANTI, P BECHI, U ARENA, G ARANGELI, AND P GENTILINI (Istituto di Clinica Medica IV and Istituto di Clinica Chirurgica Universita’ Degli Studi di Firenze, Firenze, Italy) This study was undertaken to investigate the role of bile reflux in determining the ‘alkaline reflux gastritis syndrome’ and to test whether gall stone incidence is increased after partial gastrectomy. We studied 173 patients who had had gastric surgery 10–20 years before hand. All underwent gastric endoscopy, nasogastric aspiration and liver ultrasound or biliary radiograph. Fasting bile acid reflux (FBR), bacterial charge of gastric aspirates and a remnant histology were assessed in all. Bile acid pattern in gastric aspirates was determined in 57 randomised patients by gas liquid chromatography. Sixty three patients (36%) had developed gall stones after gastric surgery; the male/female ratio was one. Secondary bile acid were higher than normal (lithocholic and deoxycholic acid were 7%±1% and 51%±4% respectively) whether gall stones were present or not. Bacterial change was increased in gastrectomised patients in comparison with normal. The 110 patients without gall stones were divided in two groups according to the presence of the ‘alkaline reflux gastritis syndrome’ symptoms. Fasting bile acid reflux and bile acid pattern did not show any significant correlation with the severity of symptoms, endoscopic pictures and histological aspects of the remnant mucosa. Moreover, response to a provocative test (Warshaw) did not discriminate between the two groups. These results show that gall stone incidence is higher in gastrectomised patients that in a normal population with a change in the male/female ratio. Secondary bile acid increase may contribute to the increased risk of gall stone. In addition, the concept of the ‘alkaline reflux gastritis syndrome’ must be questioned as symptoms were not related with endoscopic and histological pictures.

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A1238
W20
Can a poor pharmacological response to cimetidine be overcome by higher dosing or combination with pirenzepine?

M DEAKIN, J K RAMAGE, D G COLIN-JONES, AND J G WILLIAMS (Departments of Gastroenterology, RH Haslar and Queen Alexandra Hospital, Portsmouth) In order to assess the efficacy of high dose cimetidine or a cimetidine/pirenzepine combination in controlling gastric secretion in refractory duodenal ulcer we have studied the evening and nocturnal intragastric acidity, nocturnal acid, and pepsin outputs (0030-0730) of nine patients who had a poor pharmacological response to cimetidine 400 mg (C400) and failed to heal duodenal ulcers after six weeks on this treatment given bd. The patients were studied on no treatment, C400 mg, combination of C400 mg with pirenzepine 50 mg (C400P50), or cimetidine 1600 mg (C1600) all given at 23:00.

Median nocturnal pH (25-75th %iles) was 1-4 (1-4-7-8) on no treatment, 4-7 (1-8-4-8) C400 mg, 5-3 (3-9-7-8) C400P50 and 7-2 (6-4-8-1) C1600 mg. Nocturnal pepsin output was: 24-2 (23-0-95-0) IU on no treatment and 20-7 IU (3-6-37-3) on C400 mg (a non-significant change), 2-1 IU (0-5-25) after C400P50 (p<0.001) and 0 IU (0-4) after C1600 mg (p<0.001). Cimetidine 1600 mg was better than the combination in decreasing intra-gastric acidity and intragastric peptic activity (p<0.05).

Intragastric acidity and pepsin secretion can be suppressed effectively in patients with refractory ulcers and a high dose of an H2 receptor antagonist may be more effective than combination therapy.

W21
Effect of intermittent omeprazole therapy on basal and postprandial serum gastrin concentrations in duodenal ulcer patients

I F S J CROBACH, J B M J JANSSEN, AND C H W LAMERS (Departments of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands) Hypergastrinaemia is involved in the development of ECL-cell hyperplasia and tumours by long term administration of high doses of omeprazole to rats. Theoretically, intermittent omeprazole treatment may be suitable for maintenance therapy of ulcer patients. Before maintenance therapy with omeprazole can be advocated, however, the effect of such treatment on serum gastrin has to be assessed. We have studied the effect of weekly three day courses of 20 mg/day omeprazole followed by a four day period without medication for four weeks on serum gastrin in 10 patients with duodenal ulcer in remission. Basal and postprandial serum gastrin concentrations were measured before (day 1) and immediately after the three day course of omeprazole (day 4), and further on day 6 and day 8, immediately before the next course of omeprazole. In the fourth week basal and postprandial serum gastrin concentrations were measured at similar intervals that is, on day 22, 25, 27 and 29. Omeprazole did not induce significant changes in basal serum gastrin concentrations. Postprandial increments in serum gastrin on day 6 (119±24 pg/ml), day 8 (110±21 pg/ml), day 22 (114±20 pg/ml), day 25 (123±18 pg/ml), and day 27 (141±27 pg/ml) were significantly higher than on day 1 (90±22 pg/ml). There was a tendency to higher basal and postprandial serum gastrin concentrations in the fourth week compared with the first week. It is concluded that this schedule of intermittent omeprazole therapy does not result in marked basal or postprandial hypergastrinaemia and may therefore be suitable for future maintenance therapy with this drug.

W22
Differing immunosuppressive effects of azathioprine and prednisolone in maintenance of remission in autoimmune chronic active hepatitis

J J KEATING, A J STELLON, I G McFARLANE, C MCSORLEY, J NEUBERGER, P J JOHNSON, AND ROGER WILLIAMS (Liver Unit, King's College Hospital and School of Medicine and Dentistry, London) Autoimmune reactions involving cooperation between 'killer' cells (K cells) and serum autoantibodies against the liver-specific lipoprotein complex (LSP) may be involved in liver damage in chronic active hepatitis (CAH). Induction of remission by prednisolone (P) and azathioprine (A) is associated with reduction/disappearance of serum anti-LSP and, upon withdrawal of P, relapse is preceded by a rise in anti-LSP. Recent studies suggest that remission can be maintained with A alone so, in the present study, 52 patients with autoimmune CAH in remission on P were randomly allocated to receive A alone (27 patients) or continue on P + A (25 patients). At the start, 17 of the A group and 15 of the P + A group were anti-LSP negative. During a two year follow up, only one patient (in the A group) relapsed. Liver biopsies were carried out in 39 of the 51 patients showing, at worst, features of chronic persistent hepatitis, three on A alone had granulomata. There were no significant changes in anti-LSP status in the P + A group whereas 21 of the 26 A group patients who remained in remission showed large increases in serum anti-LSP levels, from a median of 1:200 (range 1:100-1:1400) to 1:1100 (range 1:100-1:2600). The findings suggest that P acts by suppressing the autoantibody response while A may act directly on K-cells.

W23
Control of hepatitis B virus infection in a high prevalence country: a cost effectiveness study

I N ROSS, P K DASS, A S THAVARASAH, AND S S NOOR (University Hospital (Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia) Control measures for hepatitis B virus (HBV) in high prevalence countries are either mass vaccination or maternal screening and vaccination of 'at risk' neonates. We examined what these measures might achieve and compared their costs, in Malaysia, where 42% of the population have had HBV. Prevalence of 'at risk' neonates was determined by screening 700 women at the onset of labour, for HBs Ag and HBs Ag by RIA. Rn, the basic reproductive rate of HBV was derived from prevalence rates of HBV markers in 1400 subjects aged 1 month to 66 years. Rn, is the average number of secondary cases arising from one primary infectious case. When Rn is <1 an infective agent becomes extinct. Horizontal transmission accounted for 96% of infections. Vaccination of vertically infected neonates would have removed only 1% of all HBs Ag carriers during the first year of vaccination. R., was =5. Elimination of HBs Ag carriers would have reduced Rn, to 3. Thus, HBV would not be eradicated. HBs Ag screening was more cost-effective than HBs Ag screening. The marginal cost of mass vaccination was >25000HBV case prevented compared with HBs Ag screening. We conclude that (i) prevention of vertical transmission is unlikely to eradicate HBV in Malaysia,
because of a large, pre-existing pool of carriers and a mainly horizontal transmission, (ii) if maternal screening is done, then use of HBe Ag is preferable and, (iii) resources allocated to screening could be transferred to a mass vaccination programme when the vaccination cost becomes £3/neonate.

W24 Reducing the incidence of non-A non-B (NANB) hepatitis in haemophiliacs

M L FLETCHER, C R RIZZA, AND J M TROWELL
(Oxford Haemophilia Centre and Nuffield Department of Clinical Medicine, Oxford)
Fifty patients who had received no blood products in the preceding year were followed after treatment with factor VIII or factor IX with serum aspartate transaminase estimations at two weekly intervals for at least 12 weeks. Twenty patients had received no previous treatment with factor VIII or factor IX concentrate.

Twenty two of the 50 patients were treated with factor VIII prepared from small donor pools (373 to 1322 donor units) with five batches in all. Thirteen had not previously received factor VIII treatment. Eleven of the 22 patients developed NANB hepatitis including six of the 13 previously untreated patients. This followed treatment with three of the five batches.

Twenty eight of the 50 patients were studied after transfusion of factor VIII or factor IX heated to 80°C for 72 hours. Seven of the 28 patients were previously untreated. None of the 28 patients developed hepatitis.

An earlier study showed that nine previously untreated haemophiliacs all developed NANB hepatitis after factor VIII treatment. Although reducing the pool size reduced the incidence of NANB hepatitis, the method of heat treating used appears to have reduced it even more effectively.

W25 Diminished responsiveness of homosexual HBV carriers with HTLVIII antibodies to recombinant alpha interferon

J MCDONALD, L CARUSO, P KARAYANNIS, L SCULLY, W HARRIS, G FORSTER, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital, London, and St Mary’s Hospital, London)
Forty one homosexual men with chronic hepatitis B were randomised into three different doses of rIFNαA, and one control group. Response was defined as a sustained loss of the HBe and HBV-DNA. None of the control patients spontaneously seroconverted. None of the treated patients with HTLVIII antibodies responded and six of the HTLVIII negative patients (33%) responded (p<0.04). The response rate was greatest (44%) in the HTLVIII negative patients who received 10 μg/m² of rIFNαA. In the HTLVIII positive patients there was no significant difference in HBV-DNA levels after three months when compared with pretreatment levels. In contrast, there was a significant reduction in HBV-DNA levels in the HTLVIII negative patients after three months of treatment (p<0.05).

We conclude that homosexual men are an important ‘at risk’ group for hepatitis B infection 44% of these patients without HTLVIII infection respond, men with HTLVIII antibodies are non-responsive to interferon.

W26 Developmental changes in a novel low molecular weight copper binding protein (LMWP) in guinea pig liver

S K S SRAI, C D BINGLE, AND O EPSTEIN
(Department of Medicine, Royal Free Hospital School of Medicine, London)
The evidence that Wilson’s disease (WD) reflects failure to switch from the fetal to adult mode of copper metabolism has prompted us to study its ontogeny. We have previously reported that the neonatal guinea pig has a copper profile similar to WD and that the particulate fraction of newborn guinea pig liver has a LMWP that is not present in adults. This study reports the pre- and postnatal changes in copper proteins from the particulate fraction of guinea pig liver. After gel chromatography, copper in the 2-mercaptoethanol solubilised particulate liver fraction resolves into three peaks; (i) void volume (VV); (ii) metallothionein (MT); (iii) LMWP. Before birth LMWP is the dominant copper binding peak with a smaller amount associated with MT and little in the VV. On the day of birth LMWP is markedly reduced but MT is unchanged. In the first 12 postnatal days LMWP and MT decrease in parallel with falling liver copper concentrations. By day 28, once adult copper levels are reached, LMWP and MT are undetectable, and copper is associated exclusively with the VV. The parallel disappearance of liver copper and LMWP indicates that this protein may have a role in copper retention during fetal development.

W27 Screening diabetics for haemochromatosis

J J A MCALEER, L INGLES, DR HADDEN, AND M E CALLENDER
(Royal Victoria Hospital, Belfast) One thousand consecutive diabetic outpatients had blood taken for serum iron and ferritin and percentage transferrin saturation. Clinical assessment and repeat blood samples were carried out on 63 patients who had either serum ferritin above the 95th percentile (438 μg/l in men and 280 μg/l in women), serum iron above 35 μmol/l or percentage transferrin saturation above 70% in men or 60% in women. Four were unavailable for review.

For 20 patients repeat results were normal. Raised results were attributed to alcohol excess in 17 patients, oral iron ingestion in two, neoplasia in three and miscellaneous causes in three.

Liver biopsy was carried out on 12 patients and two had preirritant hepatic fibrosis or cirrhosis. Liver biopsy was not clinically justified in four, and two declined biopsy. A further patient had treated haemochromatosis.

Thus, screening for haemochromatosis yielded two new cases in 1000 diabetic patients (95% confidence limits 0–7/1000) with an overall prevalence of 3/1000 (1–9/1000), which is in the range reported from studies of non-diabetic populations.

W28 Praziquantel – an active scolicidal agent

D L MORRIS, D TAYLOR, AND K S RICHARDS
(Department of Surgery, University Hospital, Nottingham and Department of Biological Sciences, University of Keele, Keele) There are as yet few compounds with systemic activity against E granulosus. We have previously used an in vitro culture system to evaluate the activity of mebendazole and albendazole. Live scolices (E granulosus) from ovine pulmonary and hepatic cysts were maintained in tissue culture. Praziquantel (PRZ) in concentrations of 10–1000 μg/l was studied together with untreated controls. Viability of scolices was assessed by microscopy/cosin exclusions at seven day intervals and confirmed by gerbil inoculation. Praziquantel in concentrations of 50 μg/l and above produced a rapid (three days) reduction in viability of scolices. Almost all treated scolices were...
dead by 10 days. Even at concentrations below 50 μg/l significant activity was seen but a dose/speed of action relationship was seen. Penetration of PRZ into intact cysts was studied by immersing cysts harvested from gerbil peritoneal infections in media containing 2000 μg/l PRZ, intra cyst concentrations were measured by HPLC. Entry of PRZ was detected within one hour and equilibration occurred shortly thereafter. Electron microscopy of scoleces treated with PRZ revealed gross damage to the tegument. Praziquantel is a very active scoliciad agent which acts more rapidly than benzimidazoles. This together with the rapid cyst entry and known pharmacokinetics suggest that praziquantel may have a role in hydatid disease for perioperative prophylaxis.

W29
Action of Cisapride on the chronic constipation of paraplegics

N R BINNIE, G CREASY, P EDMOND, AND A N SMITH (Wolfson, Gastro-intestinal Research Unit, Western General Hospital, Crewe Road, Edinburgh and Spinal Unit, Eddenhall Hospital, Musselburgh, Edinburgh) Paraplegic patients have intractable constipation. Prolonged intestinal transit and altered rectal compliance may be associated with this. The action of Cis-4-amino-5-chloro-n-2-methoxyhexamidemmonohydrate (Cisapride) has been examined in six paraplegic subjects, give both intravenously (single 10 mg dose) and orally (10 mg 8 hourly). Colonic transit was estimated by subtracting oroacal time (lactulose and expired H2 method) from oranal time (radio-opaque markers). The mean colonic transit time without Cisapride was 284.5 h; with Cisapride orally this was reduced to 148.25 h. Rectal compliance c pressure/d volume (cm H20/ml H20) was measured in the same six patients using a reproducible proctogram method (ref 1). The mean was 7.5 with a mean maximum rectal volume of 338 ml; this was reduced to 2.8 with a volume of 233 ml after Cisapride intravenously. There was no significant change in anal sphincter pressure profile. The frequency of defecation was increased but the faecal water content remained unchanged; without Cisapride 61.7%, with Cisapride 63.8% H20. This compound has an advantage effect in paraplegic subjects because it increases frequency of defecation, reduces transit time, improves rectal tone and does not cause diarrhoea or sphincter obstruction.

W30
Endoscopic balloon dilatation of colonic anastomotic strictures

N O ASTON, W J OWEN, AND D IRVING (Lewisham Hospital, London) Anastomotic strictures occur most often in the left colon. Most are caused by ischaemia or anastomotic leakage. Obstructive symptoms develop after surgery or the stricture is seen on a distal loop enema done before closure of a protective colostomy. The conventional treatment is resection. Balloon dilatation is an alternative to surgery. Using a flexible sigmoidoscope or colonoscope of 0-038 inch guidewire is passed through the stricture. A 20 mm diameter by 8 cm dilatation balloon is passed over the guidewire. The balloon is filled with dilute contrast and the stricture dilated under image intensifier control. A second balloon may be used simultaneously. Seven anastomotic strictures have been dilated. Four have developed postoperative obstruction and in three symptoms have resolved completely. There has been only partial improvement in a patient with a rectal stricture and further dilatation is planned. Three patients have had successful stricture dilatation before closure of a colostomy. There has been no complication from the procedure. Endoscopic balloon dilatation of anastomotic strictures is a simple, safe and repeatable procedure that may obviate further colonic resection.

W31
Ganglion cells in the human internal anal sphincter

N D HEATON, J R GARRETT, AND E R HOWARD (Department of Surgery and Department of Oral Pathology, King's College Hospital, London) The distribution of ganglion cells in the internal anal sphincter has been investigated in 30 subjects considered to have a normal innervation. Previous studies have shown that there is a hypoganglionic zone extending proximally from the anal valve line for 1-2 cm, before the myenteric plexus assumes a more regular appearance. There have been few reports about the distal internal anal sphincter, but it is commonly stated to be aganglionic.

Smooth muscle from the internal anal sphincter was examined histochemically for ganglion cells, using acid phosphatase and non-specific esterase staining. Ganglion cells were present in distal sphincter in all specimens examined, scattered in small groups, associated with large nerve trunks running longitudinally along the rectum. Occasional larger ganglia were found lying between the internal and external anal sphincters, as apparent continuations of the myenteric plexus and were also associated with large nerve trunks. The hypoganglionic zone proximal to the anal valve line was present in all specimens examined. Ganglion cells of the distal internal anal sphincter were typical of enteric neurones on ultrastructural examination.

It is concluded that ganglion cells are present in the distal internal anal sphincter, and that they are enteric in origin.
We therefore conclude that a positive FOB test in patients receiving NSAID treatment cannot be attributed to upper GI mucosal bleeding but should prompt a thorough lower GI examination.

W33
Evaluation of faecal occult blood tests in symptomatic patients in general practice
N C ARMITAGE, R LEICESTER, AND J D HARDCASTLE (Departments of Surgery, University Hospital Nottingham and Haslar Hospital, Gosport, Hampshire) Faecal occult blood tests (FOBT) in symptomatic patients may reduce the time to diagnosis of colorectal cancer and adenoma without altering the stage of the cancers diagnosed. Eight hundred and sixty six symptomatic patients (355 men, 511 women) in general practice were randomised into test and control groups. Test patients were given three day FOBT and control patients were managed according to the family doctor. The proportions of major symptoms were similar in FOBT positive and control patients. In the control group 22 cancers (2 stage A, 8 stage B, 10 stage C, 2 stage D) and 12 adenomas were diagnosed - predictive value (symptoms alone) 372 (9%). Seventy five of 484 (15%) of the test group had positive FOBT and 10 cancers (1 stage A, 6 stage B, 3 stage D) and 17 adenomas were diagnosed - predictive value (symptoms and positive FOBT) 27/75 (36%). In the FOBT negative group, four cancers and six adenomas have been detected - false negative rate - 27%.

The family doctors' provisional diagnoses for large bowel neoplasia were correct in only eight of 27 (30%) FOBT positive and six of 33 (18%) control group. A positive FOBT in a symptomatic patient increases the likelihood of neoplastic pathology being present four-fold and should prompt thorough investigation.

W34
Comparison of three day Haemoccult, six day Haemoccult and Fecatwin/Feca EIA tests for the detection of faecal occult blood in screening for colorectal cancer
G PYE, K C BALLANTYNE, N C ARMITAGE, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Population screening for colorectal neoplasia requires a simple acceptable test which is specific and sensitive. Immunological tests have been developed in an attempt to improve performance over established chemical tests. Faecal occult blood tests (FOBT) were offered to 7233 individuals as part of a screening programme for colorectal neoplasia. They were randomly allocated into three groups to receive either an immunological FOBT (Fecatwin/Feca EIA) or a chemical FOBT (Haemoccult) for three or six days. Individuals with a positive FOBT were offered colonoscopy.

Fecatwin/Feca EIA achieved greater compliance (60%) than either three-day (54%) or six-day (50%) Haemoccult (p<0.001). The positive rate for three-day Haemoccult (1.25%) was less than for six-day Haemoccult (2.83%) or Fecatwin/Feca EIA (3.12%) (p<0.01). Fecatwin/Feca EIA had the lowest predictive value for colorectal neoplasia (carcinomas, adenomas >1 cm) (Feca=19%, three-day Haemoccult=72% six-day Haemoccult=61%) (p<0.001).

Faecal occult blood testing for six days with Haemoccult gave the highest yield of colorectal neoplasia (six-day 17-1, three-day 9-0, Fecatwin 5-7 per 1000 screened, p<0.001) with an associated high predictive value for investigation by colonoscopy (61%) and would seem to be the method of choice for population screening.

W35
Angina pectoris: is oesophageal acid reflux a factor?
B J O'CONNOR, J R LENNON, AND J CROWE (Department of Gastroenterology, Mater Misericordiae Hospital and University College Dublin, Ireland) Oesophageal disease is suspected to aggravate angina. Recent studies showed that oesophageal acid perfusion includes myocardial ischaemia and lowers exercise angina threshold in patients with coronary artery disease.

This study examines the effect of maximal treadmill exercise (Bruce Protocol, 12 lead ECG) on both lower oesophageal pH (Syneclite probe) and myocardial performance in 20 patients with effort angina and angiographic evidence of coronary artery disease. Myocardial performance was evaluated by heart rate, blood pressure, product (RPP), ECG changes and maximal effort tolerance. All patients were studied under basal conditions (fasting, no therapy).

All had a repeat study: 10 (group A) - 30 minutes after ingestion of a standardised meal (1078 Kcal, 45% fat); and 10 (group B) immediately after intragastric infusion of 300 ml 0-1 NHCl. No patient had effort induced reflux under basal conditions whereas reflux occurred in seven of 10 patients in group A, and five of eight patients in group B with acid exposure times of 22% and 28% respectively. Mean pH fell significantly from 7-2 (basal) to 5-65 (group A) and 5-46 (group B) (p<0.01). Myocardial performance was similar at basal levels in both groups (Wilcoxson's test).

These data suggest that cardiac status is unaffected by large food intake or acid meal and that myocardial ischaemic threshold is unaltered by oesophageal acid reflux.
4-51), nor with age. In oesophagitis patients, values were significantly greater (mean 18.55, p<0.0005, Student's t on log transformed data) and were positively correlated with age (r=0.57, p<0.01). Biopsy revealed mild laryngitis in two globus patients and distal oesophagitis in six. Previous reports appear to have overestimated the importance of distal oesophageal dysmotility and GOR in globus pharyngis.

W37
Vertical gastric plication in the treatment of gastro-oesophageal reflux – an assessment in the dog and man

T V TAYLOR AND R A KNOX (Department of Surgical Gastroenterology, Manchester Royal Infirmary, Oxford Road, Manchester)

An operation in which a vertical partition is made 5-5 cm in length and parallel to the proximal gastric lesser curvature has been devised to prevent gastro-oesophageal reflux. The technique which can be simply and rapidly done increases the effective length of the ‘intra-abdominal oesophagus’, the crural sling and mucosal flap valve effect, and the sharpness of the angle of entry into the gastric reservoir. The efficiency of the lower oesophageal sphincter (LOS) is enhanced by the Bernouille effect. The gastric cross sectional area along which reflux can occur is markedly reduced by the creation of the partition. The stomach is neither opened nor divided.

The scientific basis of the operation was established in six dogs which had their lower oesophageal sphincter excised by circular myectomy before vertical gastric plication; oesophageal pH and manometry studies were carried out and vertical gastric plication prevented reflux. The operation was done in 17 patients over a two year period who were assessed clinically, endoscopically and by 24 h ambulatory pH recording. Sixteen were classified Visick I or II and ambulatory pH recordings showed a marked reduction in reflux. The operation is technically as simple, quick and safe as inserting an Angelchik prosthesis, early results are encouraging.

W38
Does the position of the probe effect the results of oesophageal pH monitoring

S J WALKER, S HOLT, C J SANDERSON, C J STODDARD AND R SHIELDS (University Department of Surgery, Royal Liverpool Hospital, Liverpool) It is conventional to position the probe used in oesophageal pH recording 5 cm above the lower oesophageal sphincter (LOS). The aim of this study was to investigate whether probe position effects the results of 24 h pH monitoring, as this may have implications for reproducibility and trials of therapy.

We studied 10 patients and five controls. All patients had symptomatic gastro-oesophageal reflux and above normal acid reflux as measured using a standard single probe technique. Two microelectrode pH probes connected to ambulatory recorders (Ormed system) were positioned in the oesophagus, one at 5 cm, the other at 10 cm above the manometrically determined LOS. The recording period was 22 hours. Percentage reflux time (total period, erect period, supine period) were analysed at the 5 and 10 cm levels for pH 3-5, pH 4, pH 4-5 using two-way analysis of variance for non orthogonal data. There was no significant difference between the results at 5 and 10 cm, for either patients or controls.

This study has shown that the positioning of the probe at either 5 or 10 cm above the LOS does not effect the results of oesophageal pH monitoring.

W39
Intravenous nutrition (IVN) and the metabolic response to surgery

H T KHAWAJA, J M JACKSON, S T TALBOT, P C WEAVER, H A LEE (INTRODUCED BY D G COLIN-JONES) (Departments of Surgery and Metabolic Medicine, St Mary's Hospital, Portsmouth)

The purpose of this study was to investigate the effect of short term IVN on the metabolic response to surgery with particular reference to the controversial nitrogen sparing effect of peripheral isoionic amino acids (IAA). Forty six patients undergoing elective abdominal surgery were randomised into three groups. Group A (n=16) received 4% dextrose-saline delivering 6 kcal/kg/day. Group B (n=15) received IAA delivering 0-15 g nitrogen/kg/day. Group C (TPN, n=15) received a central venous infusion delivering 0-15 g nitrogen and 24 non-protein kcal (50% fat, 50% glucose)/kg/day. The cumulative six day nitrogen balance (g/kg±SEM) was significantly better in group C (−0.26±0.06) when compared with group B (−0.54±0.05) and A (−0.64±0.04) which were not different. Postoperatively, group B had lower lactate*, pyruvate*, glucose*, insulin*, and higher branched chain amino acids†, total ketones‡ and urea* than groups A and C. Additionally alanine‡ was lower and free fatty acids‡ and total triglycerides‡ were higher in group B than group C. Thus group B mobilised endogenous fat but failed to spare nitrogen when compared with group A. Group B had higher ureagenesis‡ than group C which produced a better nitrogen balance‡ for a similar nitrogen intake. This evidence demonstrates the beneficial effects of TPN and does not support the use of IAA alone as a postoperative nutritional regimen.

* p<0.05, † p<0.001.

W40
New serotonin antagonist (α5HT-M receptor) blocks diarrhoea in carcinoid syndrome

M COUPE, J ANDERSON, M BARNARD, E ALSTED, S R BLOOM, AND H J F HODGSON (Departments of Gastroenterology and Endocrinology, Royal Postgraduate Medical School, Ducane Road, London) The pathophysiology of diarrhoea in the carcinoid syndrome is complex, and treatment frequently unsatisfactory. Serotonin (5HT) has been implicated in this condition. Two classes of 5HT receptor are recognised. The 5HT-D receptor is the predominant form on smooth muscle, and is blocked by classical serotonin antagonist such as methysergide. The other (5HT-M) is the predominant form on enteric neurones, and is unaffected by methysergide. It is, however, blocked by the recently developed drug ICS 205–930.

We studied the effect of 5HT-M receptor blockade in three patients with diarrhoea associated with disseminated neuroendocrine tumours. In one case of diarrhoea associated with high circulating VIP concentrations, and normal serotonin metabolism, diarrhoea was unchanged. In contrast to two patients with longstanding carcinoid syndrome there was a profound improvement in diarrhoea with both frequency and total volume being decreased. Withdrawal of ICS 205–930 resulted in a return of diarrhoea. This new 5HT-M blocker offers promise in the treatment of diarrhoea associated with carcinoid syndrome.
W41
Home parenteral nutrition in children with small bowel failure

D A KELLY, J ARMITSTEAD, AND J A WALKERSMITH (Queen Elizabeth Hospital for Children, Hackney Road, London) Home parenteral nutrition (HPN) has been successfully implemented in adults in this country but not yet established in young children. Two children with small bowel failure are reported who have been maintained on HPN for six months. JT (24 months) has microvillous atrophy and out of 20 months of TPN has spent the last six at home. RD (23 months) has a small intestinal enteropathy and had nine months of TPN with six at home. While in hospital nutritional indices (height, weight, ratio of MAC/HC) improved with caloric intake in both children but their psychosocial development was delayed by the necessary hospitalisation. Before discharge developmental delay was assessed at four months (JT) and nine months (RD). Complications in hospital included: septicaemia×3; catheter occlusion×5; the catheter was dislodged once and replaced eight times in a total of 17 months of TPN. At home, both children have maintained their somatic growth while their psychosocial development improved dramatically with both children now being developmentally normal for their age. Complications at home included a single episode of sepsis and two catheter occlusions in 12 months of TPN. There were no major problems with electrolyte disturbance or hepatic dysfunction. In conclusion, HPN should be considered for children with small bowel failure despite their limited long term prognosis not only because complications are less but also because of the dramatic improvement in psychosocial development and quality of life for both parents and children.

The effect of autologous peripheral blood T lymphocytes on the Ig secretion of isolated small intestinal mononuclear cells (IMC) has been examined. Intestinal mononuclear cells were isolated from endoscopic duodenal biopsies by enzymatic digestion with collagenase (125 IU/ml) and density gradient centrifugation. Isolated IMC were cultured for six days at a concentration of 2×10⁶/ml and secreted Ig was measured by ELISA. Mean values (µg/10⁶ cells) for IgG, IgM and IgA were 0.21±0.08, 3.82±0.83 and 10.33±2.4 (n=20) respectively.

Coculture of IMC with autologous peripheral blood T cells (PBTC) in the absence of mitogen resulted in enhanced secretion of both IgM and IgA, but had no effect on IgG production. The medium percentage increases in IgM secretion at 1:1, 1:5 and 1:10 ratio of IMC:PBTC were 71%, 49%, and 84% respectively. The percentage increases in IgA secretion were 59% (1:1), 109% (1:5), and 137% (1:10) (p<0.05). Indirect immunofluorescence showed that the T4:T8 ratio of isolated IMC was 1:0:2:1.

These results show that T lymphocytes exert an immunoregulatory influence on immunoglobulin production by human small intestinal lymphocytes.

W43
Organ culture of fetal rat small intestine for testing gluten toxicity: a reappraisal

P D HOWDLE, G M WOOD, AND M S LOSOWSKY (Department of Medicine, St James’s University Hospital, Leeds) Recent reports of organ culture of animal fetal small intestine to detect cereal toxicity have proposed its use for screening the toxicity of cereal peptides for coeliac mucosa. Some authors assessed toxicity morphologically, others by more objective biochemical means; the results were variable. We have used foetal rat small intestine organ cultures to test the toxicity of gluten fraction III (GFIII, assessing the effect morphologically and biochemically.

Small intestinal segments from 18 day old rat fetuses were cultured with and without GFIII for 48 hours. Segments before and after culture were observed histologically and significantly more segments developed definite flat villi after culture in the absence of GFIII (p=0.009), associated with significantly less stratification (p=0.014) and more columnar epithelial cells (p=0.024). Alkaline phosphatase activity fell during culture, whereas α-glucosidase activity increased, but there was no difference whether GFIII was present or not.

Gluten toxicity for fetal rat intestine was detected using morphological, but not biochemical, means. Morphological assessment was difficult, however, because of considerable variability within sections. We do not consider this type of culture to be sufficiently reliable for routine investigation of cereal toxicity, and advise caution in the interpretation of the results.

W44
Histological changes in rat small bowel transplants treated with Cyclosporin A

A J M WATSON, P A LEAR, A M P MONTGOMERY, R F M WOOD, AND M J G FARTHING (Departments of Gastroenterology and Surgery, St Bartholomew’s Hospital, London) We have previously shown that water, electrolyte and glucose transport is reduced in rat small bowel transplants. The aim of the present study was to establish whether mucosal damage could account for these changes.

Jejunal grafts from (Lew×BN)F₁ donor rats were transplanted into parental strain Lewis rats using microsurgical techniques. Control rats had a Thiry-Vella loop constructed from their own jejunum. Both transplanted and control loops were isolated from the native gut and so did not receive intraluminal nutrition. Both groups received a seven day course of Cyclosporin A (15 mg/kg/day). At nine days there was no difference in villous height or crypt depth, compared with Thiry-Vella controls (335±7±17 vs 361±9±18 g and 136±4±2 4 vs 140±2±8 g, respectively; n=6). Nor was there any difference in the number of intraepithelial or lamina propria lymphocytes (16±2±1±3 vs 12±3±0±8 cells/100 enterocytes and 8346±816 vs 7800±410 cells/mm²; n=6). At 21 days villous height in Thiry-Vella loops was reduced compared with nine days (260±0±3±8 µm, p<0.05), but transplants remained similar to controls.

We conclude that (i) mucosal damage cannot account for the transport defects in transplants; (ii) defunctioned gut mucosa, as expected, atrophies with time in this model and (iii) Cyclosporin A is a potent inhibitor of rejection in rat small bowel transplants.

W45
Glycine and glucose polymer in oral treatment

The British Society of Gastroenterology
rehydration solution (ORS): efficacy in an animal model of secretory diarrhoea

R CUNHA FERRERIA, E J ELLIOTT, J A WALKER-SMITH, AND M J G FARTHING (Departments of Gastroenterology and Child Health, St Bartholomew’s Hospital, London) It has been suggested that supplementation of oral glucose-electrolyte solutions with amino acids improves sodium and water absorption and that the substitution of glucose by glucose polymer reduces osmolality and increases water absorption. We studied the effect of an ORS (gly-ORS) containing glycine and glucose polymer (Maltodextrin: G-10) on water and solute flux in an animal model of intestinal secretion. After exposure to cholera toxin, whole rat small intestine was perfused in situ with either the gly-ORS (Na 50, K 25, Cl 40, citrate 18, gly 50, glucose 50 mmol/l, 185 mOsm/kg; n=11) or the WHO-ORS (Na 90, K 20, Cl 80, bicarb 30, glucose 111, 331 mOsm/kg; n=7). Net water secretion was reversed to absorption by both ORS but was three fold greater with gly-ORS (123±8 vs 38±8 μmol/min/g dry wt; p<0.01). Net sodium secretion occurred with both solutions but was greater with gly-ORS (−16±4 vs −6±2 μmol/min/g dry wt; p<0.01). Approximately 50% of glucose polymer in gly-ORS was hydrolysed, even though pancreatic secretions were excluded. Net glucose absorption was greater from WHO-ORS (29±1 vs 15±1 μmol/min/g dry wt; p<0.01), despite residual free glucose (17±3±1.9 mmol/l in the effluent of gly-ORS rats. Gly-ORS was superior to WHO-ORS and other commercially available ORS tested previously; its apparent beneficial effect on water absorption may be related to mixed solute composition and low osmolality.

W46–50

W46

Does a retrovirus play a role in Crohn’s disease?

J SKELLY, M REES, J F WATKINS, AND J RHODES (University Hospital of Wales, Cardiff) In a preliminary study using a cell line (55ME8) which was a hybrid of human rectal carcinoma and mouse embryo cells, antibodies were found in serum from Crohn’s patients which reacted with cytoplasmic antigen; they were shown by immunofluorescence. Antibody was detected in 50% of 71 Crohn’s, 16% of 90 ulcerative colitis, none in 30 with carcinoma colon, none in 30 with pneumococcosis and in 9% of 58 healthy controls. Subsequent work showed antigen in 14% of 94 normal controls, 50% of 102 of Crohn’s and 32% of 76 with ulcerative colitis. Measurement of antibody to 55ME8 cells by enzyme linked immunosorbent assay (ELISA) gave a mean optical density reading of 0.508, SD 0.238 for 95 normal controls, 0.604, SD 0.333 for 100 with Crohn’s disease and 0.492, SD 0.272 for 77 with ulcerative colitis.

Retrovirus antigens in 55ME8 cells were investigated using specific antiviral antisera for immunofluorescence. Antibody to the Simian sarcoma/leukaemia virus complex (SSV/SLV) gave a granular cytoplasmic fluorescence identical in appearance to that given by the Crohn’s positive sera. The anti SSV/SLV serum, and the Crohn’s positive sera reacted with a polypeptide with a molecular weight of 70 000. The identity of the polypeptide reacting with Crohn’s serum remains to be established. Results are relevant to the question that a retrovirus may play a role in Crohn’s disease.

W47

Impaired activation of the neutrophil oxidative metabolism in Crohn’s disease (CD) and ulcerative colitis (UC)

H W VERSPAGT, J ELMGREEN, A S PEÑA, I T WETERMAN, AND C B H W LAMERS (Departments of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands and Department of Gastroenterology, Herlev Hospital, Copenhagen, Denmark) Phagocytosis associated oxygen metabolism is crucial in the killing and complete breakdown of microorganisms by neutrophils. We have previously shown that neutrophils of untreated CD patients produced less hydrogen peroxide than controls. In the present study we determined the neutrophil oxidative capacity of 30 CD, 14 UC patients and 18 controls. Cells, obtained by density gradient centrifugation, were incubated with 5 oxidative stimuli (PMA, con A, zymosan, f-MLP and CSa) and the superoxide anion (O2−) and hydrogen peroxide (H2O2) production were measured (expressed in nmoles/3×106 cells/30 min). Lysates of the neutrophils were analysed for superoxide dismutase (SOD) contents by an ELISA method (expressed in ng SOD/μg DNA). Disease activity of the patients was scored by the CDAI.

Neutrophils of CD patients showed a significantly diminished maximum O2− production (430±23, p<0.05) compared with controls (516±25) whereas in UC the overall O2− production was markedly decreased (range 30±4 to 404±31, 0.05<p<0.001) irrespective of the stimulus used. The neutrophil H2O2 production in CD and UC deviated only marginally from controls. Evaluation of the neutrophil oxidative metabolism in relation to the disease activity revealed a negative correlation with the O2− production in both CD (r=−0.664, p<0.01) and in UC (r=−0.847, p<0.02). This disease activity related deficiency was accompanied by a reduced neutrophil SOD contents in CD (7.1±2.3, p<0.05) and UC (5.7±4.2, p<0.001) compared with controls (7.8±4.2) and the SOD was also negatively correlated with the disease activity (r=−0.49, p<0.01) in both diseases.

These observations clearly indicate a deficient neutrophil oxidative metabolism in CD and UC as illustrated by a reduced O2− production and SOD contents; this association is strengthened by the negative correlation with the disease activity. This neutrophil impairment might result in an inadequate antigen handling at the intestinal level contributing to the inflammatory process.

W48

Macrophage subpopulations in inflammatory bowel disease

Y R MAHDA, P GIONCHETTI, D VAUX, S PATEL, AND D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) Macrophages of the intestine are a heterogenous population with respect to morphological and histochemical criteria. This study characterises them further using a panel of monoclonal antibodies, both in normal and diseased colon. The effect of cell isolation on the proportion of subpopulations is also investigated.

Tissue was snap frozen and sections were stained using the peroxidase technique. Antibodies:— RFD1 (interdigitating cells), RFD7 (mature macrophages), RFD9 (epithelioid cells and tangible body macrophages), 3G8 (Fc receptor on neutrophils and some macrophages), 3C10 (monocytes and macrophages). For normal colon (n=10), the mean percentage (±SEM) of
positive cells in the lamina propria were:—RFD1 = 19% (±1.0), RFD7 = 20% (±1.9), RFD9 = 1% (±0.6) 3C10 = 26% (±2.2), 3G8 = 1% (±0.6). In active ulcerative colitis (n=10) and Crohn’s disease (n=6), there was a significant increase in RFD9 cells (11% (±1.1) and 8% (±2.0) respectively) and 3G8* macrophages (8% (±1.5) and 11% (±2.7) respectively). The RFD9* cells were largely aggregated in 5 out of 10 UC and in all Crohn’s tissue, occurring more frequently in the deeper layers of the lamina propria.

These findings were confirmed in mononuclear cell suspensions isolated from colon by enzymatic digestion.

W49 Oral and rectal permeability in patients with inflammatory bowel disease

R T JENKINS AND J K RAMAGE (INTRODUCED BY R H HUNT) (INTESTINAL DISEASE RESEARCH UNIT, McMASTER UNIVERSITY MEDICAL CENTRE, Hamilton, Ontario, Canada) Increased urinary excretion of 51Cr-EDTA after oral administration has been found in patients with Crohn’s disease (CD), but studies of patients with ulcerative colitis (UC) have yielded conflicting results. We investigated whether the inflamed colon shows increased permeability. Groups studied were: (a) 12 controls, (b) 12 patients with small bowel CD, and (c) 15 patients with colitis (eight CD colitis, five total UC and two left sided UC). 51Cr-EDTA (25 μCi) was given on separate occasions either orally in a bland fruit drink or rectally in normal saline via a 30 cm 8F catheter. Urine was collected for 24 h, and the total volume was counted. Excretion (median, range) after rectal administration to each group was: (a) 0.7%/24 h (0.1-1.6), (b) 0.9%/24 h (0.2-3.5; p<NS); and (c) 6.6%/24 h (1.2-21.6; p<0.0001). After oral dosing, excretion was: (a) 1.2%/24 h (0.6-2.8), (b) 2.8%/24 h (0.8-14.0; p<0.0001), and (c) 6.1%/24 h (0.9-28.3; p<0.0001). No significant difference was found between CD colitis and UC groups either orally or rectally. We conclude that in colitics abnormal permeability is shown by both oral and rectal tests. This indicates the colon is an important site of increased permeation. The oral test discriminates patients with colitis from controls as well as the rectal test (accuracy 93%). The rectal test discriminates between small bowel disease and colitis (accuracy 89%). A combined test should be evaluated prospectively in inflammatory bowel disease.

W50 Immunological findings in jejunal secretion of patients with Crohn’s disease (CD)

J F COLOMBEL, D DELACROIX, M HALPHEN, C DIVE, AND J C RAMBAUD (INSERM U54, Saint-Lazare Hospital, Paris, France and Gastroenterology Unit, Catholic University of Louvain, Brussels, Belgium) Abnormal in vitro immunoglobulins (Ig) synthesis and secretion by intestinal plasmocytes have been reported in patients with CD. The aim of this study was to compare jejunal secretion rates of polymeric IgA (p-IgA), monomeric IgA (m-IgA), IgM, IgG and secretory component (SC) in 11 healthy volunteers and six CD patients free of lesions of jejunal biopsies and having no active treatment.

Segmental jejunal perfusion was carried out using a four lumen tube. The infusion point was located near the duodenojejunal junction above an occlusive balloon. Distal collection point was 40 cm below. The intestine was perfused with a 115 mM NaCl, 10 mM KCl and 35 mM mannitol solution with PEG 4000 (1 g/l) as a dilution marker. After a 60 min equilibration period four 20 min samples were collected. Concentrations of Ig and SC were measured by immunoradiometric assay and proportions of p-IgA and m-IgA by a sucrose density gradient ultracentrifugation. Results: jejunal secretion rates (μg 40 cm⁻¹) were: IgA = 18±4; IgM = 25±4; IgG = 40±6; SC = 363±129. m-IgA = 220±44; p-IgA = 18±4; IgM = 25±4; IgG = 40±6; SC = 363±129. m-IgA = 220±44; p-IgA = 18±4; IgM = 25±4; IgG = 40±6; SC = 363±129. m-IgA = 220±44; p-IgA = 18±4; IgM = 25±4; IgG = 40±6; SC = 363±129.

We conclude that polymeric IgA secretion is lowered in patients with CS. As p-IgA is the main component of intestinal Ig secretion, our study supports the hypothesis of an abnormal intestinal immune response in CD.

W52 Prospective randomised trial of chronic sclerotherapy to prevent variceal bleeding using the same protocol to treat bleeding. Interim analysis

A K BURroughs, F D’HEGYERE, A PHILLIPS, J DOOLEY, O LEIPSTEIN, AND N MCMINnTELL (Academy of Disease Department of Medicine and Clinical Epidemiology, Royal Free Hospital, London) All but one of the controlled trials of chronic sclerotherapy (CS) have used different emergency treatments at varying time points for variceal bleeding in the control and sclerotherapy groups. Different treatments can cause different early mortality and early rebleeding rates. The effects of CS may be obscured by therapy used for acute bleeding. From January 1984 we randomised 92 cirrhotics after control of acute bleeding to CS (n=43) or no chronic...
sclerosis (n=49), who were given sucralfate (SU). Using a standardised protocol for all variceal bleeding if transfusion and glypressin did not control bleeding then emergency sclerosis or oesophageal staple transection were used in a randomised order. Characteristics of the index bleed and time to randomisation were well matched between the two groups but mean Pugh’s score was different: CS=7-95, SU=9.14. Fifty six episodes of variceal bleeding occurred in the SU group versus 45 in the CS group. There was no difference between the survival curves analysed by log-rank analysis; both were very similar to those of sclerosed patients in the controlled trials. These results suggest that if the same management is used for all episodes of bleeding the therapeutic value of adjunctive chronic sclerotherapy may prove to be small.

W53

Venous drainage of the normal gastro-oesophageal junction: a route to understanding varices

A VIANNA, P HAYES, G MOSCOSO, M DRIVER, D WESTARY, AND R WILLIAMS (Liver Unit and Department of Morbid Anatomy, King’s College Hospital and School of Medicine and Dentistry, London) A study into the venous circulation of the GOJ using 52 cadavers and three complementary techniques (cast corrosion, radiology and morphometry) allowed the demarcation of four distinct venous zones: (a) gastric zone, where the veins lie deep into the submucosa; (b) palisade zone, composed of numerous narrow parallel longitudinal vessels in the lamina propria; (c) perforating zone, characterised by treble clover shaped veins, which collect and channel laterally blood from ascending and descending intrinsic vessels to the extrinsic veins; and (d) truncal zone, composed of four or five deep lying descending large veins, which drain into the perforating zone. Venous flow appears to be bidirectional at the palisade zone, a watershed between the portal and aygous systems. In portal hypertension this venous system has to accommodate an increased cephalad portal venous flow. Preparations from cadavers with gastro-oesophageal varices showed the consequences of this adaptation. Three avenues of venous drainage were demonstrated: (1) from the stomach, through the gastric and palisade zones; (2) from extrinsic veins, through the perforating zone; and (3) via extrinsic veins alone, thereby forming para-oesophageal varices. These data may have implications for the development and rupture of gastrooesophageal varices.

W54

Placebo controlled trial of glypressin in the management of acute variceal bleeding

J G FREEMAN, I COBREN, AND C O RECORD
(Gastroenterology Unit, Royal Victoria Infirmary and University of Newcastle upon Tyne) In an open study we have shown that glypressin is significantly better than vasopressin in controlling acute variceal haemorrhage. The aim of the present study was to confirm the efficacy of glypressin and by means of a double blind placebo controlled trial compare therapy with the natural history of variceal bleeding episodes. On entering the study all patients were actively bleeding from varices confirmed by endoscopy. Patients were transfused and randomised to either 2 mg glypressin or an identical placebo injection, intravenously every four hours until bleeding was considered to be controlled followed by a further four 1 mg doses. A Sengstaken tube was passed if bleeding continued despite two doses of the drug. Thirty one bleeding episodes in 29 patients were treated. Nine patients were controlled by glypressin (60%), whereas six patients were controlled by placebo (37%; p>0.05 Fischer’s exact test). Only two of nine Child’s grade B/C patients were controlled by placebo compared with five of seven by glypressin. Deaths were higher in the placebo group (25% compared with 13%). In conclusion, one third of bleeding episodes will cease spontaneously; glypressin appears to be of benefit to patients with the more severe hepatic dysfunction.

W55

Prospective evaluation of glypressin for variceal bleeding in cirrhosis

F D’HEUGERE, A K BURROUGHES, S SHERLOCK, AND N McINTYRE (Academic Departments of Medicine and Surgery, Royal Free Hospital, London) The value of vasopressin in controlling active varical bleeding has been questioned recently; its efficacy is about 50% in both controlled and uncontrolled studies. Glypressin, a synthetic long acting analogue of vasopressin was more effective than vasopressin in a single small controlled study. We evaluated prospectively intravenous glypressin (2 mg qds for 24 hours) for active variceal bleeding in cirrhotics during the first 24 hours of admission using a standardised protocol. Study population: 208 admissions: Pugh’s grade A (47), B (82), C (79). Glypressin was not used in 132 admissions: eight due to terminal disease, seven balloon tamponade used first, and in 117 glypressin was not required. In 76 admissions (41 alcoholics) glypressin controlled bleeding at 24 hours is only 35 (46%); 63% of grade A, 38% of grade B, and 21% of grade C patients. In the whole group, control of bleeding at five days was only 29%, balloon tamponade was required in 37%, and 30 day mortality was 22%. All patients had abdominal colic, two developed heart failure which in one was secondary to a fatal myocardial infarction. The efficacy of glypressin appears no different from vasopressin, and is related to the severity of liver disease. These results suggest that randomised studies of glypressin should be undertaken to assess its efficacy taking into account the severity of liver disease.

W56

Effects of a somatostatin analogue SMS 201–995 on endotoxaemia in the rat

J N BAXTER, S A JENKINS, D W DAY, AND R SHELDERS (Department of Surgery and Pathology, University of Liverpool, Liverpool) We have recently demonstrated that a long acting analogue of somatostatin, SMS 201–995, markedly stimulates reticuloendothelial system (RES) activity in rats. As RES activity is an important defensive mechanism against infection, the aim of the present study was to investigate if SMS 201–995 could protect against endotoxaemia in rats. Eight male Wistar rats (250 g) received 2 µg SMS 201–995 sc 30 minutes before administration of 20 mg E coli endotoxin (026 B6 Bovine) ip. A further 2 µg of the analogue was given four hours after endotoxin administration. Control rats received similar doses of isotonic saline sc and endotoxin ip. All rats were bled from the tail artery eight hours after endotoxin administration, killed, the livers and kidneys removed, weighed and fixed in formal saline. The livers and kidneys of SMS 201–995 treated animals were relatively normal in appearance. In the control animals, however, the livers were markedly congested with conspicuous extravasation.
of red blood cells from capillaries. Moreover, the hepatocytes showed marked degenerative changes. Similarly the kidneys of control animals displayed lobular necrosis and capillary stains. The liver weights, kidney weight and serum levels of bilirubin and alanine amino transferase were significantly less (p<0.05, Student’s t test) in SMS 201–995 treated animals than in controls.

The results of this study suggest that SMS 201–995 may be of value in protecting against hepatic and renal damage in endotoxaemia.

W57
Studies with alcohol in the baboon
C AINLEY, A SENAPATI, I M H BROWN, C A ILES, B M SLAVIN, D R DAVIES, P W N KEELING, AND R P H THOMPSON (The Gastrointestinal Laboratory, Department of Dietetics, Department of Chemical Pathology and Department of Histopathology, St Thomas’s Hospital, London) Lieber and coworkers have produced alcoholic liver disease in adolescent baboons, with steatosis in all animals and cirrhosis in 33%. They gave the Lieber-DeCarli liquid diet with 50% of calories as ethanol, but their animals only maintained their weight and did not grow. To examine the role of nutritional factors we have attempted to reproduce these findings.

Ten adolescent baboons (colony 1) were divided into three groups: two controls; four ethanol (E); four ethanol + zinc (E+Z). All animals received the Mazuri primate diet; E and E+Z were started on ethanol – increasing to 25 g/kg/day (70% of calories), and E+Z were supplemented with 50 mg zinc/day. They were monitored by regular weighing, blood ethanol concentrations, liver blood tests and liver biopsy. Four further adolescent baboons (colony 2) were given the Lieber-DeCarli diet in which the ethanol content was progressively increased to 10 g/kg/day.

Colony 1 have been studied for up to 60 months. All animals gained weight normally. Blood ethanol concentrations ranged from 63 to 342 mg/dl, and changes in liver blood tests were small. Two E and four E+Z developed steatosis, which was severe in two E+Z, but no fibrosis or cirrhosis was seen in any animal. Colony 2 stopped growing with the introduction of ethanol to the diet, and then lost weight as the dosage was increased.

We conclude that we have been unable to produce fibrosis and cirrhosis in baboons given large amounts of ethanol. Our results suggest that nutrition is important in the genesis of such changes.

W58
Abnormal haem biosynthesis associated with unconjugated hyperbilirubinaemia in the Gunn rat
K E L MCG, F BOND, G G THOMPSON, AND M R MOORE (University of Glasgow, Department of Medicine, Western Infirmary, Glasgow) Following the observation of abnormal haem biosynthesis in Gillett’s syndrome we have studied this process in Gunn rats which have severe unconjugated hyperbilirubinaemia resembling that in Crigler-Najjar syndrome type I.

The activities of the enzymes of haem synthesis, excretion of porphyrins and precursors, and blood porphyrins were examined in eight Gunn rats (mean serum bilirubin = 142 μM, range 95–160) and eight controls (mean serum bilirubin = 5 μM, range 3–8). The activity of the penultimate enzyme of the haem pathway protoporphyrinogen oxidase (PROTO.O) was reduced with a mean value of 38% of controls in liver (p<0.001) and 24% of controls in kidney (p<0.001). In keeping with an enzymatic partial block in haem synthesis there was a two-fold increase in hepatic and seven-fold increase in renal activity of the rate controlling enzyme of the pathway 5-aminolaevulinate synthase. The Gunn rats also had increased urinary porphyrin excretion (mean = 302 μg/24 h vs control mean = 170 μg/24 h, p<0.05) and increased blood porphyrin concentration (mean 1,167 nM vs control mean 719 nM, p<0.01).

This pattern of enzymatic defect is identical to that found in Gillett’s syndrome and provides further evidence that unconjugated bilirubin impairs haem synthesis by inhibiting PROTO.O activity. This effect of unconjugated bilirubin may explain its neurotoxicity.

W59
Cytotoxic T cell responses to the nucleocapsid proteins of HBV in chronic hepatitis: evidence that antibody modulation may cause protracted infection
M PIGNATELLI, J WATERS, A M L LEVER, S IWARSON, R GERETY, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital, London) Using an autologous cytotoxicity system to study 18 HBsAg/cAg positive patients (CAH) and nine control subjects (HBsAg/cAg negative patients with no significant inflammatory liver disease). Fifteen out of 18 patients showed cytotoxicity indices above the normal range. By blocking techniques with monoclonal antibodies, to HBc (RFHBC17), HBc (RFHBC17), HLA class I (W6/32), Leu 2 (T8) T cell cytotoxicity was significantly inhibited. RFHBC17 and RFHBC1 together resulted in greater inhibition than with either antibody alone. We have also investigated the effect of passive administration of monoclonal antibodies to HBc and HBs on HBV infection in chimpanzees. Two animals received the HBV inoculum (10⁶, 10⁴CID) preincubated with either RFHBC17 or RFHBC1 and two chimpanzees received HBV alone. Passive immunisation did not protect against infection and in both cases led to an unusually prolonged hepatitis (>6 months duration).

These data suggest that two populations of T cells exist recognising HBc and HBs antigens on the hepatocyte membrane. High titre anti-HBc in the serum of patients with chronic HBV infection will modulate T cell lysis by cells sensitised to HBc. Thus HBc is the important target antigen for cytotoxic T cells mediating liver damage during the phase of HBV replication and HBs/cAb seroconversion.

W60
Influence of epidermal growth factor (EGF) on liver regeneration after partial hepatectomy in rats
P SKOVOlsen, S BOESBY, R KIRKEGAARD, K THERKELSEN, S S POULSEN, AND E NEV (Department of Surgery C, Rigshospitalet, Department of Anatomy B, Copenhagen and Department of Clinical Chemistry, Hillerød Hospital, Denmark) Epidermal growth factor stimulates DNA synthesis in cultures of adult rat hepatocytes. This effect is enhanced in the presence of insulin and glucagon. The effect of EGF on liver regeneration after 70% hepatectomy in rats was investigated. Eight to 32 hours after partial hepatectomy the concentration of EGF in portal venous blood was unchanged compared with unoperated controls. Brunner’s glands and the submandibular glands secrete EGF. Extirpation of Brunner’s glands reduced the median liver
regeneration significantly from 3-02% (2.69-3.37) to 2.45% (2.13-2.72) (wet weight of the liver remnant five days after partial hepatectomy expressed as percentage of total body weight), while extirpation of the submandibular glands had no effect. Antibody to rat EGF (ab 3124, 100 µl twice daily (sc) for five days) also reduced liver regeneration. Oral or sc administration of synthetic human EGF (5 nmol twice daily for five days) had no effect on liver regeneration, but simultaneous sc administration of EGF and insulin (15 IU twice daily) or glucagon (100 µg twice daily) increased liver regeneration significantly to 5-31% (4.86-6.30) and 4-04% (3.57-4.64) after five days. Insulin increased liver regeneration to 3.54% (3-15-4.39) and glucagon to 3.35% (2.80-3.95). The results suggest that endogenous EGF in combination with insulin and glucagon enhance liver regeneration after partial hepatectomy in rats.

(Received Human EGF was supplied by G.D. Searle Co. Ltd. and Imperial Chemical Industries, PLC, UK).

W61
Further characterisation of high molecular weight hepatotropin induced by hepatic resection

CLAIRE SELDEN, A BALSILLIE, H DARBY, AND H J F HODGSON (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) We recently described a high molecular weight hepatotrophic factor in the blood of man and rats 24 hours after hepatectomy, and report here further characterisation of the rodent substance. SDS-polyacrylamide gel electrophoresis demonstrated two major bands, MW 78 000 and 79 000. The possibility that these were high molecular weight precursors of Somatomedin peptides (IGF I and II) was dismissed by the use of specific antisera. The radiolabelled hepatotropin bound to rat hepatocytes in vitro. Selectivity for stimulation of DNA synthesis in hepatocytes, in comparison with fibroblasts or peripheral blood mononuclear cells, was demonstrated in vitro. Primary cultures of rapidly regenerating hepatocytes were strikingly more sensitive to the stimulatory effects of hepatotropin than were primary cultures of resting cells (1-5 fold at 27 µg/ml, 3-5 fold at 67 µg/ml, and 8 fold at 160 µg/ml), a phenomenon similar to that previously reported for epidermal growth factor. In its biological effects this hepatotropin has many similarities to peptide growth factors but its physico-chemical characteristics are those of a high molecular weight protein. Further study should offer new insight into control of liver regeneration after partial hepatectomy.

W62
Modulation of hepatitis B virus protein expression by interferon (IFN): homology between the precore region of HBV-DNA and a sequence regulating the cellular interferon induced antiviral system

M PIGNATELLI, A M L LEVER, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital, London) The viral proteins recognised by cytotoxic T cells have been shown to be HBe and HBe. We have investigated the effect of IFN on the expression of these proteins in HBV infected hepatocytes by screening liver biopsy specimens from 16 untreated chronic HBV carriers (HBeAg positive) and 13 patients given 7.5-10 µm² of lymphoblastoid IFN (Wellferon) from two to 78 days. Interferon produced an increase in HBeAg and a reduction in HBeAg expression in the cytoplasm and reduced membrane expression of HBsAg in infected hepatocytes. We then sought evidence of sequences in the virus genome which might be homologous with IFN sensitive sequences which have been identified upstream of several genes encoding for cellular proteins which can be induced by interferon. Such sequences were identified in the coding strand of HBV within the precore region (1821-1834 in adw subtype) and also in the non-coding strand upstream from the DNA polymerase gene (2234-2245 in adw subtype).

We conclude that it is probable that the HBV sequence showing homology to the IFN sensitive regulatory sequences of the cellular genome are responsible for the effects of HBV protein expression, produced by alpha interferon.

the value of propranolol in congestive gastropathy of portal hypertension

S W HOSKING, H KENNEDY, I SEDDON, AND D TRIGER (University Departments of Surgery, Pathology and Medicine, Royal Hallamshire Hospital, Sheffield) Histological studies have suggested that gastritis in portal hypertension is due to submucosal congestion rather than to inflammation; this has been termed congestive gastropathy. Because it does not respond to antacid therapy we have assessed the effect of D-propranolol on the lesion. Twenty four patients (Child's A 15: B nine) with endoscopic evidence of chronic gastropathy (present for at least six weeks without evidence of improvement) were given propranolol (160 mg Inderal LA daily) or placebo, with crossover to the other drug after six weeks. The order of drug administration was randomly chosen. Endoscopic assessment and gastric biopsies were taken at the start, crossover (six of 52) and end of trial (six of 52).

Twenty two patients completed the study; two withdrew (one propranolol: one placebo). Histology confirmed congestive gastropathy in all patients, but consistent changes in response to propranolol were not seen. Macroscopic appearances of mild gastropathy (snake-skin and scarlatina) did not alter with the active drug, but severe changes (cherry red spots) disappeared in four of five patients on propranolol and only one of five on placebo. Clinical bleeding from gastropathy was seen during the trial in only one patient (receiving placebo). Because cherry red spots indicate a high risk of gastrointestinal haemorrhage in portal hypertension propranolol may play a role in preventing such bleeding.

T2
Induction of remission in primary liver cell cancer (PLC) with a new thymidylate synthase inhibitor, CB3717. A phase II study

M F BASSENDINE, N J CURTIN, A L HARRIS, AND O F W JAMES (Departments of Medicine and Clinical Oncology, University of Newcastle upon Tyne) CB3717 is a new ‘non classical’ antifolate which acts by inhibiting thymidylate synthase (TS), a pivotal enzyme in the biosynthesis of DNA. We have already shown inhibition of growth of two human PLC cell-lines both in culture and xenograft models by CB3717. The cytotoxic dose of CB3717 to
PLC cells in vitro lies within that achieved in plasma after intravenous infusion in phase I clinical studies. The activity of CB3717 lead to a phase II trial.

We treated 14 consecutive unselected patients with PLC with 300 mg/m² IV every three weeks (three died after only one course, max nine courses). There were eight men, six women, aged 27 to 74 years (mean 56 years); 11 had cirrhosis, six were grade A (expected survival >14/52, eight were grade B (expected survival <14/52). Six patients showed objective response (four grade A, two grade B) with both decrease in tumour size (CT scan) and >50% reduction in alphafoetoprotein (AFP) three of these had >1 log fall in AFP; five of six of these were cirrhotic, five of six were women; a further male grade B patient showed static disease (CT scan, AFP) during nine courses. Thus of 11 patients receiving ≥two courses seven showed clinical benefit. The median survival of the grade A responders from start of therapy was 52 weeks, two still alive; the grade B responders (plus the static patient) was 40 weeks. Unwanted effects included malaise plus nausea (seven), hepatotoxicity (five), stomatitis (two), rash (two), and renal toxicity (two). Significant myoclosumpression and alopecia were not encountered. TS inhibition is a rational and effective target in PLC.

These results suggest that CB3717 will be a useful new therapeutic agent in this tumour. Further control trials are indicated.

T3 Penicillamine and cysteine protect hepatocyte membranes from acetaldehyde

A J K WILLIAMS AND R E BARRY (Departments of Medicine and Biochemistry, University of Bristol, Bristol) Acetaldehyde binds to liver plasma membranes via the formation of an intermediary Schiff base with the free amino groups of lysine residues in membrane proteins. The resulting alteration in the hepatocyte surface membrane has been shown to activate complement in man, and stimulate the neutrophil in rat. Mercaptoemic can react readily with aldehydes. We have studied the effect of two such potential therapeutic agents, cysteine and penicillamine on the binding of acetaldehyde to the hepatocyte membrane of the rat. The binding of acetaldehyde to hepatocyte membrane vesicles was studied using the incorporation of tritium from tritiated sodium cyanoborohydride. Acetaldehyde (1 mM) was incubated alone or in the presence of equimolar, or excess (~5:1 molar ratio) cysteine or penicillamine. Equimolar cysteine decreased the percentage binding from 100±4.8 (mean±SEM) to 58.9±10.8, n=6, p<0.02, and equimolar penicillamine decreased the percentage binding to 55.6±10.2, n=3, p<0.05. When both were in excess the binding was completely inhibited. N-acetyl cysteine and s-methyl cysteine in equimolar amounts caused no inhibition of binding. Therefore the presence of a free amino acid sulphhydryl group are necessary for an inhibitory effect. The inhibition of acetaldehyde binding by penicillamine and cysteine could have potential therapeutic importance in alcoholic liver disease.

T4 Is ascites caused by impaired hepatic inactivation of circulating endogenous opioid peptides?

J R THORNTON, H DEAN, AND M S LOSOWSKY (Department of Medicine, St James's University Hospital and Department of Pharmacology, University of Leeds, Leeds) We propose that the liver has a major role in the inactivation of circulating endogenous opioid peptides. These peptides are potent vasodilators, and we suggest that as has a consequence of an imperfect homeostatic attempt to maintain systemic blood pressure in response to this vasodilation, sodium and fluid retention being mediated by secondary activation of the sympathetic nervous and renin/angiotensin/aldosterone systems.

As an initial investigation of this hypothesis, we carefully collected plasma samples and measured methionine enkephalin (ME) by specific radioimmunoassay and measured equimolarly on glucose, 20 irritants with cysteine, 20 cysteine with cysteine or with a 15 healthy controls. All subjects had normal plasma creatinine. Methionine enkephalin was invariably raised in ascites (median 299 pg/ml, range 135-755) versus either non-ascites (median 40, range 30-165, p<0.001). Mann-Whitney U test) or controls (median 37, range 30-55, p<0.001). In three further patients who developed ascites, Methionine enkephalin rose on average 3.7 fold. Noradrenaline (a measure of sympathetic tone) was greater in ascites (median 5.5 mmol/l, range 1-8-20.1) versus either no ascites (median 2.8, range 1.6-4.6, p<0.001) or controls (median 1.7, range 0.9-4.7, p<0.001). Similarly, adrenaline was greater in ascites (median 0.74 mmol/l, range 0.3-2.5) versus either no ascites (median 0.41, range 0.1-1.6, p<0.005) or controls (median 0.29, range 0.1-0.9, p<0.001). Methionine enkephalin was not significantly correlated with any other of the liver biochemistry.

In conclusion, ME was raised eight-fold in ascites and we suggest that this may be a causative factor in the fluid retention of cirrhosis.

T5 A new mechanism of hepatocyte injury in acute alcoholic hepatitis

A J K WILLIAMS AND R E BARRY (Departments of Medicine and Biochemistry, University of Bristol, Bristol) Acetaldehyde binds non-enzymatically with liver membrane proteins. Acetaldehyde modified liver membranes stimulate neutrophils in rat, and activate complement in man. The effect on the neutrophil in man has not been reported. Neutrophilic infiltration of the liver is characteristic of alcoholic hepatitits. We have studied the effect of acetaldehyde-altered liver membranes on neutrophil superoxide production in man. Liver membrane vesicles were prepared from operative biopsies from six patients who provided the neutrophils. The liver membranes were exposed to 1 mM acetaldehyde, pH 7.4 for two hours at 37°C with or without reduction of the resultant adducts. Identical membranes not exposed to acetaldehyde but reduced or left non-reduced were controls.

The effect of the adduct on neutrophil superoxide production was assessed by measuring cytochrome reduction before and after the addition of superoxide dismutase. Acetaldehyde preincubation significantly increased superoxide production in response to both the reduced (from 35.5±7.1 nmol O₂/10⁶ cells/min to 128±25, mean±SEM, p<0.01) and non-reduced membranes (from 17.2±4.3, to 81±17, p<0.01). Acetaldehyde alone caused no superoxide production. Neutrophil free radical generation in response to acetaldehyde altered hepatocytes is an important potential mechanism of injury in alcoholic hepatitis.

T6 Absorption of biliary cholesterol by human gall bladder
free Ca in gall bladder bile – that is, [CaT]–[Ca$^{2+}$]+[Ca$^{2+}$], rose exponentially with increasing [BA]. The gradient (0-081) of this relationship (r=0.79, n=34; p<0.001) was much higher than that (0-032) of T-tube (hepatic) bile (r=0.65, n=133, p<0.01) indicating a greater Ca binding capacity of gall bladder bile. Possible explanations include the secretion of a Ca binding agent (possible mucus) by the gall bladder, thus decreasing the risk of Ca salt precipitation during the concentration of bile. Gall bladder bile from patients with calcified stones (n=11) did not differ from that from patients with radiolucent stones (n=41) with regard to [BA] (87.8±SD 51.2 vs 100.3±55.0); [CaT] (5.45±1.4 vs 7.1±5.7), [Ca$^{2+}$] (0.91±0.16 vs 0.88±0.30) or the relationships between [CaT] and [BA].

We conclude that these data suggest that disturbances of Ca-BA interactions per se do not play a major role in Ca gall stone formation.

### T8

#### Sodium transport in the human gall bladder: effects of secretin

M R JACyna, P E ROSS, C GALLACHER, D HOPWOOD, AND I A D BOUCHER (Departments of Medicine and Radiology, Ninewells Hospital and Medical School, Dundee) Sodium transport, metabolic rate and ATP levels were measured to assess viability in over 50 gall bladders studied.

All gall bladders studied absorbed cholesterol from the mucosal surface at rates ranging from 1-6 nmol/cm$^2$/min and proportional to the cholesterol concentration. Model biles showed a maximal rate of absorption when the lithogenic index reached 1.0 although real biles gave increased rates of absorption at lithogenic indices greater than 1. Model biles demonstrated differences between the individual bile acids but not the glycerine – taurine conjugates. Chenoedocholyxylate bile gave the highest rate of absorption (2 nmol/cm$^2$/min) compared with 1 nmol/cm$^2$/min for cholate biles.

These results show that human gall bladder absorbs cholesterol at rates proportional to the cholesterol concentration, reaching a limit when the model bile reached saturation. Real biles allowed greater absorption when bile was supersaturated and may reflect biliary constituents not present in model biles. The biliary bile acid composition also affects rate of cholesterol absorption suggesting that chenoedocholyxylate feeding may alter gall bladder absorptive function.

### T9

#### Assessment of oesophageal function using scintiscanning after eradication of varices by chronic sclerotherapy

R A J SPENCE, J A SMITH, S ISAACS, AND J TERBLANCHE (Department of Surgery, University of Cape Town and Department of Nuclear Medicine and Statistics, Groote Schuur Hospital, Cape Town, South Africa) Oesophageal function has been assessed in a group of patients with varices who had no sclerotherapy (n=15); a group of patients with varicciated varices (n=29), and a group of age and sex – matched asymptomatic controls. Assessment was done with oesophageal scintiscanning using 17-5 MBq (500 μCi) Tc$^{99m}$ in colloidal. Total transit times and individual transit times for each one third of the oesophagus were measured and compared in the three groups. When the eradicated group was compared with the control group total transit time (p=0.001); upper third (p=0.019); middle third (p=0.007) and lower third (p=0.0001) were all significantly greater in the eradicated group (Wilcoxon-Signed Rank). When the untreated variceus group was compared with the control group total transit time (p=0.022) was significantly greater in the varices group compared with the controls but the individual times for each one third did not reach statistical significance. Fifteen of the 29 patients in the eradicated group had all their sclerotherapy sessions performed via the flexible scope and their transit times were compared with those eradicated using the rigid oesophagoscope (n=14). Transit time in the lower one third was significantly longer in the flexible group. (p=0.035) (Mann-Whitney U). There was no significant difference in the other transit times.

### T10

#### Controlled trial to assess the potency of oesophageal varices during maintenance sclerotherapy

S W HOSKING, P ROBINSON, AND A G JOHNSON

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(University Surgical Unit, Royal Hallamshire Hospital, Sheffield) During maintenance sclerotherapy inadvertent injection of a thrombosed varix may cause ulceration and failure to inject a patent varix, believing it to be thrombosed, may allow further bleeding. In a pilot study, interobserver variation in diagnosing patency or thrombosis was 20%. Using an objective method of assessing patency by measuring variceal pressure, we performed a controlled trial to determine whether this method improved our sclerotherapy results. Sixty-eight patients undergoing maintenance sclerotherapy were randomised to visual assessment—not, for example, ‘flick’ sign (controls n=35), or objective pressure assessment (‘pressure’ n=33). The groups were similar with respect to previous sclerotherapy and size of varices. Based on the respective assessment, patent varices were injected. The whole procedure was repeated three weekly until all varices were thrombosed and then three monthly. During a mean follow up of 12 months, 13 variceal bleeds occurred in six control patients and one variceal bleed in one ‘pressure’ patient (p<0.05). Eight episodes of ulceration occurred in six control patients and two episodes in two ‘pressure’ patients (p<0.05). These results indicate that objective pressure assessment of varices during maintenance sclerotherapy reduces variceal rebleeding and ulceration to very low levels.

T11 Effects of an ‘elemental’ diet and different types of dietary ‘fibre’ on intestinal crypt cell production: and its correlation with plasma enteroglucagon and PYY levels

R A Goodlad, W Lenton, M A Ghatei, T E Adrian, S R Bloom, and N A Wright (Department of Histopathology, and Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road, London) Starved rats were refed with a fibre free ‘elemental’ diet supplemented with a range of dietary ‘fibres’. The crypt cell production rate (CCPR) was measured by the metaphase arrest technique. Refeeding starved rats with an ‘elemental’ diet resulted in a marked increase in CCPR in the proximal small intestine but not in the distal gut. The addition of inert bulk (kaolin) to the elemental diet had little effect on CCPR; neither did a poorly fermentable dietary ‘fibre’ (purified wood cellulose) except in the distal colon where it increased CCPR (p<0.01). A more readily fermentable ‘fibre’ (purified wheat bran) caused a large proliferative response throughout the colon and in the distal small intestine (p<0.05–p<0.001). There was no correlation between CCPR and plasma gastrin concentrations, but plasma enteroglucagon levels were significantly correlated with CCPR in almost all the sites studied (p<0.05–p<0.01). Plasma PYY concentrations also showed some correlation with CCPR, especially in the colon. Thus while inert bulk cannot stimulate colonic epithelial cell proliferation fermentable ‘fibre’ can. In addition these ‘fibres’ can also stimulate proliferation in the small intestine. Plasma enteroglucagon may be implicated in this process.

T12 Abnormal permeability mirrors jejunal morphometry

L D Juby, M F Dixon, and A T R Axon (Gastroenterology Unit, and University Department of Pathology, The General Infirmary, Leeds) In coeliac diseases changes in intestinal permeability (IP) demonstrated by the cellobiose/mannitol test are well recognised. Certain other patients have abnormal intestinal permeability, however, but ‘normal’ jejunum on routine microscopy. Using computerised morphometry we have measured the perimeter/lamina propria area index [P/LPA index] and compared this with the cellobiose/mannitol ratio in three patient groups: (i) coeliacs with villous atrophy, (ii) normal biopsy and cellobiose/mannitol test, (iii) ‘normal’ biopsy and abnormal cellobiose/mannitol test.

There is an expected difference in the P/LPA index between groups (i) coeliacs and (ii) normals (group mean 0.015±0.0019, group mean 0.043±0.0069 p<0.001). The P/LPA index in group (iii) with abnormal permeability (mean 0.035±0.0028) is significantly different from group (i) and (ii) (p<0.001 and 0.01<p<0.001). There is a significant correlation between the P/LPA index and cellobiose/mannitol ratio (correlation coefficient −0.57 p=0.001). This study indicates that the cellobiose/mannitol test reflects changes in jejunal morphometry in coeliac disease and also subtle changes in other patients not apparent on routine microscopy.

T13 Cellular basis for impaired colonic Na+ absorption in ulcerative colitis

G I Sandle and F McGlone (Department of Medicine (University of Manchester School of Medicine), Hope Hospital, Salford) Diarrhoea in ulcerative colitis is partly due to impaired colonic Na+ and water absorption, but the precise epithelial defect is unclear. Intracellular microelectrodes were therefore used to study Na+ transport properties of descending colon/rectum from patients with carcinoma (non-colitic, n=9) or active ulcerative colitis (n=3). Transepithelial voltage (Vt) and total resistance (Rt) in colitic tissues (−7±0.4 mV and 49±6 Ω cm2 respectively) were lower than in non-colitic tissues (−20±3 mV, p<0.01 and 172±23 Ω cm2, p<0.02, respectively). Basolateral membrane voltage was also lower in colitic than in non-colitic tissues (−24±5 mV vs −49±2 mV, p<0.01), suggesting impaired basolateral Na+–K+ pump activity. Apical addition of 194 K amiloride (a Na+ channel blocker) to non-colitic tissues decreased Vt, to −7±4 mV (p<0.005) and increased Rt, to 194±21 Ω cm2 (p<0.05) indicating inhibition of electrogenic sodium absorption, but had no effect in colitic tissues. Apical addition of nystatin (an ionophore which combines with membrane lipid) to non-colitic tissues decreased the apical membrane resistance, but had no effect in colitic tissues suggesting an initially high apical conductance owing to a decrease in membrane lipid content. Thus, loss of electrogenic Na+ absorption from the colon in ulcerative colitis reflects changes in the properties of both the apical and basolateral cell membranes.

T14 Rectal distension modifies upper gastrointestinal (GI) motor activity

J E Kellow, R C Gill, M De Jode, N Parnell, and D L Wingate (Gastrointestinal Science Research Unit, The London Hospital Medical College, 26 Ashfield Street, London) Disturbed upper GI transit has been reported in disorders usually assumed to be primarily colonic in origin, such as irritable bowel syndrome. We have studied the effects of rectal distension (sufficient to elicit an urge to defecate) on patterns of upper GI motor activity, as well as transit, in six healthy subjects. On day 1 gastrointestinal motility was recorded manomet-
Oesophageal—Gastroduodenal
T15–28

T15
Can failure of the Nissen fundoplication be predicted?

M M MUGHAL, J BANCEWICZ, AND M MARPLES
(introduced by M H IRVING) (University Department of Surgery, Hope Hospital, Salford) It is stated that troublesome dysphagia and ‘gas bloating’ after Nissen fundoplication is more common in patients with disordered oesophageal motility, those with a mechanically competent cardia and the ‘air swallowers’ who characteristically exhibit reflux in the upright position. We have tested this concept by analysing the results of floppy Nissen fundoplication in 79 patients with proven gastro-oesophageal reflux.

At a median follow-up period of 32 months (range six to 84 months), 66 patients (85%) had a good result (Visick 1 and 2). This included 24/27 (89%) with disordered motility, 19/24 (79%) with a competent cardia and 20/24 (83%) with upright reflux only. Twelve had a poor result because of persistent reflux in nine, severe dysphagia in two, gas bloating one and intractable post-thoracotomy pain in one. In all 12 cases the poor results were because of technical factors: disrupted or slipped fundoplication in nine, overtightened hiatus in two and post-thoracotomy neuralgia in one.

In the absence of a gross failure of oesophageal peristalsis, pre-operative oesophageal manometry and pH studies are not helpful in predicting failure of the Nissen fundoplication. The 15% incidence of poor results in our study was largely because of technical failures.

T16
pH Profile of Barrett’s oesophagus and its implications

P GILLEN, P KEEING, P J BYRNE (Departments of Surgery and Pathology, St James’s Hospital, Dublin) Barrett’s oesophagus is generally accepted as secondary to gastro-oesophageal reflux and may present with strictures, ulcers or malignant change. Twenty-four hour ambulatory pH monitoring was used to assess the severity of reflux in 21 patients with Barrett’s (seven strictures, three ulcers) and the results compared with 25 patients undergoing antireflux surgery for severe oesophagitis. All Barrett’s patients had histological proof of specialised columnar epithelium > 2 cm proximal to the gastro-oesophageal junction. The % time (mean±SEM) pH < 4 was significantly greater in Barrett’s patients than the oesophagitis group (25±0.5±3% vs 13±0.2±1%, p<0.005), as were the number of reflux episodes > 5 min duration (11±1±1.5 vs 6±5±1.2, p<0.01). Neither lower oesophageal sphincter pressure (12±8±1.6 vs 14±8±1.8) nor the total number of reflux episodes (60±5±10±6 vs 46±1±6±4) differed significantly between the two groups.

In patients with Barrett’s oesophagitis, acid clearance is impaired and leads to prolonged acid/mucosal contact time. Oesophageal strictures and ulcers and the extent of columnar change in the Barrett’s patients were related to the degree of abnormality in oesophageal acid clearance. In conclusion, patients with Barrett’s mucosa demonstrate marked acid reflux and abnormal acid clearance and should be managed by anti-reflux surgery to avoid potential complications.

T17
Omeprazole versus ranitidine in the treatment of reflux oesophagitis: a double-blind multicentre trial

E C KLINKENBERG-KNOL, J B M J JANSEN, H P FESTEN, S C M MEUWISSEN, AND C B H LAMER (Departments of Gastroenterology, Free University Hospital, Amsterdam, University Hospital, Nijmegen, University Hospital, Leiden, Grooth Ziekenhuis, s-Hertogenbosch, Holland) Omeprazole (OME) is the most potent inhibitor of gastric acid secretion currently available and may therefore be superior to H₂ receptor antagonists in the treatment of reflux oesophagitis. The effectiveness of OME in a single, oral morning dose of 60 mg or ranitidine (RAN) 150 mg bd was studied in a randomised, endoscopically controlled, double-blind trial.

Fifty-one patients with macroscopic oesophageal erosions or ulcerations were included: symptoms were recorded daily and endoscopy was repeated after four weeks and, if patients were not healed, after respectively eight, 12, and 16 weeks with a blind switch to the other medication after eight weeks. The healing rate after four weeks of treatment was: 19/25 OME-patients (76%) versus 7/26 RAN-patients (27%, p=0.002), and after eight weeks 22/25 OME-patients (88%) versus 10/26 RAN-patients (38%, p=0.003). Omeprazole was more effective in severe oesophagitis than RAN. Fifteen patients, not healed with RAN, changed medication to OME: 10 patients healed after four weeks and 13 after eight weeks. Alternatively, one of three patients, not healed on OME, healed four weeks after switching to RAN. Omeprazole was superior in the relief of heartburn (p=0.001). There were no side effects of clinical importance.

The results of this double-blind study show that OME is superior to RAN in the short term treatment of reflux oesophagitis.

T18
Laser therapy and intubation for gastro-oesophageal malignancy: practicalities and problems

N KRASNER, H BARK, A J MIRRO, AND R J WALKER (Gastrointestinal Unit, Walton Hospital, Liverpool) A combination of endoscopic Nd-YAG laser therapy and oesophageal intubation was used in the
palliation of 25 patients. There were 15 men and 10 women of mean age 71 years (range 65–85). In nine patients severe dysphagia was encountered after endoscopic intubation and the laser was required to remove tumour overgrowth in six at the upper end and in one at the lower end of the tube. In an additional two cases, repositioning of the tube was possible after laser treatment. These patients survived, swallowing well, for a further 14 weeks (range 7–26). Another group of 16 patients was treated initially with the laser and then subsequently intubated because of the length of oesophageal stricture (four), rapidity of tumour growth (six) or extrinsic tumour compression (three). Attempted intubation after prior laser therapy resulted in oesophageal perforation in three patients. Two died and these had had a fibrous stricture.

Laser treatment is the management of choice for exophytic tumours and for removal of tumour overgrowth of the tube. Also, the laser is preferable to intubation when the tumour occurs high in the oesophagus. Intubation is best applied in extrinsic tumour compression, rapidly growing tumours and poor response to laser treatment. The combination may prove helpful provided intubation is performed before the oesophagus is rendered inelastic by laser induced fibrosis.

T20 Evidence for cholinergic modulation of duodenal bicarbonate secretion

J R CRAMPTON, L C GIBBONS AND W D W REES (Department of Gastroenterology, Hope Hospital, Salford) Electrical field stimulation (EFS) is a technique used to provoke release of neurotransmitters of the enteric nervous system. We have recently described a new method where EFS is used to examine the effect of enteric nerves on duodenal bicarbonate secretion and established that EFS is a potent stimulant of alkali secretion. A 2 cm segment of bull frog (Rana catesbeiana) proximal duodenum is mounted on cannulae so that bicarbonate secretion can be measured by stat titration and EFS applied longitudinally by platinum electrodes. The response to EFS (50 V, 5 Hz, 1 TPS, 0.5 s) consists of a 50±28% (n=5, p<0.05) increase in the rate of alkalisation. This response was blocked by 10⁻⁴ M dinitrophenol (95±13% basal rate, n=6, p<0.05) and atropine, 10⁻³ M (70±7% basal rate, n=5, p<0.05) indicating the existence of enteric cholinergic neurones capable of modulating duodenal bicarbonate secretion. Further study of the response may provide additional information on the neural control of bicarbonate secretion.

T21 Further studies on the pathogenesis of acid induced pain in duodenal ulcer

J Y KANG, R GUAN, H H TAY, AND I YAP (Department of Medicine, National University of Singapore) We have previously shown that perfusion of duodenal ulcer (DU) craters with 100 ml 0·1 N HCl reproduced ulcer pain in one third of symptomatic patients— that is, the last episode of pain within 24 hours. In the present study we investigated (1) the effect of acid perfusion on non-symptomatic DU and (2) the effect of an anti-spasmodic on acid-induced DU pain. Four groups of DU patients were studied: (a) untreated symptomatic; (b) untreated non-symptomatic; (c) healed after a course of treatment; (d) treated healed. During routine endoscopy under local anaesthesia, 100 ml 0·1 N HCl was infused onto the ulcer crater or scar using a washing tube. By random allocation, group (a) patients were sub-divided into group (a1) (40 mg buscopan given intravenously prior to acid infusion) and group (a2) (no buscopan). Patients were asked to indicate if ulcer pain developed, the person assessing the pain being unaware of the group each patient was in. The numbers of patients developing pain were as follows: (a1) 13/33=39%; (a2) 9/26=35%; (b) 2/14=14%; (c) 1/6=17%; (d) 0/16=0%. Group (a1) versus groups b+c+d+p<0.05; Group (a1) versus (a2)=NS. Ninety five per cent confidence limits=29% in favour of (a2) to 21% in favour of (a1). We concluded that (1) acid infusion seldom induced pain in patients with non-symptomatic DU pain production by acid infusion probably involved a mechanism other than spasm.
Treatment was in dom order: T24
ulcer 28th plasma gastrin 20
of studies showed 20 from 20 rarely of gastrin intragastric by 23%
T23 PU, than very low reaching or ranitidine N
HAMILTON, LANZON-MILLER, S
endoscopy Hospital, London) four
mean acidity observed. In no case was massive hypergastrinacmia or achlorhydria observed.
We conclude that there is a relationship between the degree of inhibition of acid secretion caused by OME and the degree of increase in fasting plasma gastrin concentration. A level of acid inhibition higher than about 80% must be achieved before gastrin levels are affected.

T25 Alteration of H2 receptor sensitivity during maintenance ranitidine treatment
D B JONES, C W HOWDEN, D W BURGET, C SILETTI, AND R H HUNT (Division of Gastroenterology, McMaster University Medical Centre, Hamilton, Ontario, Canada) Despite maintenance H2 receptor antagonist (H2RA) treatment, 20-30% of duodenal ulcers may relapse per annum. Although compliance is a major factor in such relapse, it has been suggested that the sensitivity of the H2 receptor may change during maintenance H2RA treatment. The present study therefore examined directly the response of the H2 receptor to stimulation by the specific H2 agonist, imiprodine (IMP). Five male patients (age 38-62 years) with DU in remission underwent IMP stimulated gastric acid studies before (study day 1) and after (study day 2) three months’ RAN 150 mg nocte. Gastric acid was collected for one hour basal, and during sequential IMP infusions of 2-5, 5-0 and 10-0 mcg/kg/h for 90 min each. During high dose IMP, 50 mg of RAN was given iv over 5 min, and gastric acid collected during a further two hours of high dose IMP.

Maintenance RAN treatment resulted in an increase in basal acid output compared with pre-treatment from 1-1±0-5 to 3-1±1-1 (mean±SE) mmol/h (p=0-13). Imiprodine resulted in a stepwise increase in gastric acid secretion to a maximal of 40-45 mmol/h during IMP 10-0 mcg/kg/h infusion. At each IMP dose, there was a significant increase in acid output on study day 2 compared with study day 1 - for example, during IMP 10-0 mcg/kg/h, acid output on study day 1 was 39-3±5-1 mmol/h compared with 46-6±7-0 mmol/h on study day 2 (p=0-02). Additionally, the response to iv RAN 50 mg was accentuated by three months’ RAN treatment, causing a reduction in acid output to 9-1±1-4 mmol/h on study day 1 compared with 4-4±1-8 mmol/h on study day 2 (p=0-06).

In summary, three months’ treatment with maintenance RAN 150 mg nocte results in a significant increase in IMP stimulated gastric acid output. The accentuated response to iv bolus of RAN suggests an increased sensitivity of H2 receptors during maintenance H2RA treatment.

T26 Tissue oxygen tension measurement in the human gastrointestinal tract
W G SHERIDAN, R LOWNDES, AND H L YOUNG (University Department of Surgery, University of Wales College of Medicine, Heath Park, Cardiff) Experimental determina-
tion of gastrointestinal tissue oxygen tension (PtO2) has previously been confined to animals. In 27 patients undergoing laparotomy, PtO2 was measured at various predeter-
determined sites on the serosal surface of the gastrointestinal tract using a specially constructed modification of a Clark type oxygen electrode. This electrode, incor-
porating a thermistor for temperature compensation, has been shown to have a linear response to oxygen tension \( (r=0.995, p<0.001) \). The patients (age range 26-85 years) had an inspired oxygen concentration of 30% with a mean arterial \( PO_2 \) of 128±2-9 mmHg (mean±SD). The measured \( PO_2 \) values (mmHg, mean±SD) were: stomach 44-6±13-7, mid ileum 35-4±10-4, terminal ileum 33-5±12-8, caecum 29-3±7-6, transverse colon 36-7±9-8. \( PO_2 \) measurements at the above sites correlated with arterial \( PO_2 \) \( (r=0.70, p<0.001) \). Temporary arterial occlusion resulted in a gradual decrease in measured \( PO_2 \); reflecting the onset of tissue hypoxia. In conclusion, tissue oxygen measurement in patients using a modified Clark electrode is feasible and may have clinical applications in the per-operative assessment of tissue and organ viability.

T27

Twenty four hour ambulatory dual gastroduodenal pH profiles in health and duodenal ulcer disease

C A ERIKSEN, S A SADEK, AND A CUSCHIERI (Department of Surgery, Ninewells Hospital and Medical School, Dundee) The pathophysiology of duodenal ulcer disease remains uncertain. The presence of acid appears to be the major determining factor. This study describes continuous 24 hour simultaneous measurements of antral and duodenal bulb pH under normal physiological conditions. The data recorded by two pH electrodes and a portable microlog receiving unit were off-loaded to a computer for analysis. Ten patients (mean age 51±5 years) and seven controls (mean age 42.3 years) were studied. The mean baseline duodenal pH was significantly lower \( (p<0.03) \) in the supine, compared with erect posture \( (pH 3.4 \text{ vs } 6.3) \) in the patient group, but not in the control group \( (pH 1.7 \text{ vs } 6.9) \). Both the total number of acid peaks and the number of short lived peaks were significantly greater whilst supine rather than erect in the duodenal ulcer patients \( (p<0.03, <0.04) \).

A meal caused a gradual rise in duodenal acidity with marked and frequent fluctuations for a mean period of 1-4 hours, followed by a sharp drop in acidity. These preliminary findings suggest that duodenal acid exposure is enhanced in duodenal ulcer patients in the supine posture at night when compared to erect daytime values.

T28

Effects of truncal vagotomy and pyloroplasty and highly selective vagotomy on antroduodenal motility and transpyloric fluid movement

P M KING, A PRYDE, AND R C HEADING (Department of Medicine, Royal Infirmary, Edinburgh) Using real time ultrasound imaging, the pattern of contractions and fluid movement at the gastroduodenal junction were examined in T0 patients after truncal vagotomy and pyloroplasty (TVP). 10 with highly selective vagotomy (HSV) and 10 healthy controls given a fluid me. Antral peristaltic cycle times were similar in each group, but proximal duodenal contractions were seen to follow terminal antral contractions less frequently after TVP \( (34\%) \) than HSV \( (60\%) \) or controls \( (59\%) \) \( (p<0.05) \). Fluid movement through the gastroduodenal junction occurred as intermittent brief episodes during each cycle. Significantly more episodes of gastroduodenal flow occurred after TVP \( (mean 2.6 \text{ episodes/cycle}) \) and HSV \( (2.4) \) than in controls \( (1.7) \) \( (p<0.05) \) but their duration was similar in all groups at around 2.5 seconds. Duodenogastric flow (reflux) occurred in about 50% of cycles with no differences between the groups.

We conclude that (1) the pattern of antral contractions remains normal after TVP and HSV. (2) The pattern of gastroduodenal flow is altered by both operations, and presumably reflects proximal gastric derangement. (3) TVP but not HSV impairs antroduodenal coordination. (4) Neither TVP nor HSV significantly altered the pattern of duodenogastric reflux.

T29

Sexually transmitted disease – a new hazard for the gastroenterologist?

H A ANDREWS, J WYKE, T RAY, A ALLAN, J CLAY, R SPARKS, J ALEXANDER-WILLIAMS, M R B KEIGHLEY, AND R N ALLAN (Department of Gastroenterology and Genito-Urinary Medicine, General Hospital, Birmingham) Sexual activity in male homosexuals transmits many diseases and there may be a risk to clinicians treating male patients with rectal problems. One hundred and ten male patients attending either the rectal (75) or inflammatory bowel (35) disease clinic were evaluated, specifically, for sexually transmitted disease. Investigations include:—blood tests for syphilis, hepatitis A, hepatitis B, Chlamydia and HTLV III antibodies; rectal swab cultures for N. gonorrhoea, chlamydia and herpes simplex; stool culture and rectal biopsy. Five patients were homosexual, one with HTLV III antibodies. Serology was positive for syphilis (one), hepatitis B (three), hepatitis A (33), Chlamydia (28). Rectal swabs and stool cultures were all negative. Stool microscopy showed Giardia lamblia (one) and cryptosporidium (one). A random sample of 50 known homosexuals attending the genitourinary department showed positive results for HTLV III antibodies (four) serology for syphilis (14), hepatitis B (13), hepatitis A (one) and Chlamydia (21). Rectal swab culture was positive for gonorrhoea (one), herpes (three), Chlamydia (three). Stool microscopy showed cryptosporidium in two. Homosexuals with sexually transmitted disease were examined, sterile instruments effectively and undertaken venepuncture with care.

T30

Incidence of colonic adenomatous polyps in a necropsy series, compared with colonoscopic findings

K E WHEELATL, J P SUNTER, W K COWAN, AND M J HIGGS (Departments of Surgery and Pathology, Queen Elizabeth Hospital, Gateshead) Adenomatous polyps of the colon are generally regarded as an important predisposing condition to colorectal carcinoma. To estimate the prevalence in our area we undertook a study of the incidence of polyps in a necropsy group, and compared these findings to the patients presenting with polyps at colonoscopy.

From 610 consecutive postmortem examinations, 565 colons were examined (excluding children, cases with limited consent or autolysis), and a histological diagnosis obtained on any polyps. Adenomatous polyps were found in 196 cadavers (34.7%). None were seen below age 30, with the greatest incidence between 60 and 79 years. Seventy three per cent of the polyps were in men (overall male:female ratio of cadavers 1:5:1). Forty nine per cent of the polyps were proximal to the splenic flexure, 79% were under 1 cm diameter, and only 2% over 2 cm. Fifty four per cent of involved colons had one poly, 9% had four or more.

Colonoscopic findings in 41 consecutive
patients were reviewed, showing a very similar age and sex distribution, but 70% of the polyps were distal to the splenic flexure.

We conclude that colonic adenomatous polyps are common in our postmortem population and if this incidence is reflected in the general population, logistical problems will be enormous.

T31
Is the diarrhoea in ulcerative colitis related to a failure of colonic salvage of carbohydrate
S S C RAO, N W READ, AND C D HOLDSWORTH
(Clinical Research Unit, H Floor, Royal Hallamshire Hospital, Sheffield) The normal colon salvages unabsorbed carbohydrate by bacterial conversion to short chain fatty acids, which are rapidly absorbed along with water. In order to determine whether failure of colonic salvage of carbohydrate could contribute to the diarrhoea of unabsorbed carbohydrate we investigated the effect of a drink containing 20g lactulose on stool output and breath hydrogen production in 39 patients with unabsorbed carbohydrate subdivided according to disease activity and extent and in 13 normal controls. Each subject took a standard diet for four days and stool output was monitored throughout. Administration of lactulose on day three increased stool weight and frequency in patients with total colitis (265±143 g vs 187±118 g/day, mean±SD, p<0.01) and 3-9±2.0 vs 2-6±1.4 motions/day, p<0.01) but not in patients with distal colitis (137±113 g/day and 1-8±1-7 vs 1-7±1-1 motions/day) and in normal subjects (195±103 g/day and 1-46±0-5 vs 1-38±1-0 motions/day). The basal and peak hydrogen responses to lactulose in patients with colitis were similar to normal subjects. The mouth-caecum transit was delayed (p<0.01) in all groups of patients when compared with normal subjects. Impaired colonic salvage of carbohydrate could contribute to the diarrhoea of total colitis but not distal colitis, and this is not due to rapid transit.

T32
Eradication of adhesive E coli in ulcerative colitis (UC)
D A BURKE, S A CLAYDEN, R W LACEY, AND A T R AXON
(Gastroenterology Unit, and University Department of Microbiology, The General Infirmary, Leeds) E coli capable of adhering to human epithelial cells may be implicated in UC. Tobramycin has been studied for its ability to remove these organisms. E coli from 58 patients with UC were sensitive to Tobramycin. Frequency of in vitro mutational resistance to Tobramycin was <10⁻⁶. Safety of in vitro treatment with Tobramycin 120 mg tds for seven days and prednisolone 60 mg/day was assessed in six patients with severe UC. Peak and trough serum levels of Tobramycin remained 0-5 μg/ml. Mean percentage dose urinary excretion at seven days was 2-56%. HeLa and buccal epithelial cell adhesion of patients’ E coli were assessed before and after treatment. Serotype of five, and plasmid profiles of the sixth patient’s E coli were determined before and after treatment. One patient’s serotype and adhesion index did not change. Of those treated one required surgery, one had azathioprine and remitted, the remainder responded. No side effects, emergence of Clostridium difficile or Tobramycin resistant E coli were noted. Tobramycin can safely eradicate adhesive E coli. It is not significantly absorbed from inflamed bowel, and is unlikely to result in Tobramycin resistance amongst E coli. Eradication of adhesive E coli in UC using oral Tobramycin would appear to be a safe means of determining their role in this disease.

T33
Lymphokine activated killer cell production in patients with gastrointestinal cancer
J R T MONSON, CAROL RAMSDEN, G R GILES, T G BRENNA, AND P J GUILLOU
(Department of Surgery, St James’s University Hospital, Leeds) The in vitro stimulation with interleukin-2 of resting lymphocytes with natural killer (NK) cell characteristics results in their proliferation. This subsequently results in the generation of lymphokine-activated killer (LAK) cells, which are strongly cytotoxic towards tumour but not normal cells. Re-infusion of autologous LAK cells has produced regression of some, but not all, metastatic cancer. We have measured LAK precursors (NK activity), proliferative responses (Con A stimulated ³H-Thymidine uptake) and LAK cell generation by the lymphocytes from 27 control subjects and 27 patients with gastric and colorectal cancer (nine localised, 18 advanced). Cytotoxicity was measured against the NK target K562 and LAK cell target DAUDI before and after three days incubation with ultrapure human IL-2 (50 μ/ml).

The results demonstrate that while patients with advanced GI cancer possess only minimally impaired levels of LAK precursors (basal NK), lymphocyte proliferation and the ability to generate cytotoxic cells (stimulated NK) they remain unable to generate adequate LAK cell activity.

We conclude that this may explain the failure of LAK cell therapy to cause regression in some cases of advanced GI cancer and prompts the search for further means of augmenting this activity in these patients.

T34
Is colonic pH important in colorectal cancer?
D F EVANS, G PYE, R Bramley, T J DYSON, T W Balfour, AND J D Hardcastle
(Department of Surgery, University Hospital, Nottingham) It has been shown that enzymes important in the breakdown of bile salts to carcinogens in the colon are inactivated below pH 6-5. Colonic pH may therefore be important in the genesis of colorectal cancer. Intracolonic pH was measured in 21 patients with left sided colorectal neoplasia (14 adenoma, seven carcinoma, (49-80 years)) and compared with 23 normal volunteers (20-85 years) pH was recorded for up to 48 hours using an ingested radiotelemetry capsule (RTC) (Remote Control Systems, London) and a portable recorder (Oxford Medical Systems) during colonic transit. pH was consistently higher in both patient groups and controls on the left compared with the right side of the colon (p<0.001) (Mean pH left 7.34 (0.7 SD) right 6.52 (0.62) neoplasia left pH 6.75, (0.88), right 6.2 (0.5) normal). Colonic pH was higher in the cancer group (left colon pH 7.48 (0.19) p<0.04, right colon pH 6.65 (0.49) p<0.06) when compared with controls. In the adenoma group a similar trend was seen but this failed to reach significance (pH left 7.2 (0.71), right 6.4 (0.75). These results suggest that intracolonic pH may be important in the development of colorectal neoplasia and may explain why carcinomas develop more commonly on the left side of the colon.

T35
Pararectal lymph node involvement in rectal cancer assessed by endoluminal ultrasound
J BEYNON, D M A FOY, J L CHANNER, N J
MCC Mortensen, and J Virjee (Departments of Surgery, Medical Physics, Pathology and Radiology, Bristol Infirmary, Bristol) Assessment of pararectal lymph node involvement in rectal cancer continues to be a problem. Previous studies have shown digital examination correctly identifies only 50% of involved lymph nodes while computer tomography is also disappointing in this field. Endoluminal rectal ultrasound has been used to assess the involvement of pararectal lymph nodes in 66 patients with primary rectal cancer. Examinations have been undertaken with a rotating endo-probe and 5.5 MHz and 7.0 MHz transducers. Subsequently 57 resections were done and histological assessment compared with ultrasonic data. Sonographically, involvement was correctly predicted in 22 cases with seven false positives, while 24 cases were false with four false negatives. The coefficient of correlation between ultrasonic examination and histopathology was 0.62 (p<0.001). The accuracy for predicting lymph node metastases was 81%, the sensitivity 85%, specificity 77% and the predictive value 76%. Endoluminal rectal ultrasound is an accurate method of assessing pararectal lymph node involvement in rectal cancer and its use preoperatively enables a more accurate staging to be carried out.

T36 Does a fall in serum CEA after chemotherapy for disseminated colorectal cancer predict prolonged survival?

T G Allen-Mersh, D Niedzwiecki, B Shurgot, N Kemeny, and J M Daly (Memorial Sloan-Kettering Cancer Center, New York USA) The majority of patients with disseminated colorectal carcinoma whose serum CEA falls after cytotoxic chemotherapy show no clinical or radiological evidence of tumour shrinkage. This study has assessed the value of a fall in serum CEA as a predictor of prolonged survival after starting chemotherapy for disseminated colorectal carcinoma. CEA was measured in the sera of 329 patients with an elevated pretreatment CEA who were treated with chemotherapy for disseminated colorectal carcinoma. The CEA fell in 70% of patients with two months of starting chemotherapy. Survival in patients whose CEA fell (median 12 m) was significantly (log rank test p<0.001) longer than in patients whose CEA did not fall (8-8 m). Fifty three per cent (93/175) of patients whose CEA fell after chemotherapy were 'non-responders' (<25% clinical or radiological tumour shrinkage). Survival was significantly (p<0.04) longer in non-responders whose CEA fell (median 10-2 m) than in non-responders whose CEA did not fall (media 8-0 m). A fall in serum CEA within two months of starting chemotherapy for colorectal carcinoma is a sensitive and economical indicator of prolonged survival.

T37 Restorative proctocolectomy: the four loop W reservoir

R J Nicholls and D Lubowski (St Mark's Hospital, City Road, London) The four loop (W) ileal reservoir was developed with the aim of improving the functional results of the J reservoir, and to avoid the need for catheterisation often seen with the S reservoir. Sixty four patients have undergone the procedure between March 1983 and March 1986. There were 28 men and 36 women with a mean age of 31 years (14-52 years). Fifty seven had ulcerative colitis, six familial adenomatous polyposis, and one functional bowel disease. Mean hospital stay (including ileostomy closure) was 24±8 days. Pelvic sepsis occurred in four cases (6%) and obstruction requiring laparotomy in eight cases (13%). Other complications included reoperation for bleeding (one), wound infection (eight), anastomotic stricture requiring dilatation (four). The reservoir has been removed in one patient (one week postoperatively) with a Dukes' B rectal carcinoma, giving an overall failure rate of 1-6%. Six patients have not yet had the ileostomy closed and in six it has been closed for <1 month. Function has been assessed in the remaining 51 (mean follow up 18-6±8-9 months). Frequency of defaecation/24 hours is 3-3±1-0; night evacuation (>×1/week) 14%. Continence is completely normal in 92%, and 8% have minor leakage. Twenty per cent use anti-diarrhoeal medication. Compliance measured in 12 patients (38-5 ml/cm H2O) was significantly greater than in 11 patients with J reservoirs (18-9 ml/cm H2O) (p<0.01). All patients defecate spontaneously.

T38 Bowel dysfunction in the presence of ganglion cells

N D Heaton, J R Garrett, and E R Howard (Department of Surgery and Department of Oral Pathology, King's College Hospital, London) Abnormalities of the myenteric plexus are increasingly being recognised in patients with severe bowel dysfunction. The absence of ganglion cells in Hirschsprung's disease is well documented, but as a consequence the presence of ganglion cells in colonic biopsies is often assumed to exclude significant neuronal abnormalities. Fourteen patients presenting with neonatal bowel obstruction or severe constipation have been diagnosed as hyperganglionosis. All had neonatal onset of symptoms, and boys predominated 2:1. Associations with aganglionosis (three), enterocolitis (three), anal atresia (one), and Sipple syndrome (one) were noted. Clinically the appearance of a distended abdomen, with palpable faecal masses may suggest aganglionosis. Barium enema examination reveals dilated colon and rectum, but most striking are uncoordinated contractions occurring throughout affected colon. Pathological features include the presence of ectopic ganglia, hyperplasia of the enteric plexuses, and increased acetylcholinesterase positive nerves in the lamina propria. Twelve patients had surgical resections as emergencies or electively to relieve symptoms. Postoperative results were related to the extent of disease and the innervation at the resection margin. Hyperganglionosis is a recognisable abnormality of hindgut innervation, presenting with severe bowel dysfunction. Thus the presence of ganglion cells in colonic biopsies does not exclude significant neuronal disorders.

T39 Autosomal recessive visceral myopathy

E M Alstead, M N Murphy, A M Flanagan, A E Bishop, M H Fayadhi, and H J F Hodgson (Departments of Medicine and Pathology, Royal Postgraduate Medical School, London and Rashid Military Hospital, Iraq) A kindred with chronic intestinal pseudo-obstruction affecting 11/54 members was studied. Clinically, patients presented with recurrent intestinal obstruction in childhood or adolescence. Eight of the 11 affected individuals died before the age of 30. Pedigree analysis showed four consanguineous marriages amongst the progeny of the great-great grandparents of the affected subjects in the fifth generation, and established an autosomal recessive mode of inheritance. Barium studies demonstrated dilatation in both large and small intestine. Histological, immuno-
cytochemical and electron microscopic studies were performed on a colectomy specimen from one of the surviving affected family members. Light microscopy showed fibre degeneration with replacement by collagen and fibrous tissue in both layers of the muscularis propria and the muscularis mucosa. Myenteric plexus ganglion cells were normal in number and morphology on light microscopy and immunocytochemistry. Decreased numbers of epithelial endocrine cells containing glucagon, PYY and somatostatin were demonstrated. Electron microscopy showed disruption and disorientation of the myofilaments with increased cytoplasmic radiolucency. This confirmed a familial visceral myopathy. The family had no associated extragastrointestinal manifestations. The degeneration of the muscularis mucosa as well as muscularis propria has not been previously described.

**T41**

**Postnatal repair and intersphincteric Ivalon sponge rectopexy for the treatment of rectal prolapse**

J ROGERS and P J JEFFREY (Department of Surgery, Weymouth and District Hospital, Weymouth, Dorset) Complete rectal prolapse is often associated with faecal incontinence. Abdominal rectopexy is the standard treatment of the former and postnatal repair of the latter. Despite successful treatment of prolapse by abdominal rectopexy about a third of patients remain continent. The results of postnatal repair when used alone in cases of rectal prolapse are extremely poor.

The aim has been to design a procedure to reduce and fix a complete rectal prolapse and improve continence. The procedure combines postnatal repair with a rectopexy, placing the Ivalon sponge into the retrorectal space via the intersphincteric plane.

Twenty four patients (mean age 74 years) with complete rectal prolapse (15 of whom were incontinent to solid stool) have undergone the operation. There has been no operative mortality, nor serious morbidity. There has been one recurrence, 14 days after operation. The other 23 patients have been followed between two months and three and a half years (mean 18 months).

All patients remain continent postoperatively. This type of operation may be the treatment of choice in the elderly, where an abdominal incision is considered unwise, and in cases of rectal prolapse with incontinence.

**T42**

**Acute abdominal pain: computer aided diagnosis by non-qualified medical staff**

P C LAWRENCE, P C CLIFFORD, and I TAYLOR (University Department of Surgery, Southampton General Hospital, Southampton) The aim of this study was to explore the role of computer aided diagnosis for patients with acute abdominal pain when applied by non-qualified personnel.

The clinical features of 153 patients (median age 35, range 16–92) suffering less than one weeks’ abdominal pain were recorded. Junior doctors’ diagnostic accuracy with (65 cases) and without (70 cases) structured computer history sheets were compared with 1st year clinical medical students using structured sheets and a computer system (46 cases). These students had no previous clinical surgical experience.

Doctors’ diagnostic accuracy of 51% rose significantly to 69% with the use of structured history forms ($\chi^2=4.53$, p<0.05). Computer assisted diagnostic accuracy obtained by medical students was identical to the improved diagnostic accuracy of the junior doctors (69.5%).

In this study the doctors’ diagnostic accuracy of acute abdominal pain improved. First year clinical medical students, with no surgical experience, were able to match this improvement by using the same system. These results have implications not only for medical education but also for use of these systems by ‘para-medical’ personnel.
The British Society of Gastroenterology

A P MANNING, O R BULGIM-TOMLINSON, D J LINTOTT, AND A T R AXON (Gastroenterology Unit, and Department of Radiology, The General Infirmary, Leeds) Endoscopic retrograde cholangiopancreatography (ERCP) is a standard technique for the investigation of pancreatic disease. Changes seen in chronic pancreatitis (CP) are variable, but usually include dilatation and irregularity of the main pancreatic duct (MPD); although there may be stenoses or obstruction of the MPD its overall width is greater than normal; side branch changes may include nipping at their origins and dilatation beyond. Occasionally, however, there is diffuse and irregular narrowing of MPD and side branches giving a 'shrunken' appearance. Of 3529 ERCPs done in this department, 362 have shown changes of chronic pancreatitis with six having this 'shrunken' appearance. We present these six patients including representative radiographs to illustrate their characteristic features: the MPD is irregular and narrowed throughout its length and may be shortened; side branches, often difficult to demonstrate, are narrowed and shortened, never showing dilatation. All six patients have other confirmatory evidence of CP: none is alcoholic, one had gall stones, and two have idiopathic inflammatory bowel disease. No other aetiological factors were identified. We conclude that there is morphological variant of CP demonstrated at ERCP as a 'shrunken' pancreas which usually has no common aetiological associations.

T44
Assessment of pancreatic function using bentiromide and p-aminosalicylic acid

I M CHESNER, R A ALLEN-NARKER, N LAWSON, G V H BRADBURY, B M BUCKLEY, AND J D BERG (Department of Clinical Biochemistry and Medicine, Sandwell District General Hospital, West Bromwich, West Midlands and The Metabolic Unit, East Birmingham Hospital, Birmingham) The bentiromide test, widely used in the assessment of exocrine pancreatic function, is based on the specific hydrolysis of orally administered bentiromide by pancreatic chymotrypsin. The p-aminobenzoic acid (PABA) released is absorbed and may be measured in either urine or serum. Its specificity can be enhanced by concurrent administration of 14C-PABA, allowing an excretion index for PABA to be derived. We describe a modified test where p-aminosalicylic acid (PAS), a structural analogue of PABA, replaces the radiolabel.

In control subjects and patients with pancreatic disease we have compared excretion indices for the bentiromide test using PAS and 14C-PABA. In controls the mean excretion index using PAS was $\bar{x}=90$ (SD±12, n=19) and using 14C-PABA $\bar{x}=94$ (SD±18, n=18). There was excellent correlation between the two excretion indices ($r=0.98$, p<0.001, n=32).

These results suggest that PAS can replace 14C-PABA in the bentiromide test. The bentiromide/PAS test has important practical advantages. It does not require a radiolabel, it removes the necessity for measuring urine volume and only one analytical technique is required. Also this approach makes the test more widely applicable.

T45
The 'shrunken' pancreas: a morphological variant of idiopathic chronic pancreatitis

A P MANNING, O R BULGIM-TOMLINSON, D J LINTOTT, AND A T R AXON (Gastroenterology Unit, and Department of Radiology, The General Infirmary, Leeds) Endoscopic retrograde cholangiopancreatography (ERCP) is a standard technique for the investigation of pancreatic disease. Changes seen in chronic pancreatitis (CP) are variable, but usually include dilatation and irregularity of the main pancreatic duct (MPD); although there may be stenoses or obstruction of the MPD its overall width is greater than normal; side branch changes may include nipping at their origins and dilatation beyond. Occasionally, however, there is diffuse and irregular narrowing of MPD and side branches giving a 'shrunken' appearance. Of 3529 ERCPs done in this department, 362 have shown changes of chronic pancreatitis with six having this 'shrunken' appearance. We present these six patients including representative radiographs to illustrate their characteristic features: the MPD is irregular and narrowed throughout its length and may be shortened; side branches, often difficult to demonstrate, are narrowed and shortened, never showing dilatation. All six patients have other confirmatory evidence of CP: none is alcoholic, one had gall stones, and two have idiopathic inflammatory bowel disease. No other aetiological factors were identified. We conclude that there is morphological variant of CP demonstrated at ERCP as a 'shrunken' pancreas which usually has no common aetiological associations.

T47
Reduced biliary lipid secretion by nor-dihydroxy bile acids in rodents

J P NEOPOLEOMOS, A F HOFMANN, D GURANTZ, K PALMER, L R HAGEY, AND A R MOOSA (Department of Gastroenterology and Surgery, University of California, San diego, USA) Gall stone dissolution by chenodeoxycholate (CDC) and ursodeoxycholate (UDC) involves reduction of cholesterol (CHO) secretion but the degree of desaturation never exceeds 30-40% and the clinical results are poor. Biliary lipid secretion by bile acids (BA) is inversely related to the critical micellar concentration (CMC). As shortening of the C₃ side chain of natural C₂₅ BAs increased the CMC, the effects on lipid secretion by CDC, UDC and deoxycholate (DC) were compared with the synthetically prepared C₁₂ nor-BA homologues. Studies in the hamster showed a dramatic reduction of CHO for nor-DC, nor-CDC and nor-UDC when compared with DC, CDC and UDC: 10-4 vs 7-0, 19-1 vs 4-9 and 11-0 vs 1-7 μmol CHO/mmol BA respectively (p<0.01 at least). There was also a marked reduction of phospholipid (PL) secretion: 66 vs 38, 60 vs 28 and 57 vs 9-4 μmol PL/mmol BA respectively (p<0.01 at least). When the taurine/glycine conjugates of the C₂₅ and C₂₃ BAs were compared the reduction in biliary lipid secretion by the nor-BAs was maintained. In the rat, nor-BAs induced even less CHO secretion than PL secretion. In conclusion, nor-dihydroxy BAs are potent biliary cholesterol desaturation agents and warrant further study.

T48
Comparison of plasma cholecystokinin responses to bombesin and food in patients with pancreatic insufficiency

J B M J JANSEN AND C B H W LAMERS
Hepatology, University (Departments of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands) This study was undertaken to compare the stimulatory effects of food and bombesin on plasma CCK in nine patients with steatorrhea due to pancreatic insufficiency and nine normal subjects. Pancreatic enzyme supplementation was stopped at least three days before the studies. Plasma CCK concentrations were measured by radioimmunoassay using antibody T204, which binds to carboxy-terminal CCK-peptides containing the sulfated tyrosine region. There were no significant differences in basal plasma CCK levels (2.8±0.4 and 2.3±0.4 pM in pancreatic insufficiency and 2.4±0.3 and 2.9±0.5 pM in normal subjects). Ingestion of a liquid test meal induced significant increases in plasma CCK in both the patients with pancreatic insufficiency and the normal subjects. The integrated meal-stimulated plasma CCK secretion in patients with pancreatic insufficiency (176±26 pM 150 min) was significantly lower, however, (p=0.001) than that in the normal subjects (596±115 pM 150 min). In contrast, the integrated plasma CCK secretion during infusion of bombesin (100 ng/kg 20 min) in the patients with pancreatic insufficiency (134±23 pM 20 min) was not significantly different from the CCK response to bombesin in the normal subjects (146±28 pM 20 min). The decreased postprandial plasma CCK secretion in the presence of a normal CCK response to bombesin in pancreatic insufficiency suggests that luminal factors, probably pancreatic enzymes, play an important role in the plasma CCK response to a meal.

rats by infection with the parasite, Nippostrongylus brasiliensis. Preliminary studies by gavage showed an increased 24 hour excretion at eight to ten days postinfection compared with controls (2.5±1.6; mean % of dose, p<0.05). Thus animals were studied at three stages of infection: early (seven days), acute (10 days) and post-inflammation (21 days). Controls were non-infected littermates. Five μCi of 53Cr-EDTA was injected into a 15 cm ligated loop of jejunum in anaesthetised rats. Hydration was maintained by iv saline, and at five hours the urine, one kidney and the intact loop were counted. Mean±SEM, % of administered dose in urine (n=6) were: controls 3.4±0.6, seven days 5.2±0.9, 10 days 6.1±0.6 (p<0.05 vs control), 21 days 2.4±0.3. Kidney counts followed the same trend, higher at 10 days (p<0.05); counts in the gut did not change significantly. Myeloperoxidase activity increased in jejunal mucosa in the acute stage whereas sucrase was decreased. Ligated loops of ileum showed no changes in inflammation or permeability to the probe (means 1.0% vs 0.9%). We conclude that permeability changes are related to active inflammation, are reversible and are not seen distal to the inflamed site.

T49
Permeability of inflamed jejunum to 53Cr-EDTA in the in vivo rat
J K RAMAGE, R T JENKINS, R H HUNT, AND M H PERDUE (Intestinal Disease Research Unit, McMaster University Medical Center, Hamilton, Ontario, Canada) Increased urinary recovery of orally administered 53Cr-EDTA may be related to activity and extent of intestinal inflammation. To explore this, we measured changes in gut permeability to 53Cr-EDTA in a controlled model of jejunal inflammation produced in rats by infection with the parasite, Nippostrongylus brasiliensis. Preliminary studies by gavage showed an increased 24 hour excretion at eight to 10 days postinfection compared with controls (2.5±1.6; mean % of dose, p<0.05). Thus animals were studied at three stages of infection: early (seven days), acute (10 days) and post-inflammation (21 days). Controls were non-infected littermates. Five μCi of 53Cr-EDTA was injected into a 15 cm ligated loop of jejunum in anaesthetised rats. Hydration was maintained by iv saline, and at five hours the urine, one kidney and the intact loop were counted. Mean±SEM, % of administered dose in urine (n=6) were: controls 3.4±0.6, seven days 5.2±0.9, 10 days 6.1±0.6 (p<0.05 vs control), 21 days 2.4±0.3. Kidney counts followed the same trend, higher at 10 days (p<0.05); counts in the gut did not change significantly. Myeloperoxidase activity increased in jejunal mucosa in the acute stage whereas sucrase was decreased. Ligated loops of ileum showed no changes in inflammation or permeability to the probe (means 1.0% vs 0.9%). We conclude that permeability changes are related to active inflammation, are reversible and are not seen distal to the inflamed site.

T51
Mucus glycoprotein degrading enzymes in inflammatory bowel disease detection of a novel sialic acid O-acetyl esterase
A P CORFIELD, A J K WILLIAMS, S A WAGNER, J R CLAMP, AND R A MOUNTFORD (University of Bristol, Department of Medicine, Bristol Royal Infirmary, Bristol) A sensitive physiological assay for sialidase activity in human faecal extracts, using the main sialic acid in mammalian sialoglycoproteins, 2-6 linked N-acetylneuraminic acid to (2-6) N-acetylgalactosaminyl [3H] has been developed and optimised. The assay avoids artefacts arising with colorimetric and radioactive glyco-protein substrates.

The activity of sialidase, acylneuraminic acid pyruvate lyase, protease and non-specific esterase were assayed in 24 normal and five Crohn's disease and five ulcerative colitis patients. Significant differences were found between the two inflammatory bowel disease groups and normal for the lyase and protease, but no change in sialidase or non-specific esterase activities. This confirms previous results with synthetic sialidase substrates but provides new information regarding sialic acid metabolism with respect to lyase activity.

The degradation of colonic mucus glycoproteins rich in O-acetyl sialic acids may be governed by the release of these O-acetyl groups which block sialidase action. Accordingly a novel esterase was detected in partially purified normal faecal extracts with a mucus glycoprotein substrate. The ratio of this activity to that of sialidase was 1:100 and this may govern the initiation of mucus glycoprotein breakdown in the colon.

BASIC SCIENCE
T49–53

T50
Cholecystokinin receptor binding by human bladder myocyte membranes
P PORTINCASES, A HOWARD, G M MURPHY, AND R H DOWLING (Gastroenterology Unit, Division Medicine, UMDS, Guy's Hospital, London) The first step in CCK-induced gall bladder contraction is ligand binding of the peptide by myocyte membrane receptors. This has been studied little in animals but never in man. Because gall bladder emptying in response to CCK is impaired in gall stone patients, we wished to see if this was because of changes in myocyte membrane receptor activity (number and/or activity). To date we have homogenised fresh gall bladder muscle (five pooled samples from 25 gall stone patients), prepared plasma membrane fractions either by Percoll spontaneous density gradients or by ultracentrifugation (25×000–200 000×g), checked their purity by measuring the membrane marker enzyme 5'-nucleotidase (5'-NT) and by electron microscopy, and studied total and reversible binding of [3H]-CCK₄₋SO₄. Using Percoll gradients, total CCK binding was 8.4±5 SD 4.3 fmol/ng protein (3.3–15.9%) and after adding 100 nmoles CCK₄₋SO₄, reversible receptor binding was 41±12.8% of total, but enrichment of the fraction with 5'-NT was poor. With both 25 000 and 200 000 g ultracentrifugation, there were membrane ribbons and vesicles by EM, a 3-5 fold enrichment of 5'-NT; 0-6-2.8 fmol/mg prot. (1.3-2.3%) total CCK binding, of which 51-90% was reversible. These preliminary studies have shown for the first time in man, CCK binding by gall bladder myocyte membranes similar to that reported in animals. These methods will be used to correlate CCK binding with in vivo and in vitro studies of gall bladder contraction in man.
T52
Luminal alkalinisation by rat caecum in vitro

S P CANFIELD (INTRODUCTION BY B P CURWAIN (Department of Physiology, St Mary's Hospital Medical School, London)) This study investigates the ability of rat caecum to alkalinise a luminal solution under in vitro conditions.

The serosal surface was bathed in a HCO₃⁻ buffered saline gassed with 95% O₂/5% CO₂ (pH 7.4) at 35°C and the luminal with a similar but unbuffered solution gassed with 100% O₂ (pH=7.2). This change was every 15 min, luminal alkalinisation was determined by titration and expressed as H⁺ loss in μmol cm⁻² h⁻¹.

The luminal saline became more alkaline at a rate of 7.3±0.69 μmol H⁺ cm⁻² h⁻¹. Replacement of the HCO₃⁻/CO₂ buffer with HEPES/100% O₂ caused a fall (p<0.01) in rate from 6.4±0.54 to 0.75±0.25 μmol H⁺ cm⁻² h⁻¹ (n=4) which was reversible. Gassing the luminal side with 95% O₂/5% CO₂ changed the initial pH of the luminal saline from 7.2 to 4.6 but had no effect on alkalinisation; with 95% O₂/5% CO₂ 5.7±0.43; with 100% O₂ 5.95±0.08.

Alkalinisation by tissues mounted with the serosal side facing the unbuffered solution was 2.98±0.52 μmol H⁺ cm⁻² h⁻¹ (n=5), lower (p<0.01) than tissues from the same animals where the mucosal surface faced the unbuffered solution (9.1±1.27 μmol H⁺ cm⁻² h⁻¹, n=4).

Rat caecum in vitro alkalinises a luminal solution by a process which depends upon serosal HCO₃⁻.

T53
Hydrophobic adhesion of E coli (EC) in ulcerative colitis (UC)

D A BURKE AND A T R AXON (Gastroenterology Unit, The General Infirmary, Leeds) E coli from patients with UC possess a mannose-resistant adhesive property demonstrated by both buccal epithelial (BEC) and HeLa cell adhesion. Pathogenic E coli with adhesive properties have an increased surface hydrophobicity. The fimbrial adhesins CFA/I and CFA/II typically associated with enterotoxigenic E coli can be identified by haemagglutination. Slide haemagglutination typing of 74 colitic E coli isolates, using 5 types of red blood cell revealed a variety of haemagglutination patterns including those expressed by normal stool and enteropathogenic E coli 43-2% showed no mannose-resistant haemagglutination with any source of red blood cell. No CFA/I or CFA/II type pattern was found in any colitic E coli. The salting out method was used to assess hydrophobicity of E coli from 42 colitics and 15 controls. The mean (±SEM) lowest molar dilution of ammonium sulphate resulting in autoglutination for colitic E coli was 0.93 M±0.16 compared with 2.45 M ±0.25 for controls (p<0.0001). Bacterial adhesion negatively correlates (p<0.001). E coli grown at 18°C show a significant decrease in BEC adhesion (p<0.01) and hydrophobicity (p<0.001). The salting out method differentiates between colitic and control E coli. The hydrophobicity of colitic E coli is due to the expression of an adhesion unidentifiable by haemagglutination but with properties similar to the adhesins of intestinal pathogenic E coli raising the possibility that E coli in patients with UC may have pathogenic potential.

GASTRODUODENAL
T54-63

T54
Studies of gastrin in patients with the intestinal type of gastric cancer

G DEN HARTOG, J B M J JANSEH, D J SCHAARDENBURG, E J F LAMBERTS, D M V D BOOMGAARD, J KREUNING, AND C B H W LAMERS (Departments of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands) Patients with atrophy of the antral mucosa have low serum gastrin responses to bombesin because of reduced antral gastrin concentrations. As this condition is suggested to predispose to the intestinal type of gastric cancer, we have measured bombesin stimulated serum gastrin concentrations and antral gastrin contents in 21 patients with the intestinal type of gastric cancer and we have compared the results with those found in 30 dyspeptic patients without endoscopic or histologic abnormalities, 12 patients with either the diffuse type or cardiac cancer and 17 patients with a benign gastric ulcer. Bombesin 100 ng/kg, was infused over 20 min and plasma for gastrin measurement (RIA) was obtained at 0, 0.5, 10, 15, and 20 min. Gastrin was also measured in extracts of antral biopsies. In patients with gastric cancer or gastric ulcer, the biopsies were taken from non-affected sites. The lower level of normal was defined as the 10th percentile of the dyspeptic patients (control group).

Abnormally low gastrin responses to bombesin were found in nine of 21 patients with the intestinal type of gastric cancer (p<0.05), in two of 12 patients with the diffuse type or cardiac cancer (NS) and in three of 17 patients with gastric ulcer (NS). The antral gastrin content was abnormally low in 10 of 21 patients with the intestinal type of gastric cancer (<0.05), in one of 12 patients with the diffuse type or cardiac cancer (NS) and in four of 17 patients with gastric ulcer (NS). It is concluded that patients with the intestinal type of gastric cancer have, in contrast with those with the diffuse type or cardiac cancer and those with benign gastric ulcer, an abnormally low serum gastrin response to bombesin. This low response is not caused by cancerous involvement of the antrum, but by low gastrin content of the antral mucosa.

T55
Genetic and dietary factors in the pathogenesis of gastric cancer (GC). Study of a high incidence family

F FARINATI, F COSTA, M SCAPOLU, C VENTURI-PASINI, M BORTOLAMI, F DE LAZZARI, F CARDIN, F DI MARIO, AND R NACCARATI (Cattedra di Malattie dell'Apparato Digerente, Università di Padova, Padova, Italy) A ‘gastric cancer’ family, in which father, mother and three of the nine children were affected by gastric cancer, was studied in order to evaluate the pathogenetic role of genetic, dietary and environmental factors. Eighteen subjects, including all living siblings and the grandchild aged over 30 underwent endoscopy and biopsies; gastric juice samples were tested for pH, nitrates and, partly, CA 19-9 (RIA). Blood samples were tested for blood groups, HLA antigens, pepsinogen group I and gastrin. The water sources of the family were tested for nitrates, nitrates, and bacteria. An accurate history regarding dietary habits was collected. All siblings were affected by chronic atrophic gastritis (CAG) and/or intestinal metaplasia (IM); two of nine presented mild epithelial dysplasia. Intestinal metaplasia was also present in two of nine grandchild whose age was 35. The nitrate, nitrite and bacteria content of the wells used by the family were normal. In the diet, lack of fresh vegetables (and, there-
Hypertrophic gastrophy is a rare condition characterized by the overproduction of prostaglandin E2 (PGE2) in the stomach. The overproduction of PGE2 can contribute to the development of hypertrophic gastric mucosal folds. These findings are relevant to the pathogenesis of hypertrophic gastrophy and to potential effects of longterm therapy with PGE2 analogues.

T57 Difficulties in the diagnosis of adenocarcinoma of the stomach in routine practice

M Deakin, D G Colin-Jones, and M Vessey (Department of Gastroenterology, Queen Alexandra Hospital, Portsmouth, and Department of Community Medicine and General Practice, Radcliffe Infirmary, Oxford) A detailed retrospective assessment was made of 342 cases of adenocarcinoma of the stomach diagnosed in Portsmouth and Oxford during 1979 and 1980. Stage 1 and 2 disease accounted for only 46/342 (13.3%) of tumours diagnosed and only nine patients (2.6%) had early tumours.

Most patients including those with early tumours presented with weight loss and abdominal pain and in 72% within three months of onset of symptoms. During the year up to diagnosis 232 patients underwent 247 barium meals with a false negative rate of 26% for cancer detection and 125 patients underwent upper gastrointestinal endoscopy on 141 occasions with a false negative rate of 13%. The false negatives had different bases, radiology missed lesions completely whilst endoscopy observed them only to conclude erroneously that they were benign.

Symptoms in gastric cancer do not develop early, so early diagnosis in symptomatic patients is essential. The false negative results contributed to delays in no less than 20% of the cases investigated. Awareness of the failings of the two diagnostic modalities is important if more cases of gastric cancer are to be diagnosed at a treatable stage.

T58 Endoscopic aspiration cytology of gastric lesions

C J H Ingoldby and R J Hall (University Department of Surgery, St James's Hospital, Leeds) The limitations of endoscopic biopsy in the diagnosis of gastric cancer are well recognised. The addition of brush cytology improves diagnostic accuracy but only surface cells are sampled. Needle aspiration cytology allows sampling of the deeper layers of the stomach. We have developed a technique, using a flexible varices injection needle to obtain cell aspirates, and have compared results with the two conventional methods.

Initial studies confirmed that cells could be aspirated at endoscopy. Sampling of an operative specimen was then carried out at multiple sites on and around a gastric carcinoma and compared with subsequent histology. Needle aspiration obtained readable samples at all sites and corresponded in every case with histological findings.

Comparative studies were therefore done on 19 benign or malignant gastric lesions in 16 patients undergoing endoscopy. Successful aspirates were obtained from 19 lesions. The technique was quick and easy. All three methods provided the same diagnosis in 15 lesions. In two instances cancer was shown on biopsy alone but not on cytology, but in two instances aspiration cytology alone correctly revealed the presence of cancer.

We conclude that endoscopic aspiration cytology is a simple technique and its addition to conventional sampling improves diagnostic accuracy.

T59 Post-trial surveillance of mortality in bleeding peptic ulcer disease

K E Wheatley, S Brearley, P W Dykes, and M R B Keighley (The General Hospital, Birmingham) Between October 1980 and September 1983 we conducted a randomised trial of the timing of surgery in bleeding peptic ulcer disease. This demonstrated no mortality in patients under 60 with early or delayed surgery, but early surgery was associated with a significantly lower mortality in older patients. This trial has, however, been criticised on statistical grounds. Since the completion of the trial we have adhered to a policy of early surgery in the over 60 group and delayed surgery in the under 60 group and surveyed the mortality rates.

In the 27 months to May 1986, 200 patients were admitted with definite haematemesis and/or melaena from peptic ulcers. Eighty one patients were under 60 years (56 duodenal ulcers (DU), 25 gastric ulcers (GU)) and 119 were over 60 (64 DU, 55 GU). There were nine deaths overall (4.5%) with all deaths in the older group (7.6%).

There were 41 emergency operations
with two deaths (4.9%), both in the over 60 group (2/29 – 6.9%).
We conclude that under our current policy we continue to have a low mortality rate in bleeding peptic ulcer disease and an acceptable postoperative mortality. Patients below 60 years of age continue to show zero mortality.

T60
Relief of gas bloat syndrome by gastrointestinal stimulation
F C Campbell, D H Cook, Geraldine Blanch, and A Cuschieri (Department of Surgery, Ninewells Hospital and Medical School, Dundee) In gas bloat syndrome (GBS), the retrograde passage of swallowed air is prevented by the oesophagogastric ‘valve’ created by antireflux surgery. Postprandial gastric distension and discomfort result but there is no effective treatment. While stimulation of stomach emptying and transit of contents through small bowel could alleviate symptoms, this method could theoretically cause ‘dumping’ and reactive hypoglycaemia.
In 10 patients with severe gas bloat syndrome baseline symptoms were evaluated by scored linear analogue scale – the worse the symptoms, the higher the score. In response to a solid meal, baseline gastric emptying and intestinal transit were evaluated by isotope scintiscan and 
H2 breath test respectively. Sequential blood glucose assays were taken for three hours after the solid meal. All patients were then given cisapride, a new stimulatory prokinetic drug, 4 mg iv initially then 10 mg orally tds for one week. Symptomatic and objective tests were repeated after treatment. Symptom score fell from \( \pm SEM = 29.7 \pm 7.7 \) before (B) to \( \pm SEM = 29.7 \pm 7.7 \) after (A) treatment (*p<0.02). Transit times diminished from \( \pm SEM = 156 \pm 23 \) mins (B) to \( \pm SEM = 97 \pm 9.7 \) mins (A) (*p<0.006) and gastric emptying times fell from \( \pm SEM = 44 \pm 6.2 \) (B) to \( \pm SEM = 38 \pm 6.4 \) (A) (*paired Student’s t test). Blood glucose levels were unaffected by cisapride.
We conclude that cisapride relieves symptoms of gas bloat syndrome by gastrointestinal stimulation, but it does not induce reactive hypoglycaemia.

T61
Relation of gastric mucosal surface pH to luminal acid in gastric and duodenal ulcer patients
B J Z Danesh, M L Lucas, J M Rawlings, and R I Russell (Institute of Physiology, University of Glasgow and Gastroenterology Unit, Royal Infirmary, Glasgow) It is recognised that a neutral mucus-bicarbonate gel layer protects gastric mucosal surface against luminal acid. This study examines the relation of gastric antral mucosal surface pH to luminal acid in 34 endoscopically normal (controls), 22 gastric ulcer (GU) and 25 duodenal ulcer (DU) patients. Gastric (fundal and antral) mucosal and luminal pH was measured, using a flexible electrode introduced through an endoscope. The subjects were divided into those with high and low fundal and antral luminal pHs. In subjects with fundal luminal pH higher than 2.5 (and antral pH greater than 4.0) the antral mucosal pH (mean ± SEM) was neutral and similar in the 3 groups: 7.17±0.07 in controls (n=10), 7.05±0.05 in GU (n=10) and 7.09±0.04 in DU (n=9). In those with fundal luminal pH below 2.5; however, the antral mucosal pH was again neutral (pH 7.00±0.20) in GU (n=12) but not in controls (n=24) (pH 4.7±0.42) p<0.01) or DU patients (n=13) (pH 5.90±0.46) (p<0.05). In the latter subgroup those who had antral luminal pH below 4.0, the antral mucosal pH was again higher (pH 6.49±0.41) in GU (n=4) than in controls (pH 3.8±0.43, n=12) and DU (pH 4.3±1.85, n=4).
This study has shown that in contrast with DU and control subjects, patients with gastric ulcer disease can maintain a neutral mucosal microclimate in the face of a high fundal luminal acidity.

T62
Effect of submandibular glands and synthetic human epidermal growth factor (EGF) on healing of gastric ulcers in rats
P Skov Olsen, S S Poulsen, K Theerkelsen, and E Nexø (Department of Surgery C, Rigshospitalet, Department of Anatomy B, University of Copenhagen and Department of Clinical Chemistry, Hillerød Hospital, Denmark) In rats sialoadenectomy decreases the synthesis of DNA in gastric mucosa and the resistance of the gastric epithelium to damaging agents such as bile salt solutions. Epidermal growth factor is secreted in an exocrine manner from the submandibular gland. We have previously shown that oral administration of EGF can prevent the development of experimental gastric lesions in the rat. The effect of extirpation of the submandibular glands and the effect of oral administration of synthetic human EGF on healing of chronic gastric ulcers in rats was investigated. Removal of the submandibular glands delayed healing of chronic gastric ulcers when examined after 50, 100, and 200 days. Oral administration of synthetic human EGF increased gastric ulcer healing when examined after 25 and 50 days of treatment. The effect of synthetic human EGF was comparable with that of cimetidine. Combined administration of synthetic human EGF and cimetidine further enhanced healing of gastric ulcers compared with the effect of each substance. Neither synthetic human EGF nor removal of the submandibular glands influenced gastric acid secretion. This study shows that the submandibular glands influence healing of chronic gastric ulcers and suggest that EGF participate in healing of gastric ulcers in rats.
(Synthetic human EGF was supplied by G D Searle Co, Ltd. and Imperial Chemical Industries, PLC, UK.)

T63
Clinical and ultrastructural studies in duodenal pseudomelanosis
J Y Kang, A Y T Wu, J L S Cha, A Wee, I E Sutherland, and R Horii (Departments of Medicine, Pathology and Zoology, National University of Singapore and Department of Renal Medicine, Singapore General Hospital, Singapore) The presence of a spotty brownish-black pigmentation in the duodenal mucosa on endoscopy, termed duodenal pseudomelanosis, has been described in eight previous case reports. We have studied seven more patients: four men and three women, aged 28-79 years. Five were on maintenance haemo- or peritoneal dialysis, one had undergone renal transplantation while the seventh was anaemic. Six of the seven were on oral iron supplementation. There were no symptoms attributable to the pigmentation. In five, the pigment was positive with the Perl’s iron stain (P+ve) but negative by the Masson-Fontana method for melanin (MF-ve); one was P-ve MF+ve; while in another, P+ve MF+ve pigment became P+ve MF+ve one year later. At electron microscopy MF+ve pigment comprised characteristic anguilar membrane-bound structures while MF-ve pigment contained more rounded or irregularly-shaped granules. Electron probe x-ray analysis demonstrated the presence of iron in P+ve as well as P-ve pigment.
MF+ve pigment had high sulphur content but MF–ve pigment had little or no sulphur. Duodenal biopsies from 32/46 uremic patients (on oral iron but endoscopically normal) contained iron compared with 22/120 non-uremic subjects (p<0-001). We postulate that, in uremic subjects taking oral iron, duodenal pseudomelanosis may represent a disorder of iron transport from the duodenal mucosa. Iron-containing pigment with a high sulphur content may become MF+ve.

**LIVER POSTERS**

**T64**

Urban clustering of primary biliary cirrhosis

J F MAYBERRY, J GIGGS, H L SMART, AND P J TOGILL (University Hospital of Nottingham and University of Nottingham, Nottingham) Between 1970 and 1984 38 patients with primary biliary cirrhosis were diagnosed in the greater Nottingham area which has a population of 573 000. The diagnosis was accepted on the basis of classical histological changes. During this period 14 additional patients were found to have positive antimitochondrial antibody titres by their general practitioners, but no liver biopsy was performed. These patients were not included in the study. The overall incidence of primary biliary cirrhosis was 0-44/10^5/year. Between 1970 and 1984 24 patients died giving a prevalence for the disease of 4-210^5. The majority of the patients were women (ratio 19:1). The age specific incidence rose to a peak of 5-210^5/year in the 65–69 age group.

In all cases a detailed residential history was obtained from the patient or a close relative and this was analysed using data obtained from census enumeration districts. There was clear evidence of clustering of cases in the town and this was significantly associated with the water supply in the two areas of Clifton and Stapleford. Further studies may elucidate an important environmental factor in the development of primary biliary cirrhosis.

**T65**

Sexual dysfunction and sex hormone changes in liver disease. A controlled study of alcoholic vs non-alcoholic disease

P BANNISTER, J OAKES, P SHERIDAN, AND M S LOSOWSKY (Department of Medicine, St James’s Hospital, Leeds) Men with liver disease are hypogonadal and feminised. European workers consider the liver disease and American workers consider alcohol consumption the major factor. We investigated sexual dysfunction and sex hormones in three groups of men; control (n=22), alcoholic liver disease (ALD) (n=22), non-alcoholic liver disease (NALD) (n=24). The liver disease groups were matched for age, drug therapy, disease severity and complications. Men with ALD had significantly more sexual dysfunction. Androgen concentrations were changed in ALD and NALD, more so in the ALD group. Data is mean±SD: Control vs ALD vs NALD.

Testosterone; 18–1±5–2 vs 6–6±4–8 vs 12–9±6–0 nmol/l; NALD vs control p<0–01; ALD vs control p<0–001; NALD vs ALD p<0–005.

Androstenedione; 3–8±1–7 vs 8–12±2–8 vs 5–46±2–47 nmol/l; NALD vs control p<0–02; ALD vs control p<0–001; NALD vs ALD p<0–005.

Dehydroepiandrosterone-sulphate; 6–78±3–2 vs 1–27±1–6 vs 1–71±1–7 nmol/l; NALD vs control p<0–001; ALD vs control p<0–001; ALD vs NALD p<0–5.

Oestradiol concentrations were raised only in the ALD group; 96±5 vs 177±189 vs 94±50 pmol/l. ALD vs control p<0–05. In this, the first controlled study, liver disease per se causes sexual dysfunction and sex hormone changes but these changes are amplified by ethanol.

**T66**

Cytological diagnosis of hepatic dysfuntion after liver transplantation

R M KIRBY, J A YOUNG, S G HUBSCHER, W B CUTHBERTSON, A B JAIN, AND P McMCMASTER (Queen Elizabeth Hospital, Edgbaston, Birmingham) Sixteen patients have been studied after 19 liver transplants by fine needle aspiration cytology in combination with Menghini needle biopsies. Eighty seven specimens were examined. Thirty nine of these followed histological biopsy and allowed direct comparison once the cytological diagnosis had been made. Eleven baseline aspirations were done immediately after perfusion of the graft.

Rejection was diagnosed by a rise in liver aspirate lymphocytes, plasmablasts and plasmacytes compared with peripheral blood. There were 36 diagnoses of rejection. Twenty nine of these were matched with histology; 28 confirmed rejection. Thirty eight cytological diagnosis did not suggest rejection. Ten were matched against histology. Six of these confirmed the absence of acute rejection, three suggested 'mild' or improving rejection. Two patients were not treated for rejection because of mild biochemical changes and one incident was treated despite spontaneously improving biochemistry. The 36 biopsies with no histology, showing the absence of rejection were done in the absence of clinical suspicion of active acute rejection. The presence of macrophages preceded or accompanied serious graft disease including chronic rejection and graft ischaemia.

Cytological examination of liver grafts carries a high sensitivity and specificity for acute rejection.

**T67**

Natural killer cell activity in hepatocellular carcinoma: in vitro and in vivo response to interferon

A A DUNK, D NOVICK, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital School of Medicine, London) Natural killer (NK) cells may be important in the host defence against cancer and reduced NK activity has been found in patients with a variety of different cancers. In a 51 chromium release assay we have measured the in vitro NK cytotoxicity of peripheral blood mononuclear cells (PBMCs) isolated from patients with hepatocellular carcinoma (HCC) against K562 cells, and have examined the effects of α-interferon (IFN) on NK function both in vitro and in vivo. At all effector:target (E:T) ratios studied, NK cytotoxicity in HCC patients (n=17) was significantly lower than patients with cirrhosis (C: n=13) or normal controls (NC: n=12 – for example, at E:T=50:1, % cytotoxicity (mean±SEM) HCC**=26±3±3, C**=45±6±2, NC=53±8±4. *p<0–05 vs C, p<0–01 vs NC, **p<0–05 vs NC). Natural killer activity in HCC did not correlate significantly with either serum AFP concentration or patient performance score. Natural killer activity in all groups could be increased by prior incubation of PBMCs with IFN but this was significant only in HCC patients, where 10 IU/ml of IFN increased NK cytotoxicity from 36±9±10 to 52±8±2%. E:T=50:1, n=5, mean±SEM, p<0–05. Further increases in IFN concentration failed to further increase NK activity. Natural killer activity was measured before and 24 hours after...
2.5 mU/m² of IFN was given to four HCC patients. Natural killer cytotoxicity (mean±SEM) rose from 27.5±8.6 to 60.9±5.2% (p=0.05).

We conclude that natural killer activity is reduced in HCC. This is not explicable on the basis of underlying cirrhosis, or related to serum AFP level or poor patient condition. Natural killer cytotoxicity in HCC can be increased in vitro and in vivo by small doses of IFN.

T68
Multiple logistic analysis of Pugh’s criteria for early mortality from variceal bleeding. Comparison with other modified Child’s classifications

A K BURROUGHS, F D’HEGEGERE, A PHILLIPS, and N MCINTYRE (Academic Department of Medicine and Clinical Epidemiology, Royal Free Hospital School of Medicine, London) Modified Child’s classifications (MC) in cirrhotics using grades A, B, and C are commonly used to assess prognosis, and 30 day mortality after variceal bleeds. Component criteria of MC are statistically a good index of overall prognosis, but have not been validated as prognostic indicators after variceal bleeding. Moreover, simple comparison of the same grades using different MC may be misleading because of different systems of grading. We compared prospectively in 132 cirrhotics bleeding three MC (Campbell, Pugh and Cello). There was great variation in grading: grade A 6% to 42%, grade B 28% to 36% and grade C 21% to 66%, with similar differing proportions of deaths at 30 days (n=29) in each grade. The prognostic value of several variables including Pugh’s criteria (PC) for 30 day mortality after variceal bleeding was analysed using multiple logistic analysis. All PC correlated univariately: bilirubin p=0.004, asites p=0.0002, encephalopathy p<0.0005, prothrombin time p<0.02, albumin p<0.08. Only one other factor correlated: early rebleeding p=0.003. Bilirubin, ascites, encephalopathy, and early rebleeding had independent prognostic value. Thus PC are statistically valid prognostic indicators for 30 day mortality after variceal bleeds. A uniform system of grading, however, must be adopted for clinical use.

T69
Prospective randomised trial of endoscopic sclerotherapy versus oesophageal staple transection for acute variceal bleeding. Single interim analysis

A K BURROUGHS, F D’HEGEGERE, A PHILLIPS, K E F HOBBS, and N MCINTYRE (Academic Department of Medicine, Clinical Epidemiology and Surgery, Royal Free Hospital and Medical School, London) Emergency sclerotherapy (ES) for variceal bleeding has relegated surgery to second line treatment in many centres, although very few randomised studies exist comparing ES and surgical treatment. We randomised cirrhotics to ES or oesophageal staple transection (OST) if bleeding was not controlled with transfusion and gypsyxan at any time within five days of admission. There were 200 admissions (125 patients): Pugh’s grade A (47), B (80), C (73). In 82 admissions bleeding was not controlled: 12 not randomised (eight not eligible, four moribund): 70 randomised (63 patients) – 35 to OST, 35 to ES: grade A (nine), grade B (25), grade C (36). The two groups were well matched as regards clinical status, severity and duration of bleeding. Mortality at 30 days was 34% (12 of 35) in both groups (1A, 4B, 19C) analysed by intention to treat, and 27% (OST) and 31% (ES) related to treatment received. Emergency sclerotherapy (≤ injections) failed to completely control bleeding in 15% (five admissions – one survived); OST in 3% (one admission – survived). Fatal complications were similar. These results show that OST has a similar mortality to ES. Emergency sclerotherapy was less effective, and there was a high mortality in patient failures. Prediction of ES failures and/or early changes to alternative therapy may improve survival in acute variceal bleeding.

T70
Randomised controlled double blind trial of lactitol and lactulose in acute hepatic encephalopathy in cirrhotic patients

G HAWLEY AND M V MORGAN (Academic Department of Medicine, Royal Free Hospital, London) Lactitol is a non-absorbable disaccharide available as a powder which, in open comparison, is as effective as lactulose in the treatment of chronic hepatic encephalopathy but is better tolerated. Twenty five cirrhotic patients needing treatment for 28 episodes of acute hepatic encephalopathy were blindly randomised to either lactitol (n=15) or lactulose (n=13) dispensed as solutions identical to colour, taste, pH, and osmolarity containing either 75 g/100 ml lactitol or 50-6 g/100 ml lactulose. The initial dose of 0.75 ml/kg was adjusted to produce two semi-soft stools per day. Patients were assessed 12 hourly for five days. Patient groups were comparable on entry to the trial. During the trial, significant improvements occurred in clinical and psychometric performance and in the EEG in the majority of patients in both groups. At the end of the trial 67% of patients in the lactitol and 69% in the lactulose group were clinically normal. At 24 hours, however, 33% of lactitol patients but only 8.2% of lactulose patients had improved significantly (p<0.05). Both drugs are effective in the treatment of acute hepatic encephalopathy, but patients treated with lactitol responded more quickly.

COLORECTAL
T71–77
Epithelial cell proliferation kinetics of colorectal mucosa in patients with polyps of the large bowel

M PONZI DE LEON, P DI DONATA, L RONCUCCI, M G AMORICO, C SACCHETTI, G MALAGOLI, M PERINI, L CODELLUPI, AND A FERRARI (Istituto di Patologia Medica, Istituto di Radiologia, Cattedra di Gastroenterologia, Universita di Modena, Modena, Italy) In normal subjects the cytoproliferative activity of colonic mucosa is limited to the lower portion of the crypts and almost absent in the surface. In subjects at high risk for colorectal cancer (such as members of families with adenomatosis coli or Lynch syndromes) cell proliferation is observed in the whole body of the crypt. It is not known if this abnormal proliferative pattern is also observed in the more common patients with solitary or multiple polyps. Thus, we purposed to investigate the proliferative pattern of large bowel mucosa in subjects with adenomas.

Twenty eight patients with polyps and 15 healthy controls entered the study. During endoscopy small samples of mucosa were taken at 10–15 cm from the anus and incubated with ³H-thymidine (1–5 μCi/ml) for one hour at 37°C. After exposition of Kodak AR 10 films and histology, each
intestinal hemicyt was divided into five longitudinal compartments from the fundus to the surface. For each hemicyt total cells, cells for each compartment and labelled cells (in phase S of the replicative cycle) were counted.

In total, 11 948 cells were counted in patients with polyps and 5471 in controls. Labelling index (% of labelled cells) was 11.2±2.5% SDM in the polyps group and 9.5±2.5% in controls (NS). In the first and in the second compartments the ratio between labelled and unlabelled cells was not different between the two groups. In the third compartment the ratio was higher in the polyps group (0.10±0.13 vs 0.09±0.12, p<0.02) and even higher in the most superficial compartments (0.40±0.07 vs 0.20±0.07, p<0.01).

We conclude that a significant increase of the cytoproliferative activity in the most superficial portion of the large bowel mucosa (3', 4' and 5' compartments) has been found in patients with adenomatous polyps. These findings might be of relevance in order to define the predisposition to colorectal cancer in this population at risk.

T72 Role for endogenous androgen in the development of colorectal adenomas?

W S L STIBBINGS, M J G FARTHING, J R RUDDEFOOT, T E ANDERSON, G P VINSON, J M A NORTHOVER, AND R F M WOOD (Professorial Surgical Unit and Departments of Gastroenterology and Biochemistry, St Bartholomew's Hospital Medical College, London) Necropsy and colonoscopic studies have shown that colorectal adenomas occur more frequently in men than women. To evaluate the potential effect of androgens on the development and growth of human colorectal adenomas, the prevalence and concentrations of cytosolic androgen receptors (AR) were analysed in 26 adenomas and 19 samples of normal mucosa by a hybrid ligand receptor binding assay. Scatchard analysis was used to determine the binding specificity and tissue was considered AR positive at receptor concentrations ≥5 fmol/mg cytosolic protein. Androgen receptors were detected in seven of the adenomas (26-9%) and in six of the normal mucosa samples (31.6%). In the adenomas, AR levels were low ranging from 6 to 31 fmol/mg cytosolic protein, and dissociation constants (Kd) ranged from 0.17±2.7×10−9 M, comparable with the Kd of AR in human prostate (6±4×10−9 M).

Six of 13 adenomas (46%) excised from men had positive receptor binding activity, whereas only one of 13 (7.7%) from women was positive (p<0.03). Fisher's exact test. There was no significant correlation between AR levels and patient age or between adenoma size, histological type or degree of dysplasia. In normal mucosa, AR levels ranged from 7−33 fmol/mg and Kd's ranged from 0.24−3.1×10−9 M. There was no significant difference between either AR prevalence or levels in the adenomas and the normal mucosa. The sex difference was exclusive to the adenomas. These results suggest that endogenous androgen may play a role in the adenoma-carcinoma sequence early in the promotional process.

T73 Plasminogen activator activity in the colonic polyadenocarcinoma sequence

P A F DE BRUIN, H W VERSPAEGT, G GRIFFIOEN, J H VERHEIJEN, M NAP, AND C B H W LAMERS (Departments of Gastroenterology and Hepatology, Department of Pathology, University Hospital and Gauibus Institute TNO, Leiden, The Netherlands) Malignant changes are often accompanied by alterations in activity and composition of the plasminogen activators (PA). To study the relation between PA expression and the development of colorectal cancer, we determined tissue-type plasminogen activator (t-PA) and urokinase-type plasminogen activator (u-PA) activity in normal mucosa (n=78), polyps (n=76) and adenocarcinomas (n=70) of the colon. Tissue obtained from surgical resection or polypectomy was homogenised and analysed for both PA activities by (a) SDS-PAGE followed by PA identification from lysis areas in a fibrin-plasminogen gel overlay (zymogram-technique); (b) t-PA and u-PA activity measurements in an enzymatic assay using plasminogen, a chromogenic substrate and selective quenching with monospecific antibodies to determine both activators (expressed as enzymatic units, mean±SEM).

Zymograms of normal mucosa revealed PA activity exclusively at MW=65 000 (t-PA) whereas in adenocarcinomas this activity was decreased and a second stronger activity occurred at MW=50 000 (u-PA). The enzymatic assay confirmed these observations by a significant reduction in t-PA activity (0.65±0.06 vs 2.2±0.16, p<0.001) and a corresponding increase in u-PA activity (0.55±0.05 vs 0.13±0.01, p<0.001) in the adenocarcinomas when compared with normal mucosa. The contribution of u-PA to the total PA-activity (% u-PA) in normal colon mucosa was 5±2±5%, whereas in adenocarcinomas the % u-PA was significantly increased to 47±7±5% (p<0.001) with a specificity and sensitivity of respectively 98.8% and 95.8%. Adenomatous polyps showed values of % u-PA (20±2±13) which were intermediate as well as significantly different (p<0.001) from those of normal mucosa and adenocarcinomas.

This study shows that the sequence of normal mucosa-polyp-adenocarcinoma in the colon is associated with a parallel increase in u-PA activity. Thus PA measurements in intestinal tissue might be helpful in the early detection of colorectal cancer.

T74 Calcium has a protective role against the development of colorectal tumours

G V N APPLETON, P W DAVIES, J B BRISTOL, AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Carcinogenesis in the large intestine is promoted by both intrarectal administration of sodium deoxycholate and small bowel resection. Oral supplements of calcium reduce the mitogenic effect of fatty acids and bile acids on large bowel mucosa, and calcium is antitropic to human colon. The role of intraluminal calcium in preventing colonic tumour formation was tested in 60 male Sprague-Dawley rats weighing 185±6±9±2 (SEM) given a six weeks course of azoxymethane 15 mg/kg/wk and then submitted to either an 80% jejunoileal resection, or simple transection and resuture of the bowel. Within each group half the animals had 24 g/l calcium lactate added to the drinking water. Twenty five weeks postoperatively the number of colonic tumours per animal was recorded. Among rats with transection calcium supplements more than halved tumour numbers from 4±3±1±0 to 1±8±0±8 (p<0.02). As expected jejunoileal resection increased tumour yield - by 65% in rats drinking normal water (p<0.05), and 105% in the animals with added calcium (p<0.05 - but again calcium reduced the number of tumours from 6±9±1±0 to 3±7±1±2, a fall of 46% (p<0.02). Increased dietary levels of calcium tend to blunt the carcinogenic effect of massive enterectomy, conceivably by binding tropic substances such as bile acids. Calcium protects against...
the development of colorectal neoplasia and this may be important in man.

T75

Value of screening postcholecystectomy patients for colorectal neoplasia

R J MOOREHEAD, J O M MILLS, H K WILSON, AND S T D MCKELVEY (Department of Surgery, The Queen's University of Belfast, and Department of Radiology, Royal Victoria Hospital, Belfast, and Ulster Hospital, Dundonald) Cholecystectomy may increase the risk of developing colorectal adenoma and carcinoma. Patients over 60 years of age who have undergone cholecystectomy more than 10 years previously are thought to be particularly at risk.

We are undertaking a prospective study of 100 patients to determine the incidence of colorectal neoplasia a decade after cholecystectomy. To date 84 patients (mean age 68.4±6.4 years, men 28, women 56) have been investigated by sigmoidoscopy and barium enema examination. The interval since cholecystectomy was a mean of 12.8±SD 4-2 years. Control observations were made on 84 age and sex matched subjects undergoing hospital and non-hospital postmortem examination.

Thirteen postcholecystectomy patients had tumours (nine with adenomas >1 cm, four with carcinoma). In the control group three had adenomas >1 cm and none had carcinoma. The difference is statistically significant (p<0.05 (χ² test).

The results to date confirm that cholecystectomy increases the risk of developing colorectal neoplasia. Further studies are needed to determine if younger patients and those with shorter postoperative intervals are at similar risk. Surveillance for large bowel tumours is indicated in older postcholecystectomy patients.

T76

Tumour cell DNA content as an indication of early recurrence in colorectal cancer

N C ARMITAGE, K C BALLANTYNE, JUDITH WRIGHT, AND J D HARDCASTLE (Department of Surgery, University Hospital Nottingham) Tumour cell DNA content as measured in paraffin embedded material has been shown to influence the survival of patients with colorectal cancer, independent of pathological stage and histological grade. We have measured prospectively tumour cell DNA content in both fresh and paraffin embedded material in 109 patients with one or three years follow up.

DNA content was measured by flow cytometry on disaggregated tumour samples using ethidium bromide/mithramycin (E/M) for fresh, and diamidino phenyl indole hydrochloride (DAPI) for paraffin embedded material. There was 89/110 (81%) agreement between the two methods with DAPI more accurate in identifying abnormal cell populations.

Fifty seven (52%) tumours had an abnormal DNA content – 52 (47%) aneuploid, five (5%) tetraploid. There was no relationship with pathological stage or histological grade. Of 59 patients whose tumours had no evidence of metastasis (Dukes' stages A and B 11 (19%) have developed local or distant recurrence – 8/27 (30%) aneuploid, 0/4 tetraploid and 3/28 (11%) diploid tumours.

Prospective measurement gives a similar proportion of tumours with abnormal DNA content as found retrospectively. Patients undergoing potentially curative surgery with aneuploid tumours appear to have an increased risk of developing early recurrence.

T77

Can DNA ploidy be estimated histologically in colorectal adenocarcinomas?

J T KENT, J S LOWE, N C ARMITAGE, K C BALLANTYNE, AND J D HARDCASTLE (Department of Surgery and Department of Pathology, University Hospital, Nottingham) Subjective histological grading of colorectal carcinomas is not a powerful indicator of patient survival. Tumour cell DNA content (ploidy) has been shown to be of independent prognostic value, but flow cytometry is limited in application to specialist centres. Using computer aided morphometry, the mean nuclear profile area (300 nuclei) was measured in 51 moderately differentiated stage B colorectal carcinomas.

The results were compared with the evaluation of DNA ploidy made by flow cytometry. Twenty six (51%) of the tumours were DNA aneuploid. The mean nuclear profile area for the aneuploid tumours was 62.9 μm² compared with 48.3 μm² for the diploid (p<0.00011, t=-7.4, 49 dof). The mean nuclear profile area was found to be greater than 53.5 μm² in 24 (92%) of the aneuploid tumours, but only four (16%) of the diploid.

A simple algorithm was constructed from these findings to estimate DNA ploidy at routine histology. Nuclear size was determined using an eyepiece graticule, and DNA ploidy was correctly estimated in 38/51 (74%) of the tumours. Tumour ploidy is related to tumour size, and this simple histological technique may distinguish aneuploid tumours with improvement of subjective grading.

T78-80

OESOPHAGUS

T78

Effects of ranitidine and of sleeping posture on symptoms and endoscopic appearances in patients with severe peptic oesophagitis

C GORDON, N HADDLEY, D LONG, R MACPHERSON, B BEATS, AND R F HARVEY (Gastroenterology Unit, Frenchay Hospital, Bristol) After an initial symptomatic assessment and oesophagoscopy, 71 patients (43 men and 28 women) with gastro-oesophageal reflux and severe peptic oesophagitis (defined as ulceration with slough formation) were entered into a double blind trial of ranitidine 150 mg twice daily or placebo for a period of six weeks. The effect of elevation of the bed on the 20 cm blocks was tested separately by randomly allocating 36 of the 71 patients to this therapy, irrespective of whether they were on ranitidine or placebo.

Thus there were four groups of patients (placebo, flat; placebo, blocks; ranitidine, flat; ranitidine, blocks). In these groups, symptoms improved overall in 26-6, 58-8, 76-5 and 86-7% respectively, and healing of more than half the ulcerated area was seen in 46-2, 76-5, 70-6 and 93-3% respectively. All symptoms studied (retrosternal and epigastric pain, reflux and dysphagia) were significantly improved by ranitidine, as were endoscopic appearances. The additional beneficial effect of elevation of the head of the bed, independent of the effect of ranitidine, was statistically significant for all symptoms except dysphagia.

We conclude that: (1) ranitidine improves the symptoms and promotes healing of severe reflux oesophagitis. (2) Elevation of the head of the bed is beneficial in severe reflux oesophagitis. (3) These two effects are independent and complementary.
T79
Arterial vascularisation of the oesophagus
D LIEBERMANN-MEFFERT, U NEFF, U LUSCHER, AND M ALLGOWER (Kantonsspital, Department Chirurgie, Spitalstrasse 21 Basel, Switzerland 4031; Creighton University, Omaha, Nebraska, USA) Blunt cervico-oesophagectomy, an increasingly used operation for oesophageal cancer, caused only exceptional mediastinal bleeding. The oesophageal blood supply was studied in 16 human cadavers by injecting plastic compounds into the Aorta. Three-dimensional corrosion casts showed: (1) the proximal third of the oesophagus was well supplied by pairs of arteries branching from the inferior thyroid artery and by a bunch of small tracheo-oesophageal arteries arising from the aortic arch. (2) The middle oesophagus, a 16 to 24 cm long section, was supplied by only one and rarely two unpaired small arteries arising directly from the thoracic aorta. This area was mainly supplied by minute collaterals coming from the proximal and distal oesophagus and located in the submucosa. (3) The distal oesophagus and cardia were well supplied by a number of branches originating from the left gastric and splenic arteries. Phrenic arteries did not supply the oesophagus and intercostal branches only twice. The poor extraparial blood supply to the thoracic oesophagus explains why ‘blunt oesophageal dissection’ in smaller oesophageal tumours caused no mediastinal bleeding and why oesophageal anastomotic leak is frequent.

T80
Oesophageal ulcers associated with doxycycline therapy
SAEED ADIB-BAGHERI (INTRODUCED BY R E POUNDER) (Gastroenterologist, PO Box: 71345–1443, Shiraz, Iran) Over a period of 16 months, 56 patients, 41 women and 15 men, aged 17–47 years developed retrosternal burning pain and odynophagia after taking doxycycline hyclate. The drug was used mainly for pelvic inflammatory disease, upper respiratory, urinary tract, and skin infections. Hundred milligram blue capsules in majority of patients taken twice a day, the last dose, before retiring and usually with less than a glass of water. Within one to seven hours after one of the evening doses the patients woke up with severe low or midretrosternal burning pain made worse on swallowing saliva, taking liquid, or solid food. In most patients odynophagia lasted for four to six days, but dysphagia persisted for another three to four days. In all patients symptoms disappeared within eight to 14 days.

Oesophagoscopy carried out in 35 of these patients showed; large serpiginous, single or multiple ulcers involving part or the whole circumference of the mucosa. Ulcers, usually 22–26 cm from incisors and for a length of 3–8 cm were biopsied. Histologic examination of ulcer margins showed; basal cell hyperplasia and spongiosis of the squamous cells, but acute inflammatory cell infiltration and necrosis were present in ulcer bases. Ten of these patients underwent repeat endoscopy three to four weeks after their initial examination and no trace of lesions could be found. None of these patients had history for reflux or previous history of dysphagia, and none developed symptoms after taking morning medication. A video tape of the ulcers, and after improvement at endoscopy is available.

T81
Mucosal permeability to sugars in vitro in coeliac and Crohn’s disease
D J DAWSON, A M DUNNE, R W LOBLEY, J NOTMAN, M MAHON, AND R HOLMES (University Department of Gastroenterology, Manchester Royal Infirmary and Department of Anatomy, University of Manchester, Manchester) To differentiate surface area effects from mucosal permeability changes we have studied the total uptake, mucosal permeation and mucosal permeability (permeation corrected for surface area) of mannitol and raffinose in jejunal biopsies from controls (n=48), coeliac in relapse (13) and remission (11), and patients with small intestinal Crohn’s disease (12).

In coeliaics in relapse, mannitol permeation was reduced vs controls (median 0.59 vs 0.90 μl/mg dry wt, p=0.0006), raffinose permeation was increased (0.51 vs 0.31, p=0.009) and permeability to both sugars was increased (mannitol 2.54 vs 1.21, p=0.009; raffinose 2.38 vs 0.5, p=0.0001). In coeliaics in complete remission, permeation and permeability for raffinose but not mannitol remained abnormal (raffinose permeation 0.38, p=0.04; permeability 0.72, p=0.02). In Crohn’s disease, mannitol permeation was reduced (0.69, p=0.02) but raffinose was unchanged. Permeabilities to both sugars were normal.

The results are compatible with transcellular uptake of mannitol (surface area-dependent) and paracellular uptake of raffinose (surface area-independent).

We conclude (1) transcellular uptake is reduced in untreated coeliac disease and returns to normal on treatment; (2) paracellular uptake of both sugars is increased in untreated coeliac disease and may remain abnormal following treatment; (3) in Crohn’s disease only the transcellular route is affected.

T82
Increased rates of spinal trabecular bone loss in patients with inflammatory bowel disease
R MOTLEY, E O CRAWLEY, W D EVANS, C EVANS, J RHODES, AND J E COMPSTON (Departments of Gastroenterology, Pathology and Medical Physics, University Hospital of Wales and University of Wales College of Medicine, Cardiff, Glam) Low bone mineral content (BMC) in spinal trabecular bone and cortical bone in the radius has been demonstrated in approximately one third of patients with inflammatory bowel disease (IBD). We have carried out repeat measurements of BMC after one year to determine the rate of bone loss in these patients. Bone mineral content was measured in spinal trabecular bone by quantitative computerised tomography and a cortical radial bone by single photon absorptiometry. The reproducibility of both methods is 2–3%.

Twenty seven patients (15 women) aged 23–78 years were studied. In 18 patients, changes in spinal trabecular BMC were similar to those observed in controls: however, nine patients, four men, aged 23–73 years (mean 41) showed accelerated rates of bone loss ranging from 8–50% of the initial BMC (mean 27%). All but two of these had received steroids over the preceding year; seven of the nine patients had small bowel IBD with resection. Only one patient showed an increased rate of cortical bone loss at the radial site.

Our results show rapid spinal trabecular bone loss over a relatively short period of time in some patients with IBD and suggest that steroid therapy may be an important contributory factor. Further studies are...
required to identify patients at risk and establish effective prophylaxis.

T83  
Transport of bile salts (BS) by enteric and non-enteric microorganisms and their effect on growth  
C E W HALLIDAY, O D PREDLAC, C CLARK, AND M J G FARTHING (Department of Gastroenterology, St Bartholomew's Hospital, West Smithfield, London) We have shown previously that BS stimulate growth of Giardia and are taken up by an energy dependent, saturable process. The aims of this study were to determine (1) if BS are actively transported by Giardia and (2) whether BS uptake and the effects of BS on growth are specific to Giardia. To determine the intracellular concentration of BS, intracellular volume of Giardia was estimated by [14C]-urea diffusion. The effect of BS on growth of Giardia, Trichomonas vaginalis and E coli was assessed. Kinetics of BS uptake were determined with sodium glycocholate (GC) (0-1-5 mmol/l) and tracer [14C]-GC. Intracellular volume of Giardia was 1-85±0-25×10^{-14} l. Uptake of GC from 2 mmol/l GC was 17-9±0-9 mmol/10^9 trophozoites/30 min. The calculated intracellular concentration was 9-7 mmol/l, suggesting that GC was actively transported against a five-fold concentration gradient. Ox bile stimulated growth of Giardia, inhibited Trichomonas but had no effect on E coli. Glycocholate uptake by Trichomonas and E coli was a saturable process. (Trichomonas Km 5-19 mmol/l, Vmax 4-10 nmol/mg protein/30 min; E coli Km 0-154 mmol/l, Vmax 0-24 nmol/mg protein/30 min) but was substantially less than uptake by Giardia (Km 1-11 mmol/l, Vmax 18-04 nmol/mg protein/30 min) (4-75 times). Thus BS stimulate growth and are actively taken up by Giardia, but the biological relevance of intracellular BS accumulation remains to be determined.

T84  
Episodic nature canine terminal ileal emptying  
R C SPILLER, M L BROWN, AND S F PHILLIPS (Gastroenterology Unit, Mayo Clinic, Rochester, Min, USA) The effect of previously described patterns of terminal ileal motility have been quantified in the present study by means of gamma-scintigraphy. 0-3 mCi of 99mTc DTPA was injected via an ileal cannula 50 cm from the ileocolonic junction (I-CJ) at the following times (all in duplicate): (a) during phase I of the interdigestive myoelectric cycle (IDMEC), (b) 10 min before a 400 kcal meal, (c) two hours postcibal (pc), and (d) four hours pc. Gamma scans were obtained every 4 min while simultaneous myoelectric activity was recorded from serosal electrodes. During phase I of the IDMEC isotope remained immobile while migration of phase III down the study segment was associated with sudden movements, boluses of isotope entering the colon when phase III was 12±9 cm from the I-CJ. Phase III occurred every 113±7 min (mean±SEM) and cleared 48±7% of ileal isotope into the colon. The time for 50% of isotope to enter the fasting colon (T50) was 111±11 min (n=6). Postprandially colonic filling was similarly episodic; some boluses (six of 27) were associated with discrete clustered contractions but most (17/27) occurred during irregular phase II-like concentrations. Immediately after eating (study B) ileal activity rose transiently in six of 10 studies but T50 was increased to 207±16 min (p<0.02). T50 at four hour pc was 91±31 min (n=8), significantly shorter than at two hour pc, 162±25 min (n=8) or study B (both p<0.01). We conclude that episodic fasting ileal emptying is clearly related to the IDMEC, postprandially emptying is also episodic but less clearly related to propulsive motor patterns.

T85  
Orocaecal transit time in health and in thyroid disease  
M V TOBIN, R A FISKEN, R T DIGGORY, A I MORRIS, AND I T GILMORE (Gastroenterology Unit, Royal Liverpool Hospital, Liverpool) The lactulose H2 breath test is a simple, non-invasive method of determining the oro-caecal transit time (OCTT) but its reproducibility and clinical application remain uncertain. After assessing its reproducibility by duplicate studies in 12 normal subjects using lactulose 30 g in a liquid meal, we studied OCTT in 17 patients with thyrotoxicosis, 14 of whom were retested after being rendered euthyroid, and in six patients with myxoedema, four of whom were repeated after replacement therapy. The mean OCTT in controls was 86-7±15-9 (mean±SEM) minutes and after four weeks, 84-1±11-9 mins. The mean coefficient of variation for transit time within individuals was 8-6±3-0 (range 0-28%). Hyperthyroid patients had a transit time significantly faster than controls, 51-1±4-4 minutes p<0.01, but after treatment returned to normal (82-0±7-0 min). In six patients with hypothyroidism the OCTT was 96-7±13-3 mins, and in four retested after thyroxine replacement it did not change. Our results show that the OCTT (1) measured by this breath test is reproducible, (2) is significantly faster than normal in thyrotoxicosis and approaches normal after treatment and (3) in hypothyroid patients is similar to controls. It is likely that in thyrotoxicosis but not in myxoedema the OCTT is a major factor in the disturbed bowel habit.

T86  
Critical rise in breath hydrogen in evaluation of intestinal transit  
F C CAMPBELL AND A CUSCHIERI (Department of Surgery, Ninewells Hospital and Medical School, Dundee) The hydrogen [H2] breath test of intestinal transit relies on caecal fermentation of an ingested non-absorbable saccharide with liberation of H2 which is absorbed and exhaled in breath. There is no uniform 'critical rise' in breath H2 although values of three or 10 parts per million (ppm) have been suggested. This study investigates test reliability according to the level of 'critical rise'. Fasting sample variation and correlation with disease state have been considered. In 26 healthy volunteers and 43 patients with symptomatic diarrhoea (21 postgastrectomy syndrome, 12 visceral autonomic neuropathy, 10 irritable bowel syndrome) multiple fasting breath samples were taken before a liquid test meal of 10 g isotonic lactulose. Breath samples were taken at 10 minute intervals afterwards for up to six hours. Fasting variation increased in proportion with initial fasting H2 value (Kendall au=0-42; p<0-001). Variation between fasting samples exceeded 3 ppm in 15 of 35 subjects with initial fasting H2 >9 ppm. No differences of transit time were observed between patients and volunteers with a critical rise of 3 ppm. A rise of 10 ppm distinguished the two groups, with shorter transit times in the patients (p<0-01 Mann Whitney). We conclude that a critical rise of 3 ppm is inadequate to overcome fasting H2 breath variation and has poor correlation with disease state. A minimum rise or 10 ppm is suggested.
Is TPN related hepatobiliary dysfunction secondary to deprivation of enteral stimulation

W P Morgan, P Truskeit, M Rose, and J M Ham (Departments of Surgery, Royal Hallamshire Hospital, Sheffield and Prince of Wales Hospital, Sydney, NSW) We have previously reported a model of TPN in the pig, in which cholestasis and gall bladder ‘sludge’ occurred. The present study was to determine whether the administration of TPN by methods causing enteral stimulation altered those findings. Intravenous, intragastric and intravenous plus cholecystokinin infusions of TPN were administered to young pigs. Their effect upon bile flow, bile salt excretion, liver histology, the character of gall bladder bile and the lithogenic index of hepatic duct bile was compared with controls. Bile flow and salt excretion were assessed by their response to sequential intraportal infusions of taurocholic acid (TCA) and secretin. The pattern and magnitude of the bile flow and salt excretion responses to TCA differed in the TPN groups compared to controls, but not to one another. Regression analysis of the relationship between bile flow and bile salt excretion suggested that the bile salt independent fraction of canalicular flow was significantly less in all three TPN groups compared with controls. Gall bladder bile was normal in controls but viscid and particulate in the majority of TPN pigs. The livers of the TPN animals showed marked centrilobular fatty infiltration. The lithogenic indices of hepatic duct bile were low in all groups. We have failed to show enteral stimulation alters hepatobiliary dysfunction in TPN.

Plasma prednisolone concentrations after oral administration in inflammatory bowel disease: correlation with anatomic extent and therapeutic efficacy

C A Rodrigues, E M Nabi, C Spiliadis, P B McIntyre, V Phongsathom, J E Lennard-Jones, A Rosen, and M J Willoughby (St Mark’s Hospital, London, King’s College, London and Lister Hospital, Stevenage, Herts) Prednisolone absorption was studied after a 20 mg oral dose, given as uncoated tablets, in 13 normal subjects (five women, eight men), eight patients with ulcerative colitis, and 21 patients with various types of Crohn’s disease, all receiving prednisolone therapy. Normal subjects showed a peak plasma level (PPL) of 285±4 SE ng/ml, a time to peak (TTP) of 105±2 minutes, and an area under the curve (AUC) of 1389±11. Corresponding values in the various disease categories (significance of differences from normal) were as follows: Ulcerative colitis: PPL 343±11 ng/ml (NS), TTP=209±11 minutes (p<0.05), AUC=1422±31 (NS). Colonic or ileocolic Crohn’s (n=6): PPL=335±23 ng/ml (NS), TTP=205±10.5 minutes (p<0.05), AUC=1546±90 (NS). Terminal ileal Crohn’s, including anastomotic recurrence (n=5): PPL=312±13 ng/ml (NS), TTP=183±3 minutes (p<0.05), AUC=1368±22 (NS). Jejunoileal or extensive ileal Crohn’s disease (n=10, six with previous resection): PPL=255±10.5 ng/ml (NS), TTP=220±12 minutes (p<0.05), AUC=1216±22 (p<0.05). Patients with extensive small bowel disease had a significantly lower PPL (p<0.05), and AUC (p<0.05) than the other patient groups. These results show delayed prednisolone absorption in all patient groups, and that decreased absorption is confined to patients with extensive small bowel Crohn’s disease. In eight patients with steroid dependent disease, similar absorption studies were done, with the minimum dose required to maintain remission. Despite variation in this dose between patients, the plasma prednisolone levels obtained were similar in all patients, and about half those obtained with a 20 mg dose.

Double blind controlled comparison of balsalazide and sulphasalazine in maintenance therapy of patients with ulcerative colitis

P B McIntyre, C A Rodrigues, J E Lennard-Jones, J G Barrison, J G Walker, and J H Baron (St Mark’s, St Mary’s, and St Charles’ Hospital, London) Balsalazide (BSZ) is a pro-drug which releases 5-aminosalicylic acid (SASA) and 4-aminobenzoylalanine (an inert carrier) in the intestine in man. Balsalazide was compared with sulphasalazine (SSZ) (both 1 g bd orally) in the maintenance in remission of patients with ulcerative colitis (UC). Seventy-five patients (51 men, 24 women) mean age 43 yr (range 19-79 yr) with UC were randomly allocated to either treatment (41BSZ, 34SSZ) for six months. The groups were similar in respect of age, sex, smoking, duration and extent of disease. Four patients defaulted (2BSZ, 2SSZ) leaving 39 on BSZ and 32 on SSZ for analysis. Two other patients on SSZ withdrew with side-effects. Remission rates at six months (59% (95% CI 42-74%) BSZ, 73% (95% CI 54-88%) SSZ) were not significantly different (χ²=1.0, p>0.05). Seventeen patients previously experienced minor side-effects from SSZ. Nine of 32 patients on SSZ and three of 39 on BSZ
reported side effects in this study (p=0.048 Fisher’s exact test). One patient with a skin eruption on SSZ did not react subsequently to open BSZ. Mean haemoglobin concentrations, similar on entry, increased after six months with BSZ (0.2 g/dl) but decreased with SSZ (0.5 g/dl) (p<0.001). Balsalazide may be as effective as SSZ in the maintenance of UC in remission and has fewer side effects.

T91
Reversal of sulphasalazine induced seminal abnormalities after substitution with 5-ASA (Mesalazine)
S RILEY, V MANI, M GOODMAN, B MANDAL, AND L A TURNBERG (University Department of Medicine, Hope Hospital, Salford and Leigh Infirmary, Bury General, Mossall Hospital, Manchester) Seminal abnormalities are commonly found during sulphasalazine (SZP) treatment. Although these changes are reversible after withdrawal of the drug this may result in disease relapse. Animal studies suggest that 5-ASA, the active component of SZP, does not impair fertility.

We have studied 16 patients with chronic ulcerative colitis in clinical remission taking 2–3 g SZP daily. Each patient produced three samples of semen at weekly intervals and of the 48 samples analysed 40% showed oligospermia, 40% an increased number of abnormal forms and 90% impaired motility.

Eight patients substituted enteric coated 5-ASA (Mesalazine) for SZP (dose equivalence 400 mg 5-ASA=1 g SZP) for a minimum period of three months. One patient developed a salmonella associated colitis relapse while the others remained well. Improvement in sperm count (p<0.05), motility (p<0.02) and morphology (p<0.02) occurred in all cases.

Suboptimal improvement of motility prompted re-evaluation in two patients after 12 months 5-ASA and in these further improvement occurred. These studies demonstrate that treatment with 5-ASA allows the recovery of seminal abnormalities induced by SZP in patients with colitis.

T92
Clostridium difficile (CD) and ulcerative colitis (UC)
D A BURKE AND A R AXON (Gastroenterology Unit, The General Infirmary, Leeds)

Clostridium difficile has been implicated in relapse of UC. Controversy exists, however, over the diagnostic and therapeutic implications for its role in UC. Sixty two of 77 patients (42 men, 35 women age 19–75 years) with UC in relapse were able to provide stool before treatment and within 12 hours of attending hospital. One patient with typical pseudomembranous colitis after antibiotics was not included. Four had received antibiotics other than sulphasalazine (SS) before the onset of their symptoms. Thirty five were taking SS. One patient was culture positive, toxin negative, after antibiotics; another with detectable toxin (one in two) but culture negative had not received antibiotics. Six with no initial stool sample were CD culture negative during treatment. Fifty seven (25 in patients) were assayed during their treatment period; two had received antibiotics and became culture positive, but toxin negative, the remainder were all negative. Three patients required emergency colectomy, all of whom were CD negative initially. By undertaking culture and toxin assay before treatment and any significant hospital exposure, this study shows that CD is not a cause of relapse in UC and is not secondarily acquired during relapse unless exposed to antibiotics. SS does not predispose to acquisition of CD. There is no role for routine screening or treatment of CD in UC.

T93–104

Diet and the Gut

T93
Effect of chilli ingestion on the gastro-duodenal mucosa
J Y KANG, I YAP, AND T C LIM (Department of Medicine, National University of Singapore and the Department of Medicine III, Singapore General Hospital, Singapore) Chilli ingestion may lead to dyspepsia. The aim of the present study was to determine whether acute ingestion of chilli causes macroscopic gastro-duodenal mucosal damage. Eighteen healthy male subjects were studied after a normal control endoscopy one week previously. By random allocation, six subjects took 20 g ground dried chilli (Capsicum annuum), another six 2 tablets of aspirin 300 mg each, while the last six acted as controls. Endoscopy was done six hours later by two endoscopists simultaneously using the lecture scope. The endoscopists were unaware of which group each subject was in and recorded their results independently. The gastric body, gastric antrum, duodenal bulb and duodenal second part were assessed as follows: normal – 0; erythematous patches or streaks – 1, haemorrhages – 2, and erosions – 3. For each subject, the four grades were added to give a composite score. There was 95% agreement between the two endoscopists. The total scores for each of the three groups were: chilli – 2; aspirin – 3; control – 4. Chilli vs aspirin – p<0.01 by the Wilcoxon’s rank sum test; aspirin vs control – p<0.01; chilli vs control – not significant. All six subjects who took chilli reported nausea while five experienced abdominal discomfort. One of the six subjects who took aspirin experienced abdominal discomfort. We conclude that although chilli ingestion is associated with gastrointestinal symptoms, it does not lead to macroscopic gastroduodenal mucosal damage.

T94
Somatostatin analogue (SMS 201–995) inhibits early rapid gastric emptying after truncal vagotomy and drainage
N PARR, S GRIME, S A JENKINS, M CRITCHLEY, J BAXTER, AND C MACKIE (Departments of Surgery and Nuclear Medicine, University of Liverpool and Royal Liverpool Hospital, Liverpool) Somatostatin infusion, while improving symptoms of early dumping in patients, has been reported to accelerate gastric emptying (GE) of liquids in healthy volunteers. We have investigated the effects of a long acting analogue of somatostatin, SMS 201–995, on GE in five dogs after truncal vagotomy and pyloroplasty and in four patients suffering from dumping or diarrhoea after truncal vagotomy with drainage.

Gastric emptying was assessed using gamma camera imaging of 15% dextrose labelled with 99mTc-DTPA. Studies were done with and without prior administration of SMS 201–995 (0.05 mg SC). Each animal study was duplicated.

In both dogs and patients GE without prior administration of SMS 201–995 was biphasic with an early rapid component. Gastric emptying at 10 min was 35±6% (mean±SEM) for dogs and 84±5% for patients. Administration of SMS 201–995 significantly inhibited GE during this period, being 12±3% for dogs (p<0.02; Student’s paired t test) and 44±10% for
patients (p<0.05). By the end of the test period, however, (dogs – 60 min, patients – 30 min) the differences in GE between studies with and without SMS 201–955 administration were not significant (dogs: with=25.5±%, without=35±%; patients: with=62±14%, without=88±6%). These results show that SMS 201–955 inhibited rapid early GE of liquids after truncal vagotomy. Inhibition of this magnitude has not previously been achieved, except by revisional surgery.

T95
Blood glucose, plasma motilin and gastric emptying

S I GRAINGER, J SCOBIE, J PETRANYI, J J GAUNT, AND R P H THOMPSON (Gastrointestinal Laboratory, The Rayne Institute, St Thomas’ Hospital, London) Gastric motility is enhanced by hypoglycaemia and diminished by hyperglycaemia; the mechanism might be because of altered levels of peptides that modulate motor activity of the gut.

We have measured plasma motilin and gastric emptying of radiolabelled poached egg white twice in eight diabetic patients on different days at blood glucose levels of 3 and 11 mmol/l, maintained by dextrose/insulin infusion for at least two hours. Vagal tone was assessed from heart rate variations during deep breathing and plasma motilin was measured immediately before the labelled meal.

Vagal tone was unaffected by blood glucose level. At the lower level, however, gastric transit was faster in every patient (median area under emptying curve 5360 vs 5639, p<0.01), chiefly because of the shorter gastric lag times (median 23 vs 34 min, p<0.10). Plasma motilin levels tended to be higher (mean (SE) 28 (9) vs 16 (4) pmol/l, p=0.08).

Therefore ambient blood glucose concentration influences gastric transit of food and may thus regulate food intake. General changes in vagal tone are not involved; changes in motilin level may be causal or simply secondarily reflect enhanced gastroduodenal motility.

T96
Postvagotomy diarrhoea is more than gastric incontinence

S A RAHES, V SMIRIOTIS, T HAWKINS, C W VENABLES, AND J D A JOHNSTON (University Department of Surgery and Freeman Hos-
pital Medical Physics Department, Newcastle upon Tyne) It is generally believed that postvagotomy diarrhoea is caused by gastric incontinence. This is based on the results of intubation studies and outdated radioisotope techniques which may have underestimated the early emptying phase. We have re-investigated this hypothesis using a computerised gamma camera system to measure emptying of a 50% glucose drink. Plasma volume changes (haematocrit method) were also measured. Fifteen patients 3+ years after truncal vagotomy and pyloroplasty were studied, divided into two distinct clinical groups – seven with postvagotomy diarrhoea (A) and eight without (B).

The drink provocated diarrhoea attacks in seven of seven in group A but only one in eight in group B (p<0.001). Early gastric emptying was rapid in both groups (median T1/2: 6 minutes vs 8.8 minutes; p=NS). Six of seven in group A and six of eight in group B emptied more than half of the glucose within 10 minutes (p=NS). The maximum fall in plasma volume was greater in group A (median fall: 13% vs 8%; p<0.01). This fall did not correlate significantly with any parameter of gastric emptying. We conclude that gastric incontinence does not necessarily lead to diarrhoea. These results suggest that therapy should be aimed at reducing fluid shift into the intestine rather than attempting to slow gastric emptying.

T97
Expression of class II antigens in coeliac jejunal mucosa

A M P MONTGOMERY, C NAVARRETE, AND P J KUMAR (Department of Gastroenterology, St Bartholomew’s Hospital and Department of Immunology, The London Hospital, London) Class II antigens have distinct functions in immunoregulation (DR in stimulation, DO in suppression), whilst their expression on non-immunological cells has implications for antigen presentation and autoimmunity. These functions suggest a role for these antigens in the immunopathogenesis of coeliac disease. Serial sections of jejunal mucosa from controls (six), treated coeliacs (six) and untreated coeliacs (six) were used in three stage immunoperoxidase techniques using new monoclonal antibodies to DR and DO and mononclonals to DR and T-cell subsets. In controls and treated coeliacs villous enterocytes were DR negative (DO ), weakly DP positive (DP’) and strongly DR’ but in untreated coeliacs were strongly positive for all antigens. Crypt enterocytes were DO and DP’ and weakly DR’ in controls and treated coeliacs, but strongly DR’ and weakly DP’ in untreated coeliacs. The intensity and extent of distribution was DR’>DP’>DO. Intra-epithelial lymphocytes (IELs) were negative for class II antigens in controls and treated coeliacs with a Tc’/Tc ratio of 2:3. In untreated patients >80% of IELs were DR’ DP’ with a Tc’/Tc ratio of 1:1.

In conclusion, untreated patients have increased class II expression on enterocytes and IELs. This has implications for gluten presentation, in vivo activation (only activated T-cells express class II) and autoimmunity.

T98
Mucosal permeability to gluten is normal in treated coeliac disease

D J DAWSON, A M DUNNE, R W LOBLEY, J NOTMAN, M MAHON, P M RAWCLIFFE, AND R HOLMES (University Department of Gastroenterology, Manchester Royal Infirmary and Department of Anatomy, University of Manchester, Manchester) Abnormal intestinal permeability to gluten may be implicated in the aetiology of coeliac disease. We have measured the 10 minute uptake and mucosal permeation of 3H-labelled peptic tryptic fragments of gluten and bovine serum albumin (BSA) into jejunal biopsies from treated coeliac patients (n=9) and controls (n=11). The acute effects of the proteins on sugar permeability were also measured. Peptic hydrolysis during incubation was inhibited by a combination of aprotinin, bestatin, and captopril.

Mucosal permeation of gluten was greater than that of BSA in controls [median (IQR) 0.46±0.39, range 0.20–0.88] vs 0.48±0.39, range 0.20–0.84] but in coeliacs [0±0.29, range 0.02–0.68] and not in controls [0±0.29, range 0.02–0.68] vs 0.46±0.39, range 0.20–0.84]. Mucosal permeability to gluten (permeation corrected for mucosal surface area) was not significantly different from that for BSA in either group, but BSA permeability was increased in coeliacs (p<0.03). Neither gluten nor BSA had a significant effect on the permeation or mucosal permeability for mannitol or raffinose.

These results provide no support for abnormal peptide permeability or for a selective mucosal defect in gluten permeability in treated coeliac disease.
Gliadin has no acute effects on the permeability of other solutes in vitro.

T99
Coeliac disease and malignancy

M R LANE, P PRIOR G K T HOLMES, AND R N ALLAN (General Hospital, Birmingham)
The increased risk of malignancy in coeliac disease is now well accepted, whether this risk is reduced with the use of gluten free diets remains unknown. The long-term outcome among 210 patients studied in 1976 who presented with biopsy proven coeliac disease before 1973 has been reassessed. One hundred and eighty one (85%) have been followed up to 1985 or death, 63 patients have died (32%). There have been 38 examples of malignancy in 35 patients of whom three remain alive. There have been 14 lymphomas, 13 arising within the GI tract, but no further lymphomas have been diagnosed in the last 10 years, three oesophageal and four oesophageal carcinomas have occurred (two oesophageal) in the last 10 years. There have been no small bowel carcinomas. The increased risk of patients with coeliac disease developing GI lymphoma, and carcinoma of the oesophagus and oesophagus is confirmed. (Relative risks to be presented). The absence of any examples of new lymphoma in the last 10 years is a significant change in the pattern of malignancy and perhaps a consequence of the gluten free diet.

T100
Cellular hypersensitivity in coeliac disease to a synthetic dodecapeptide sequence from A-gliadin that resembles an early protein of human adenovirus 12

J A KARAGIANNIS, J D PRIDDLE, AND D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) A sequence analogy has been reported between a region (residues 206-217) from A-gliadin of Scout 66 wheat and the early protein Elb of human adenovirus type 12 (residues 384-395). Cross-reactivity was shown between Elb, A-gliadin and a synthetic heptapeptide comprising A-gliadin residues 211-217.

Cell mediated immunity to a peptide comprising A-gliadin residues 206-217, prepared by solid phase synthesis, was studied at 33, 11 and 5.5 µg/ml using a two-stage migration inhibition assay. Peripheral blood mononuclear cells were prepared from eight patients with coeliac disease in remission on a gluten free diet. Control studies were undertaken at 33 µg/ml using eight healthy controls matched for age and sex and a group of patients with inactive ulcerative colitis or Crohn’s disease who were not receiving immunosuppressive therapy. At 33 µg/ml the migration index (MI) was 0.74 (SD 0.09) for coeliacs compared with 0.97 (SD 0.12) for healthy controls (p<0.001). No significant difference was found between healthy controls and patients with inflammatory bowel disease (p>0.05). A dose response effect was seen in coeliacs. At 33 µg/ml MI was 0.74 (SD 0.09), at 11 µg/ml MI was 0.87 (SD 0.06, p<0.008 compared with 33 µg/ml) and at 5.5 µg/ml MI was 0.94 (SD 0.05, p<0.002 compared with 11 µg/ml).

This synthetic peptide elicits a cellular immune response in coeliac patients which appears to be disease specific.

T101
Influence of energy and nitrogen contents of enteral diets on nitrogen balance: a double blind prospective controlled clinical trial

R G P REES, T M COOPER, P G FROST, AND D B A SILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Although enteral nutrition is an accepted form of nutritional support, controlled trials have highlighted difficulties in achieving positive N balance in patients receiving ‘standard’ polymeric diets (1 kcal/ml, 5-6 N/l). In this prospective double blind controlled trial we investigated whether nitrogen balance can be improved by administering diets supplying higher energy density (1-5 kcal/ml) with either moderate or substantial increases in nitrogen. Forty three patients requiring nasogastric feeding were randomised to receive 2 l/d of one of three diets supplying the following total energy (kcal) and N (g): 2000 and 12-6 (gp I, n=13); 3000 and 15-6 (gp II, n=14); 3000 and 18-8 (gp III, n=16). Groups compared well for duration of feeding (gp I, 10-8±SD 6-2 d; gp II, 11-6±6-2; gp III, 11-9±6-6). There was no significant difference in average daily N balance between gps I (−4-0±9-8 g) and II (−1-8±7-2). In contrast, significantly better daily N balance was achieved in gp III (+1-6±5-6) compared with gps I (p<0.001) and II (p<0.003).

These findings confirm that in routine clinical practice, widely used ‘standard’ diets supply insufficient energy and nitrogen for positive N balance. Significantly better results cannot be achieved with more energy alone (1-5 kcal/ml), but also substantially more N (9-4 g/l) is required.

T102
Small intestinal response to ‘elemental’ and ‘complete’ liquid feeds

D G MAXTON, E U CYNK, AND R P H THOMPSON (Gastrointestinal Laboratory, The Rayne Institute, St Thomas’ Hospital, London) Liquid amino acid elemental diets may be effective in Crohn’s disease by producing bowel rest. Substitution with whole protein complete feeds would improve palatability and reduce cost. We therefore compared jejunal and ileal structure and ‘in vivo’ jejunal absorption in rats (n=7) fed isocoloric amounts of normal chow, a complete feed (ENSURE: ENS) and an elemental diet (Vivonex-HN:V). Animals fed V gained less weight than ENS or N (N 44±3.3, ENS 45±5.6 vs 90±19.9 g; mean±SEM, both p<0.005). ENS and V feeding increased jejunal total and mucosal weight above N (n=23±2.4 vs ENS 28.5±3.0, p<0.01, vs V 29.2±5.0, p<0.05 and N 10.3±0.4 vs ENS 12±1.9, p<0.02, vs V 11.8±2.0, p<NS mean±SEM mg/cm/100 g bw for total and mucosal weight respectively), with DNA and protein less so. Jejunal sugar absorption was also higher in ENS and V groups. Conversely, terminal ileal weight was reduced by ENS and partially V diets (N 18-2±3.0 vs ENS 13±1.4, p<0.05, vs V 11±1±8, p<0.001 mean±SEM, mg/cm/100 mg bw).

We conclude that both elemental and complete liquid diets increase proximal and reduce distal intestinal mass, but elemental feeds reduce ileal weight more profoundly. This property may be important for the therapeutic effect of elemental diets in inflammatory bowel disease, and is probably due to the availability of luminal nutrients.

T103
Bicarbonate in oral rehydration solutions (ORS): a double blind controlled trial in children with gastroenteritis in the United Kingdom

E J ELLIOTT, J A ARMISTEAD, M J G FARTHING, AND J A WALKER-SMITH (Academic Department of Child Health, Queen Elizabeth Hospital for Children, London and Department of Gastroenterology, St Bartholomew’s Hospital, London) Bicarbonate is added
to ORS for (i) correction of acidosis and (ii) promotion of sodium and water absorption. Nevertheless, there is little objective evidence to support its inclusion. Forty children aged 5 years old with acute gastroenteritis for < seven days were randomly allocated to receive either ORS containing bicarbonate (group I: Na 35, K 20, Cl 7, HCO₃⁻ 18, glucose 202 mmol/L, 312 mOsm/kg; British National Formulary) or an identical solution, except that bicarbonate was replaced by chloride (group II). Groups were matched for age, sex, ethnic origin, duration of diarrhea and nutritional status. On admission, degree of dehydration biochemical and haematological parameters were similar. Forty percent had viral and 20% bacterial pathogens. All children were successfully treated without complications. Oral rehydration solution intake by the groups was similar. Clinical outcome, as judged by speed of rehydration, stool frequency, duration of diarrhea and length of hospital stay was the same in both groups. After 24 hours of ORS there was no difference between groups I and II in serum bicarbonate (20.5±0.6 vs 19.6±0.6 mmol/L respectively), venous pH (7.38±0.02 vs 7.36±0.01), urea and electrolytes. Oral rehydration solution without bicarbonate was effective for rehydration and correction of acidosis in these children with gastroenteritis in the UK Exclusion of bicarbonate would simplify production, increase stability and reduce cost of ORS, without apparent impairment of efficacy.

**T 104**
Pharmacological manipulation of postoperative ileus: results of a placebo controlled double blind clinical trial

S A Sade, C Eriksen, C A Cranford Jr, and A Cuschieri (Department of Surgery, Ninewells Hospital and Medical School, Dundee) Postoperative ileus after abdominal surgery contributes to hypoaemia and chest infection, and may delay recovery after abdominal surgery. Attempts at pharmacological manipulation have included adrenergic blockade and cholineresterase inhibition. The synthetic peptide ceruletide has been shown to reduce postoperative intestinal paralysis. The effect of this agent on the postoperative course was investigated in a placebo controlled double blind randomised clinical trial involving 82 patients undergoing elective abdominal surgery.

On completion, 42 patients were found to have received ceruletide (Cer) as an iv infusion (2 ng/kg/min) and 40 patients placebo (P) infusion administered on the first postop day. The two groups were similar in respect of age, sex, operation, extent of bowel handling and serum electrolyte profile. Six patients in the Cer group and five patients in the P group passed flatus by the morning of the second postop day. Significantly more patients in the Cer group passed flatus on the second vs the third day (11/36, 5/26) when compared with the P group (5/35, 10/30) (χ² = 10.11, p<0.01). Significantly more patients in the P group complained of abdominal cramps on day 3 when compared with day 2 in the P group (16/29, 8/34) than in the Cer group (8/26, 11/36) (χ² = 5.62, p<0.02).

These results indicate that ceruletide enhances the return of peristaltic activity in patients with uncomplicated postoperative ileus.

**INFLAMMATORY BOWEL DISEASE**
**T 105**
Cardiff incidence of Crohn's disease continues to rise

J D Rose, J Rhodes, G Williams, G M Roberts, and J F Mayberry (University Hospital of Wales, Cardiff and City Hospital, Nottingham) The incidence of Crohn's disease in the City of Cardiff has been recorded from 1934 and has risen from 0.18/10⁵/year for the period 1931–35 to 4.92/10⁵/year for the period 1976–80; a total of 281 patients were identified between 1934 and 1980. From diagnostic records in the Departments of Pathology, Radiology, Outpatient Clinics and from the Area Health Authority 115 new patients with Crohn's disease resident within the City at the time of the diagnosis were identified between 1981–85. The individual yearly incidences/10⁵ of the population were 6-4 in 1981, 7-1 in '82, 9-3 in '83, 6-4 in '84 and 11-8 in '85 with a mean for the 5-year period of 8.2/10⁵/year.

Analysis of the distribution of disease at the time of diagnosis showed all forms were increasing. Of the 115 patients, 42 had ileocaecal disease, 43 ano-colo-rectal disease, six small bowel and 21 a combination of small and large bowel disease. This distribution of disease does not differ significantly from the previous quinquennial figures. The increase in disease at all sites suggests that the figures are not distorted by inclusion of patients who would previously have been labelled ulcerative colitis. The figures show that the incidence of Crohn's disease continues to rise and current values are among the highest recorded in the world literature.

**T 106**
Potentially pathogenic character of E coli (EC) in inflammatory bowel disease

D A Burke and T R Axon (Gastroenterology Unit, The General Infirmary, Leeds) Mucoosal adhesion is a virulence factor of pathogenic EC. Using the buccal epithelial cell adhesion assay, a quantitative assessment was made of the mannos-resistant adhesive property of EC isolates from 50 patients with ulcerative colitis in relapse (median buccal epithelial cell index=43%), nine in remission (30%), 13 with Crohn's disease (53%), 11 patients with infectious diarrhoea (14%) and 22 controls (4-5%). There is no significant difference between the buccal epithelial cell indices of colitides and both controls (p<0.0001) and those with infectious diarrhoea (p<0.00%). Similarly for the Crohn's patients. The median buccal epithelial cell index of the inflammatory bowel disease patient samples compares with the buccal epithelial cell index of 47% for the enteropathogenic EC ES5171.

The buccal epithelial cell assay offers a simple and rapid screening technique that differentiates between inflammatory bowel disease and control EC due to the expression of a potentially pathogenic characteristic in the EC of patients with inflammatory bowel disease. Eighty six per cent of patients with inflammatory bowel disease carry EC with a buccal epithelial cell index >25% compared with 0% controls.

This observation supports the hypothesis that EC have a role in the pathogenesis of inflammatory bowel disease.

**T 107**
Plasmid profiles in E coli isolated from IBD patients

M R Lane, P E Pease, and R N Allan (Department of Medicine Microbiology, Medical School, Birmingham and The Gastroenterology Unit, General Hospital, Birmingham) Plasmids, extrachromosomal DNA elements, found in bacteria mediate many functions including virulence. We have
examined plasmid profiles of *E. coli* from patients with inflammatory bowel disease to search for a putative ‘disease-related’ plasmid.

Forty-three isolates from 27 patients with ulcerative colitis (UC), 17 from 12 with Crohn’s disease (CD) were compared with 44 isolates from 25 control patients. Plasmids were extracted using alkaline lysis at 56°C, cellular protein precipitated with phenol and removed by centrifugation and the plasmids separated by electrophoresis in 0-7% agarose.

The average number of plasmids per isolate were controls (4-2), UC (3-12) and CD (2-35) (p<0-05). These reductions in plasmid number were due to significant loss of small plasmids (<3-6 Kb pairs). Within the UC group isolates from active colitis contained more plasmids than those with inactive disease (4-09 vs 2-09 p<0-05).

Sulphonamide resistance did not affect plasmid numbers, but did seem to account for the presence of plasmids common to several isolates. The increased number of plasmids found in active UC when compared with inactive UC supports the concept of plasmid mediated factors influencing the activity of ulcerative colitis.

T108
Colonic mucin subclass defect in ulcerative colitis: real or artefact?

M. Rhodes, N. Parker, P. Patel, and C. K. Ching (University Department of Medicine and Walton Hospital, Liverpool) It has been suggested that ulcerative colitis results from defective colonic mucus. Podolsky and Isselbacher recently reported a selective depletion of one of six mucin subclasses defined by discontinuous gradient ion-exchange chromatography of purified colonic mucus obtained from patients with ulcerative colitis in remission (Gastroenterology 1984; 87: 991-8). The significance of this finding depends on the interpretation of the ion-exchange chromatography.

We have analysed mucus obtained from colonic resection for carcinoma (n=6). Mucin was purified by homogenisation, centrifugation, Sepharose 4B gel filtration and caesium chloride density gradient centrifugation. Discontinuous gradient ion-exchange (DEAE cellulose and Pharmacia mono Q) with six salt steps yielded six mucin fractions but continuous gradient ion-exchange yielded only three major fractions. This shows that the six mucin subclasses previously reported are largely artefacts of the six salt steps used. Furthermore, comparison with ion-exchange chromatographs of highly purified bovine submaxillary mucin suggests that at least two of the six subclasses may not be mucins.

The previous findings may therefore simply reflect mucin depletion and further work is needed to elucidate colonic mucus glycoprotein abnormalities in ulcerative colitis.

T109
Can rectal biopsy distinguish acute self-limiting colitis from early inflammatory bowel disease

M. C. Allison, S. J. Hamilton-Dutoit, P. Dibollon, and R. E. Pounder (Academic Departments of Medicine and Histopathology, Royal Free Hospital School of Medicine, London) It can be hard to distinguish acute self-limiting colitis (ASLC) from inflammatory bowel disease (IBD) in a patient presenting for the first time with diarrhea and/or rectal bleeding. We identified 72 such patients who presented in one health district between 1978 and 1983, in whom biopsy of inflamed rectal mucosa had been performed. Follow up information was obtained for 64 patients of whom 37 had definite IBD. The other 27 had no further symptoms or treatment, and were considered to have had a single episode of ASLC. All original biopsies were evaluated blindly by two independent observers for the presence of eight criteria reported to be highly discriminant between ASLC and IBD. Crypt distortion and lymphocytic infiltration were commonly seen, but were only 75-80% predictive of IBD. Epithelial surface erosions, crypt atrophy or lymphoid aggregates beneath the crypts each had 82-90% specificity for IBD. Isolated basal giant cells or epithelioid granulomata, although present in only 11 biopsies, had 100% predictive value for IBD.

The discriminant features recorded in this study can distinguish ASLC from IBD in rectal biopsies from most new patients with colitis. Only the presence of basal giant cells or epithelioid granulomata, however, is diagnostic of IBD.

T110
The pill, smoking and inflammatory bowel disease – results from the Royal College of General Practitioners (RCGP) Oral Contraception Study

Richard F. A. Logan, Clifford R. Kay, and Louise Scott (Department of Community Medicine and Epidemiology, The University of Nottingham Medical School and the Royal College of General Practitioners, Manchester Research Unit, Manchester) Recent studies have suggested that contraceptive pill use is associated with a two to four-fold increased risk of Crohn's disease (CD) and Vesse et al. have also found a two-fold increased risk of ulcerative colitis (UC). We have examined prospectively collected data on pill use, smoking and the development of CD and UC available from the RCGP contraceptive study which has recorded all new morbidity occurring in 46,000 married women followed since 1968. After excluding 13 cases where the diagnosis was not confirmed CD had developed in 42 and UC in 78 women. Annual incidence of CD (10/100,000) and UC (19/100,000) were in keeping with expected figures. There were small increases in rates of both CD and UC in current pill users compared with non-users (Ratio of rates (RR)) for CD=1.6. p>0.05, RR for UC=1.5, p>0.05). Rates of CD and UC in ex-users were similar to never users. Analysed by smoking habit, recorded at entry, the incidence of CD was higher in smokers and that of UC lower. The incidence in non-smokers, smokers of <20/day and smokers of >20/day of CD was respectively 8, 13 and 18/100,000 and of UC respectively 22, 16, 13/100,000 – results consistent with previous studies of smoking in CD and UC. In this the largest study of pill users there were only small increases in risk of CD and UC in pill users which were not statistically significant and disappeared after stopping the pill.

T111
Mucosal T lymphocytes and HLA-DR expression in ulcerative colitis

I. K. Trejosiewicz, S. Badr-el-Din, D. J. Oakes, R. V. Healey, G. Janossy, and M. S. Losowsky (Department of Medicine, St. James’s University Hospital, Leeds and Academic Department of Immunology, Royal Free Hospital, London) Mucosal immunoregulatory T lymphocytes are thought to play a major role in ulcerative colitis (UC), although their subset distribution and relationship to MHC antigens has not been extensively studied. We have used double label immunofluorescence of cryostat sections of colonoscopy biopsies with combinations of monoclonal antibodies in 21 UC patients (10 with total
colitis) and 30 controls. Although large individual variations in both groups were observed, there were no statistically significant differences between patient and control groups in either intraepithelial or lamina propria compartments in terms of CD4:CD8 (T4:T8) ratio, nor of co-expression of CD5 (T1) antigen by CD4⁺ (T8 suppressor/cytotoxic) cells. However, there was increased expression of the CD7 (T2 ‘T blast’) antigen by CD4⁺ (T4 helper/inducer) cells in those patients where the epithelium was strongly positive for expression of MHC Class II antigens (HLA-DR and HLA-DQ). Moreover, whereas the epithelium of control patients was invariably negative for Class II antigens, in the majority (58%) of UC patients, the epithelium was strongly HLA-DR⁺ and HLA-DQ⁺, especially in patients with total colitis (87%), irrespective of treatment or duration of illness. Class I MHC antigens (HLA-A, B, C) were expressed apparently equally by enterocytes in UC and control groups. These data suggest that local immunostimulation of CD4⁺ helper/inducer cells may be linked to the possible antigen-presenting capabilities of MHC Class II⁺ enterocytes, especially in total colitis, and thereby result in the maintenance of the chronic inflammatory state.

T113
Predictive value of intraepithelial lymphocyte counts in childhood enteropathies

C J TAYLOR (Department of Child Health, Alder Hey Children’s Hospital, Liverpool)

Changes in intraepithelial lymphocyte (IEL) numbers have been found to correlate with active coeliac disease. If specific, IEL counts may be of value in childhood enteropathies, where subtotal or severe partial villous atrophy is not infective, especially with cow’s milk protein intolerance (CMPI) or after gastroenteritis. To evaluate the use of IEL counts a supervised gluten challenge was performed on 116 children initially diagnosed as coeliac on the basis of characteristic jejunal biopsy and an apparent response to gluten exclusion. Counts were performed by a single observer on routinely processed 4 μH&E sections. Results were expressed as IELs/100 enterocytes.

Forty nine per cent of patients failed to relapse on challenge with one late relapse on two year follow up. Reappraisal of these cases suggested alternate diagnoses, of which CMPI (16%) or post enteritis (20%) were the most common. Intraepithelial lymphocyte counts in confirmed coeliacs were high at diagnosis (67±16) (mean ±SD) fell on diet [28±15] and rose on challenge [64±20]. These changes were significant (p<0.01 using paired t test). Raised IEL counts at diagnosis were also found in patients with CMPI and giardiasis but a significant fall on diet only occurred in CMPI patients (p<0.05). Only patients showing mucosal relapse – that is, confirmed coeliacs, showed a significant increase in IELs post challenge compared with counts on a gluten free diet. While an increase in IELs showed good correlation with mucosal relapse on challenge a high count at diagnosis was of insufficient specificity to obviate the need for gluten challenge.

T114
Restorative proctocolectomy J pouch ileoanal anastomosis: a single surgeon’s experiences over two and a half years

M R B KEGHLEY (The General Hospital, Birmingham) Thirty two patients have had a J pouch ileoanal anastomosis since October 1983 (three polyposis, 25 ulcerative colitis, four megacolon): 20 had a previous colectomy and 12 a single stage proctocolectomy (five had no stoma). There were no deaths: 12 patients (37%) had surgical complications (pelvic sepsis, six, bleeding one, rectovaginal fistula one, high fistula-in-ano one, intestinal obstruction two, electrocutaneous fistula three). The pouch has been removed in two (sepsis, bleeding) and a loop ileostomy raised in three (rectovaginal fistula, short bowel syndrome, sepsis) three patients are awaiting ileostomy closure.

Of 25 whose intestinal continuity has been restored the median frequency of defection is 5-7 during the day, and only eight rise at night. Only one patient wears pads (only at night). Fourteen patients take antiarrhoeals and 11 require dietary restriction. None have sexual dysfunction. Three patients have features of Crohn’s disease in the colectomy specimen. Median duration of convalescence is 6-2 months (2–18 months). Improvements in surgical technique which seem to have reduced morbidity include: stapling leaving a long rectal stump at the original colectomy, mucosectomy from above, extensive vascular mobilisation of the iliac blood supply, preservation of the ileocolic artery and removal of the entire rectal cuff.
index, ESR or mucoproteins, or depressed serum proteins or haemoglobin is therefore reported. All of the patients except one were started on a dose of 15 mg/kg/day for two weeks after which the dose was progressively decreased until termination after a maximum of one year. Only five of the patients responded to treatment, the remainder having shown no clinical improvement, deteriorated or failed to absorb the drug. Two of the patients who initially appeared to respond relapsed during maintenance treatment and one required surgery. Two further patients required surgery but the remainder responded to corticosteroids sometimes dramatically. The most common side effect has been hyperaesthesia, which occurred in most patients, but this improved when the dose of the drug was decreased. One patient developed mild nephrotoxicity, which was dose dependent and reversible. 

In conclusion, in our experience Cyclosporin A appears to be of low efficacy and has only a limited place in the treatment of Crohn’s disease.

T116
Controlled multicentric therapeutic trial of an unrefined carbohydrate, fibre rich diet in ‘Crohn’s disease’

JEAN K RITCHIE, JANE WADSWORTH, J E LENNARD-JONES, AND ELIZABETH ROGERS (St Mark’s Hospital, London) Between 1.9.80 and 31.8.83, 352 patients with inactive or mildly active Crohn’s disease but on no drug therapy apart from sulphasalazine were entered from 39 hospitals into a prospective trial to assess the effect of two different diets on disease activity. The clinical condition was assessed at three monthly intervals using a scoring system and dietary intake recorded every six months. One hundred and sixty two patients were randomly allocated to diet A (unrestricted sugar low fibre) and 190 diet B (ideally no sugar high fibre).

During the two year trial period 21 patients required surgical treatment (diet A 14; diet B seven). Thirty nine patients were admitted to hospital (A 21, anal surgery only two: B 18, anal five) and 36 required out patient treatment with anti-inflammatory or antibacterial drugs (A 15: B 21). Seventy w eight patients withdrew/ were withdrawn before completion of the trial. The withdrawal was caused by worsening of symptoms (including weight loss) in 22 (A two: B 20), dietary non-compliance in 24 (A four: B 20) or for unknown or irrelevant reasons in 32 (A 16: B 16). The 178 patients who completed the trial without incident complied well with the diets prescribed (Median change in sugar intake A =76 G/week (NS): B =372 G/week (p<0.001). Median change in fibre intake A =-3 G/week (NS): B =+48 G/week (p<0.001) at two years. The clinical score deteriorated in 52 (A 24: B 28) was unchanged in 12 (A 11: B one) and improved in 114 (A 55: B 59).

Thus, a greater number of patients failed to continue with diet B and no clear difference in the clinical course was observed in patients who accepted the two different types of dietary advice.

T117
Raw soya flour produces a marked increase in cholecystokinin (CCK) release in man

J C BOJARSKI, C J SPRINGER, AND J CALAM (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Rats fed on raw soya meal develop increased plasma CCK and pancreatic hypertrophy and cancer. Cholecystokinin stimulates pancreatic growth and soya beans contain trypsin inhibitors which remove inhibition of CCK release by trypsin. The relevance of this effect to man, however, has been questioned on the basis that soya trypsin inhibitors are partially inactivated by human gastric juice and react less with human trypsin compared with rat trypsin.

Eight normal subjects ate scrambled egg on two occasions plus 5 g of soya flour in apple sauce every 30 min. On one occasion flour was raw and on the other it had been heated resulting in a fall from 34 to 3 mg in trypsin inhibited/g of flour. Cholecystokinin was measured in C18 Sep-pak extracts of plasma using a bioassay on dispersed rat pancreatic acini.

Raw flour produced a substantial and sustained increase in plasma CCK with a two hour integrated CCK response of 21.1±6.6 pmol/l (mean±SE) compared with 6.6±2.6 pmol during ingestion of cooked flour (p<0.01, Wilcoxon matched pairs test, p also <0.05 at four time points).

This result is of interest because a recent rise in the incidence of pancreatic cancer coincides with a massive increase in soya products in our diet.

T118
Total pancreatectomy – diabetes and enzyme replacement

J P LINEHAN, D C BROWN, A B KURTZ, AND R C G RUSSELL (Departments of Surgery and Medicine, The Middlesex Hospital, London) Total pancreatectomy will relieve the symptoms of end-stage chronic pancreatitis but it reputedly results in dangerous ‘brittle diabetes’. This has not been our impression, therefore we have reviewed our experience in relation to diabetic control and enzyme replacement.

Twenty two patients are under review after undergoing total pancreatectomy for benign disease (follow up 4–80 months); eight standard total pancreatectomy (TP) and 14 duodenum-preserving total pancreatectomy (DPTP). They were compared with age and sex matched insulin-dependent diabetic controls for HbA1, percentage ideal body weight (%IBW) and insulin requirement/kg/day. Bowel frequency and enzyme replacement was assessed.

Total pancreatectomies weighed less than controls (median %IBW 89.7, 115.6, p=0.004) and had lower insulin requirement (medians 0.49, 0.64, p=0.024). DPTPs did not differ from controls. HbA1 did differ in any group. There were five severe hypoglycaemias in the TPs (three during periods of profound steatorrhoea) compared to one each in DPTPs and controls. Twelve patients had normal bowel action and have stable diabetes; two on Pancrex V Forte (30 and 150 tabs/day) and 10 on Creon (median 52.5/day, range 18–80). Ten are increasing their enzyme dose.

Adequate pancreatic enzyme replacement is essential to prevent diabetic instability, and if attained diabetic management is straightforward.

T119
Endoscopic biliary prosthesis in 102 poor risk patients with carcinoma of the pancreas

A G SPEER, P B COTTON, L P DINEEN, AND R P A’HERN (Department of Gastroenterology, The Middlesex Hospital and Cancer Research Campaign Centre, King’s College Hospital, London) Between May 1983 and March 1986 102 patients with low biliary obstruction caused by carcinoma of the pancreas were considered for palliation with an endoscopic biliary prosthesis.
These were high risk patients judged unsuitable for surgery – median age 76 years (35–95); median bilirubin 378 μmol/l (27–907); 25 patients (25%) had renal impairment and 17 patients (17%) had previous unsuccessful attempts at surgical (14) or percutaneous (3) relief of obstruction. Three patients had such advanced disease that endoscopic intervention was judged not indicated and all three died within seven days. Stenting was attempted in 99 patients and was successful in 88 (89%). The external diameter of the prostheses used was 11.5 Fr gauge – 9, 10 Fr – 71 and 8 Fr – 8. The serum bilirubin fell satisfactorily in 87 patients (89% of attempted procedures). The 30 day mortality for successfully inserted prostheses was eight patients (9%). Complications occurred within two weeks of the procedure in nine patients (9%) mainly cholangitis. The median survival of patients with successfully inserted stents was 21 weeks (mean 25 weeks). Prosthesis blockage requiring endoscopic replacement occurred in 26 patients (29.5% of those at risk). Duodenal obstruction requiring surgical bypass developed in two patients. A Cox regression analysis identified increased age and high white cell count as having a significantly adverse effect on survival. Age ≤80 years median survival 24 weeks (mean 28.6), age > 80 years median survival 18 weeks (mean 18) (p=0.006). White cell count ≤6.5 cells/ml median survival 24 weeks (mean 31.3), white cell count > 6.5 median survival 20 weeks (mean 21.2) (p=0.04). Endoscopic insertion of a biliary prosthesis is an effective technique in high risk patients with low malignant strictures.

T120
Monoclonal antibody imaging of pancreatic cancer

K C BALLANTYNE, A C PERKINS, G PYE, AND J D HARDCASTLE (Departments of Surgery and Medical Physics, University Hospital, Nottingham) The first commercially available monoclonal antibody preparation for tumour imaging is Imacis-1 (International CIS). It is a combination of fragments F(ab)₂ of two monoclonal antibodies, anti-CEA and 19–9 radiolabelled with Iodine-131 and it is recommended in the detection of recurrent gastrointestinal cancer. As both of these antibodies are frequently expressed by pancreatic cancer, we have evaluated the ability of this antibody cocktail to image previously diagnosed pancreatic cancer.

Ten patients were studied (seven men, three women). All had a laparotomy diagnosis of pancreatic cancer, five had metastases and the diagnosis was confirmed histologically in a further three.

Serum CEA and Ca 19–9 levels were measured, 70 MBq of radiolabelled antibody administered, and imaging performed after 48–72 hours. Positive tumour uptake was demonstrated in eight of 10 patients: four primary cancers, one of three liver metastases and three of three abdominal metastases. In two patients with ascites diffuse intra-abdominal uptake was also seen. Serum Ca 19–9 levels were particularly raised in patients whose cancers were successfully imaged.

This study suggests that immunoscintigraphy using Imacis-1 may have a role in the investigation of patients with suspected pancreatic cancer.

T121
Results of an aggressive surgical approach to hilar cholangiocarcinoma

N S HADjis, I S BENJAMIN, AND I H BLUMGART (Department of Surgery, Royal Postgraduate Medical School, London) Of 128 patients admitted with hilar cholangiocarcinoma, 27 underwent curative resection. There were 11 local recurrences of the ductal confluence and 16 liver resections (extended right lobectomy 12, left lobectomy three, extended left lobectomy one). The 30 day hospital mortality was 7.4%. None of the 11 patients submitted to local excision, and only one of 18 patients who did not have previous surgery or preoperative biliary drainage, died in hospital. The mean survival for the 24 patients who left the hospital is 22.5 months. Sixteen patients died at six to 80 months, with a mean survival of 24 months; 13 of them had local recurrence. Eight patients are alive, with a mean survival of 20 months (range 10–45). The quality of life according to defined criteria was much improved.

The results show that radical resection can be accomplished with a low mortality and can be expected to significantly prolong survival. It appears, however, that current surgical methods alone cannot control the disease locally, and a study of the place of adjuvant radiotherapy after a curative resection is suggested.

T122
Preliminary results of a multicentre prospective trial of fresh frozen plasma in the treatment of acute pancreatitis

T LEES, M HOLLIDAY, D HEATH, T HUNT, J SCOTT, D WITHERS, M C A BRETt, AND A W HALL (Departments of Surgery and Pathology, University of Leicester, Leicester) An uncontrolled clinical study and animal work suggests fresh frozen plasma (FFP) reduces mortality in acute pancreatitis, possibly by replenishing the plasma antiproteinase system. A prospective controlled randomised clinical trial is underway to explore this possibility. Patients with acute pancreatitis have prognostic markers measured and are randomised to receive either FFP (2 units per 24 hours for 72 hours) or purified protein fraction (1 bottle per 24 hours for 72 hours) as part of the intravenous fluid therapy. Serum α₁ antiproteinase and α₂ macroglobulin levels are measured on days 1, 3, and 7.

To date 113 attacks of acute pancreatitis have been randomised – 56 FFP and 57 colloid control. The two groups are well matched in all clinical criteria including predicted severity of pancreatitis. No significant difference has yet been shown between the two groups in clinical outcome (five deaths in each group). Both show a significant rise in α₁ antiproteinase levels from days 1 to 3 and this is not influenced by administration of FFP. α₂ macroglobulin levels show a significant fall in the colloid control group from days 1 to 3 (p<0.02) but remain substantially unaltered in patients receiving FFP (p=0.91, two-tailed Mann-Whitney Ranking Test). Relatively low volumes of FFP have been shown to prevent the usual depletion of serum α₂ macroglobulin in acute pancreatitis and this may have therapeutic implications.
developed their first recurrence of pain more than a year postoperatively. At two years, pre-operative flatulence was reduced from 67% to 42%, distension from 58% to 36%, reflux type indigestion from 60% to 42% and nausea from 63% to 21%. There was little change, however, in the incidence of these symptoms at one and two years and in at least a third of the patients they were new. Exploration of the bile duct (19%) did not appear to affect symptomatic outcome and of 15 patients referred back to hospital with persistent symptoms none has yet been shown to have a retained stone.

It is concluded that apparently non-specific symptoms are less common after cholecystectomy. Early postcholecystectomy symptoms may improve with time but some patients only develop symptoms after an interval.

T124
Outcome of endoscopic sphincterotomy for papillary stenosis
D CARR LOCKE, I BAILEY, J NEOPTOLEMOS, T LEES, AND D HEATH (Departments of Surgery and Gastroenterology, Leicester Royal Infirmary, Leicester) The benefits of endoscopic sphincterotomy for presumed papillary stenosis are controversial. Out of 454 ERCPs for postcholecystectomy symptoms, 32 patients with persistent biliary pain have undergone endoscopic sphincterotomy (ES) for ‘papillary stenosis’. There were 28 women and four men with a mean age of 51 years (range 31–72 years). The outcome has been independently reviewed at one to six years and compared with diagnostic factors. In two patients ES was not possible because of severe fibrosis. After ES, 18 patients were significantly improved (group A), 11 unchanged and one worse (group B). Significantly different individual criteria between patients in group A and group B were: CBD diameter > 10 mm (15 vs 1, p<0.001), delayed drainage of contrast, > 30 minutes after ERCP, (11 vs 2, p<0.01) but not abnormal LFTs, (6 vs 1, NS). Two or more factors were present in 13 patients in group A and only one patient in group B (p<0.01). Manometric studies were performed in nine patients, five in group A and four in group B, all showing abnormally high sphincter of Oddi pressures.

We conclude that duct dilatation and delayed drainage of contrast appear to be good indicators of outcome, but the place of manometry is unclear.

T125
Endoscopic removal of stones from the common bile duct: the whole truth
M E LAMBERT, D F MARTIN, AND D E F TWEEDLE (Departments of Surgery and Radiology, University Hospital of South Manchester, Manchester) There is still doubt about the morbidity and mortality of endoscopic removal of gall stones, largely because of concern about the accuracy of audit. Three hundred and fifty-six patients with proven stones were referred during 1981 and 1985 for endoscopic treatment which was carried out by two clinicians. In 26 patients (7.3%) a cholangiogram could not be obtained, in three because of failure to intubate the second part of the duodenum (0.8%) and in five because of failure to locate the papilla (1.4%). Twenty of these patients underwent operations; three of them dying. In seven of the 330 in whom a cholangiogram was obtained, the stones were too large for endoscopic removal (2% of the 356). Three hundred and fifteen (88%) underwent successful endoscopic sphincterotomy and in 281 (79%) all stones were eventually removed after a mean of 1-98 ERCPs (range 1–7). There were four deaths directly attributable to the procedure (1-1%) and 43 complications (6-4% of ERCPs but 12-1% of patients). The results continue to improve: between 1981 and 1985 the proportion of patients in whom stones were successfully removed rose from 79% to 91%, the number in whom the procedure failed, resulting in operation, fell from 21% to 8% and the complication rate fell from 13% to 7% per patient.

T126
Efficacy of ceruletid treatment for retained common bile duct stones
S A SADEK and A CUSCHIERI (Department of Surgery, Ninewells Hospital and Medical School, Dundee) The synthetic peptide ceruletid induces maximal relaxation of the sphincter of Oddi and has been reported to be effective in the management of retained CBD stones after cholecystectomy. The treatment which entails an intravenous infusion of ceruletid (2 ng/kg/min in saline for one hour) during pressure controlled saline infusion through the long limb of the T-tube, was evaluated in 23 patients treated in several district general hospitals. The success of the procedure was assessed by repeat T-tube cholangiography. Passage of stones into the duodenum was documented in 12 patients (52%) with complete clearance in eight (35%). The radiological stone size ranged from 3–15 mm. There was no correlation between a successful outcome and size of retained stones. The flow rate of the saline T-tube infusion during ceruletid treatment was 55-3 ml/min, SD 21-1. There was an inverse correlation between the CBD pressure during ceruletid controlled saline T-tube infusion and successful stone passage. When the pressure remained below 25 cm H2O, a successful outcome was obtained in all the cases as opposed to two of eight patients in whom the pressure exceeded this level (27–45 cm H2O). Ampullary impaction of the stone was encountered in two patients. These results are superior to those obtained by mono-octanoate and indicate that this simple method of treatment should be tried before more invasive methods for this problem.

T127
Prospective trial of pre-operative endoscopic sphincterotomy (ES)
D L CARR-LOCKE, J P NEOPTOLEMOS, AND D P FOSSARD (The Leicester Royal Infirmary, Leicester) In a prospective study, 120 patients were randomised to ES followed by surgery (group I) or to surgery alone (group II). The groups were well matched with respect to age, sex and biochemical and clinical risk factors. Five were incorrectly entered into the trial and six were subsequently withdrawn because surgery was refused in five (group I) and one had ES alone following a myocardial infarct (group II). There remained 50 patients in group I and 59 patients in group II. The overall mean age was 61 years (range 20–83 years) and the mean serum bilirubin was 120 μmol/l (range 5–474 μmol/l). Failure to carry out ES or clear the CBD of stones occurred in seven patients in group I (14%), whereas retained or recurrent stones occurred in six patients in group II (10%). Major complications in group I occurred in seven patients (14%) including two deaths compared with five patients (8-5%) including one death in group II. Nine other patients had minor complications in group I (18%) and nine patients in group II (15%).

In conclusion, these results do not support the routine pre-operative use of ES in patients with CBD stones who are otherwise suitable for biliary surgery.
T128  
Morbidity and mortality of common bile duct exploration  
W G SHERIDAN, H O L WILLIAMS, AND M H LEWIS (Department of Surgery, East Glamorgan General Hospital, Pontypridd, S Wales) Only limited data exist on the morbidity of common bile duct (CBD) exploration in UK surgical practice. We have therefore carried out a retrospective review of 257 patients who had CBD exploration in one hospital over a 15 year period. One hundred and eighty patients (45-9%) developed one or more complications as follows; septic complications (19-5%) (includes a 15-9% wound infection rate), cardiorespiratory complications (16-7%), wound dehiscence or incisional hernia (3-9%), T-tube complications (3-5%), haemorrhagic complications (2-3%), urinary tract problems (2-3%), prolonged ileus (1-9%), postoperative pancreatitis (1-9%), renal failure (1-2%), hepatic failure (0-4%). Thirty seven patients (14-4%) had retained stones, discovered before discharge from hospital in 20 (7-8%) and later in the remainder. Postexploratory cholangiography did not significantly reduce the incidence of retained stones. Of 12 patients who had choledochoscopy, none had retained stones. Five patients (1-9%) died, death being because of postoperative pancreatitis in two and to sepsicaemia, bile peritonitis and myocardial infarction in the remainder. In conclusion, CBD exploration has a high associated morbidity, particularly because of septic complications and a high retained stone rate, for which choledochoscopy may offer the best solution.

GASTRODUODENAL  
T129-138

T129  
Sudden deaths at home from peptic ulceration – a hitherto unrecognised phenomenon  
A L BLOWER and C P ARMSTRONG (Leighton Hospital, Crewe, Cheshire) There are over 4000 deaths annually from peptic ulceration in this country. Many die before medical treatment is possible. All sudden deaths from peptic ulceration since 1972 have been studied in South Cheshire; population approximately stable at 250 000. Data were obtained from necropsy reports, hospital, and general practitioner records. Ninety one at home deaths occurring accounted for 37% of all ulcer related deaths. Patients were grouped into three five year periods: 1972–76 (21), 1977–81 (32) and 1982–86 (38). The mean ages were similar at 70-8, 70-7, and 73-4 years respectively. Men were in the majority in the first period whereas women were more common in the last five years. Duodenal and bleeding ulcers predominated in the first period in contrast with gastric and perforated ulcers in the last five years. Non-steroidal anti-inflammatory drug use increased from 37% to 46% and then to 87% in the last five years.  
These figures emphasise the previously unrecognised importance of including all home deaths in future studies of peptic ulceration. In the study period there have been marked epidemiological changes. Patients dying at home from peptic ulceration are now more likely to be women with a perforated gastric ulcer. Most of the subjects are now using anti-inflammatory drugs which we believe are responsible for these changes.

T130  
Impact of histamine H2 receptor antagonists upon admissions for peptic ulceration within the Northern region (1971–84)  
C W VENABLES, K DENHAM, AND R A MCNAY (Department of Surgery, Freeman Hospital, Newcastle upon Tyne and Northern Regional Statistics Section) Early studies showed a reduction in gastric surgery after the introduction of cimetidine but there have been no longer term studies or data on medical admissions. We have analysed all discharges or deaths (of over 48 hours admission) for peptic ulcer (PU) in the northern region for the period 1971–84. These have been subdivided by type, treatment, ulcer category and area. Trends have been analysed by comparing three time periods (1971–75, 1977–80, and 1981–84). The results show that there is a continuing reduction in all surgical admissions (Elective DU 70%; GU 50%; emergency DU 37%; GU 19%; perforated DU 20%) except perforated GU (+60%) when 1981–84 was compared with 1971–75. There was a similar trend in medical admissions (elective DU 61%; GU 25%; emergency DU 23%) with a 61% rise in emergency GU admissions. Subdividing the region into five geographical areas revealed comparable trends in all areas except that the rise in emergency GU admissions did not occur in Cumbria. These findings confirm a continuing impact on admissions for PU from the introduction of histamine H2 antagonists.

T131  
Which ulcer patients are likely to present with bleeding?  
K MATTHEWSON, S PUGH, AND T C NORTHFIELD (Gastroenterology Units, St James Hospital, Balham and University College Hospital, London) The factors which determine whether a peptic ulcer presents with pain or bleeding are unknown. We have prospectively evaluated patient features (age, sex, smoking, alcohol, and analgesic consumption, and previous history of peptic ulceration) and endoscopic features (ulcer number, site, diameter, depth and nature of ulcer base) in 106 unselected patients presenting with acute bleeding and 58 presenting with pain who were found to have peptic ulcers at endoscopy. As patients with bleeding were older (median age 65 vs 51, p<0.001), other statistical comparisons were age corrected. Patients with bleeding were more likely to have taken non-steroidal anti-inflammatory drugs (NSAIDs) within the previous four weeks (59% vs 20%, p<0.001) and to have an ulcer greater than 20 mm in diameter (27% vs 6%, p<0.01), but there were no significant differences regarding sex, smoking, alcohol intake, incidence of multiple ulceration, ulcer depth, ulcer site, or nature of ulcer base. Although there was no significant difference in the overall incidence of a previous ulcer diagnosis, bleeding patients were more likely to have had a previous ulcer complication (bleeding or perforation) (20% vs 0%, p<0.001). We have therefore shown for the first time that ulcer patients who present with bleeding rather than pain are three times as likely to have taken NSAIDs recently; they tend to be older, are more likely to have had a previous ulcer complication and are more likely to have a large ulcer.

T132  
Occurrence of pain in peptic ulcer haemorrhage: relation to age and non-steroidal anti-inflammatory drugs  
I M CHESSER, L E RHODES, AND R D MONT-
GOMERY (Department of Medicine, East Birmingham Hospital, Birmingham). It has been claimed that haemorrhage from peptic ulcer tends to be painless in the elderly, and also in patients taking non-aspirin non-steroidal anti-inflammatory drugs (NANSAIDs). We have reviewed the records of 254 consecutive cases of endoscopically proven bleeding ulcer, concerning abdominal pain on presentation and during the preceeding six months and also the ingestion of NANSAIDs as recorded on positive questioning. With insufficient data in 18 cases, 236 were analysed (38 taking NANSAIDs). Overall 58% had no pain on presentation and 36% had no pain then or in the preceeding six months. There were no differences between GU and DU or between the sexes. Pain was unrelated to NANSAID ingestion in DU or GU or in any age group. Of patients with no pain during the six months 21% were taking NANSAIDs and of those with pain 20% were taking NANSAIDs (44% and 40% respectively in patients over 70 years old). Ulcers tended to be painless over the age of 70 compared with under 50 ($\chi^2=3.934$, p<0.05).

NANSAIDs do not reduce pain in ulcers which bleed. Hence the previously confirmed tendency for NANSAID-associated ulcers to present with haemorrhage indicates a genuinely increased bleeding risk in such ulcers, rather than a selective under estimation of their prevalence.

T133

Campylobacter positive and campylobacter negative gastric ulcers (GU) – have they a different aetiology?

H J O’CONNOR, M F DIXON, J I WYATT, AND A T R AXON (Gastroenterology Unit and University Department of Pathology, General Infirmary at Leeds, Leeds). About 30% of GU patients are Campylobacter (CLO) negative on gastric biopsy. The signficance of this finding is at present unclear and possible differences between CLO-positive and CLO-negative GU have not been evaluated. In this study, gastric biopsies from 58 patients with untreated GU were blindly assessed for the presence of CLO and also scored for severity of reflux gastritis (RG). We have previously shown that RG 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 histological features were each graded from 0 (normal or absent) to 3 (severe) and the sum of the grades used to assign each patient a ‘reflux score’ (0–15). Forty three patients (74%) were CLO-positive and 15 CLO-negative. Of the CLO-negative GU, nine had a reflux score >10 compared with only five of those CLO-positive ($\chi^2$, p<0.001). Furthermore, CLO-negative GU showed significantly higher reflux scores (mean±SD) than CLO-positive GUs (10±9.4 vs 8±1.2; 3, p<0.001).

These results suggest that there may be fundamental differences between CLO-positive and CLO-negative GU. The evolution of GU in CLO-positive patients may be related to CLO-induced gastric mucosal injury whereas in CLO-negative subjects enterogastric reflux may be the prime aetiological factor.

T134

Effect of enprostil on basal and postprandial serum gastrin levels in patients with antral G-cell hyperfunction, Zollinger-Ellison, syndrome and normal subjects

I F S J CROBACH, J B MJ JANSSEN, AND C B HW LAMERS (Departments of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands). Enprostil, a synthetic dehydro-prostaglandin E2, inhibits serum gastrin levels in normal subjects and patients with duodenal ulcer. The present study was undertaken to assess the effect of Enprostil on basal and postprandial serum gastrin concentrations in patients with hypergastrinaemia and gastric acid hypersecretion of antral (antral G-cell hyperfunction) or tumour (Zollinger-Ellison syndrome) origin. Basal and postprandial serum gastrin concentrations were measured after 70 $\mu$g Enprostil or placebo orally in five patients with antral G-cell hyperfunction (four men, one woman, 22–44 years, BAO 11–0–19 mmol/h), in three patients with Zollinger-Ellison syndrome (three men, 19–52 years, BAO 28.0–45.0 mmol/h) and in five normal subjects (five men, 33–65 years).

Enprostil reduced basal serum gastrin concentrations in all five patients with antral G-cell hyperfunction (230±52 to 145±34 pg/ml), in two or three patients with Zollinger-Ellison syndrome (1269±427 to 1048±445 pg/mg), and in all normal subjects (51±9 to 41±7 pg/ml). The percentage reduction in antral G-cell hyperfunction (37±12%) was slightly higher than in Zollinger-Ellison syndrome (17±19%) and normal controls (19±7%). The postprandial gastrin secretion was inhibited by Enprostil in all subjects (228±316 to 709±154 pg/ml 2h in antral G-cell hyperfunction, 454±1774 to 578±342 pg/ml 2h in Zollinger-Ellison syndrome and 660±128 to 199±50 pg/ml 2h in normal subjects). The percentage inhibition was slightly higher in Zollinger-Ellison syndrome (13±45%) than in antral G-cell hyperfunction (69±13%) and normal subjects (70±19%). It is concluded that Enprostil inhibits postprandial gastrin secretion not only in normogastrinaemic subjects but also in patients with antral cell hyperfunction or Zollinger-Ellison syndrome.

T135

Highly selective vagotomy (HSV) and duodenal ulcers resistant to $H_2$-blockers

J N PRIMROSE, A T R AXON, AND D JOHNSTON (University Department of Surgery and Department of Medical Gastroenterology, The General Infirmary, Leeds). Our aim was to establish whether HSV provides effective treatment for the DU which fails to heal on $H_2$-blocker (H$_2$B).

In a prospective study of HSV (1978–83), 141 patients were operated on for uncomplicated DU and had satisfactory pre- and postoperative acid studies. In 52, the DU had failed to heal despite six weeks on full dose H$_2$B (group R), 14 patients relapsed on maintenance therapy (RM), 63 remained healed on H$_2$B (H) but relapsed frequently off therapy and 12 did not receive H$_2$B (N).

The overall recurrence rate was 7.5% at two years and 15% at four to five years. There were eight recurrent ulcers (RU) among 45 of 52 group (R) patients who attended for follow up at two years (17%) and 10 RU among 25 of 40 patients at four to five years (40%). In the ‘RM’ group, there was no RU (0%) either at two years among 13 of 14 patients or four to five years among nine of 10 patients. In the ‘H’ group, there was one RU among 63 patients at two years (2%) and one among 40 of 48 patients at four to five years (3%). In the ‘N’ group, there was one RU in 10 of 12 patients at two years (10%) and one in seven of eight patients at four to five years (14%).

Recurrence was more common in the ‘R’ than in the ‘H’ group, both a two year (p<0.02) and at four to five years (p<0.01), and was independent of surgeon and preoperative BAO and PAO. An ulcer that fails to heal on $H_2$-blockers represents
Famotidine, a new H₂ receptor antagonist, restores levels of cytoprotective prostaglandin E₂ in the peripheral blood of patients with peptic ulcer disease.

J P Walsh, W J Maxwell, F P Hogan, and P W N Keeling (Department of Clinical Medicine, Trinity College Medical School, St James' Hospital, Dublin 8) Prostaglandin E₂ (PGE₂) has been shown to play an important role in the maintenance of the gastroduodenal defense mechanisms. A deficiency of PGE₂ has been shown in mucosal biopsies, gastric juice and peripheral blood of patients with duodenal ulcer disease (DUD). The aims of this study were to examine the effect of a new H₂ receptor antagonist (H₂-RA), Famotidine (FAM), on PGE₂ biosynthesis by peripheral blood mononuclear cells (PBMC) of patients with DUD. Twenty patients with endoscopically proven active DUD entered a double blind, placebo controlled randomised trial of FAM (40 mg nocte) or placebo for six weeks with repeat endoscopic examination to assess ulcer activity. Fasting peripheral blood samples were taken before and after six weeks treatment. Freshly isolated PBMC (Hypaque-Ficoll) were stimulated with opsonised zymosan for 30 mins at 37°C. Prostaglandin E₂ concentration in the supernatants were measured by radioimmunoassay.

The results from both active and placebo treatment DUD groups were compared with those from healthy controls and it was found that PGE₂ levels in the pretreated DUD groups were depressed significantly compared with that found in control subjects. Placebo 15±4±±6; FAM 14±3±1±7, (n=10) vs Control 27±8±3±3 (n=43); ng/10⁶ monocytes. X±SEM. p<0±01 Student’s t test. After six weeks treatment 62-5% of the placebo and 90% of the FAM group had healed. Despite healing PGE₂ biosynthesis by PBMC remained depressed in the placebo group (12-9±2±7), however, but were normalised in the FAM treated patients (27-5±4-6). In a previous study we found that in 20 DUD patients treated with Cimotidine (800 mg nocte for four weeks), all healed but PGE₂ levels remained depleted. In conclusion, FAM in contrast to other H₂-RA appears to restore peripheral blood cell biosynthesis of cytoprotective PGE₂ at six weeks in patients with DUD.

T137
Simple and effective treatment for postvagotomy diarrhoea
S R Aimes, V Smirniotis, E J Wheldon, C W Venables, and I D A Johnston (University Department of Surgery, Newcastle upon Tyne) The treatment of postvagotomy diarrhoea is often unsatisfactory. Cholestyramine has been reported to be effective but is unpleasant to take and may have undesirable long term effects. In this study cholestyramine has been compared with loperamide in treating this condition. Thirty three patients with persistent diarrhoea were studied: group A = truncal vagotomy+drainage (n=22); group B = truncal vagotomy+drainage plus cholecystectomy (n=11). Patients were randomised to receive a course of either cholestyramine 4 g bd or loperamide 4 mg mane, after which treatment was stopped for one week and the patient crossed-over to the alternate drug. Diary records of diarrhoea were kept throughout the study. After reassessment patients received their preferred treatment for a further four weeks, dosage being adjusted for best control.

In group A only one of 22 found cholestyramine effective and 11/22 complained that it was intolerable or made diarrhoea worse. In group B eight of 11 found cholestyramine effective (p<0-01; Fisher Exact Test). Loperamide was effective in 16/22 of group A and nine of 11 group B, the latter patients preferring it to cholestyramine.

We conclude that the prophylactic use of low dose Loperamide given once daily is a simple, safe and effective treatment for post-vagotomy diarrhoea. Cholestyramine is useful in patients who have also had a cholecystectomy, but is their second line treatment.

T138
Insulin test (IT) as a predictor of recurrent ulceration (RU) after highly selective vagotomy (HSV): comparison with the value of measurement of BAO and PAO
J N Primrose and D Johnston (University Department of Surgery, The General Infirmary, Leeds) Though the IT is widely used as an indicator of incomplete vagotomy and future RU, it is tedious and unpleasant. The aim of this study was to determine whether similar information could be derived from simpler measurement of BAO and PAO(K) before and after operation.

Bile acid output and the responses to insulin and pentagastrin were measured in 38 patients with RU after HSV for DU, and in 101 patients without RU more than five years after HSV for DU. In each patient BAO and PAO(K) were measured before HSV; and BAO, PAO(K) (except in a few unfit people) and PAO(K) one week after HSV.

The IT (Hollander) was “positive” in 34% of the RU patients compared with 8% of non-RU. The best discriminant using BAO/PAO was a reduction of <50% in the PAO following operation. This was “positive” in 53% of RU but also in 28% of non-RU. Other discriminants were even less specific.

Although the IT was less sensitive than other indicators of recurrence it is much more specific if the incidence of recurrence after HSV is low the insulin test has better predictive value than BAO or PAO(K): it would be premature to abandon it.

P1
Development of colonic transport processes in infancy: the influence of aldosterone
H R Jenkins, T R Fenton, M O Savage, M J Dillon, and P J Millar (The Hospital for Sick Children, St George’s Hospital and The Institute of Child Health, London) Aldosterone is of critical importance in the regulation of Na⁺ conservation by both kidney and colon. Little is known, however, of the ontogeny of these processes in the human infant. Using the technique of non-equilibrium rectal dialysis we have investigated rectal Na⁺ absorption in 25 premature infants and neonates (N, 30±44 weeks gestation), 15 infants (1, 1±12 months) and 14 older children (C, 1±7 years). Na⁺ absorption was highest in N (274 nmol/cm²/min±ISD) compared with I (200±56) and C (149±42). Plasma aldosterone was markedly elevated in N (7570±2500 pmol/l) compared with infant reference levels (790±210). Urinary Na⁺ wasting was apparent in the preterm infants in group N. Plasma aldosterone and Na⁺ absorption was also studied in infants...
with end-organ unresponsiveness to aldosterone (7200±210, Na+ 90±4), aldosterone deficiency (O, Na+ 60±46) and secondary hyperaldosteronism (1300±346, Na+ 281±52). These data suggest that colonic Na+ transport processes are efficient in early infancy and that aldosterone is a major regulatory hormone. In the preterm infant prior to 34 weeks gestation renal tubular Na+ reabsorptive mechanisms are poorly developed and the colon is the major organ of Na+ conservation. The consequences of diversionary surgery and colectomy should be carefully considered in this age group.

F2
Endoscopic biliary prosthesis in the palliation of malignant biliary obstruction – a randomised trial

H A SHEPHERD, A DIBA, A P ROSS, M ARTHUR, G ROYLE, AND D COLIN-JONES (Winchester, Southampton and Portsmouth Hospitals) Plastic endoprostheses, inserted transhepatically or endoscopically into the bile duct, are alternatives to surgical bypass for the relief of malignant biliary obstruction. We report an ongoing randomised trial which compares endoscopy with surgery in the palliation of malignant obstruction of the distal bile duct.

Eighty three patients have been referred and 46 (55.4%) have been randomised. Exclusions were, preferred treatment (59.2%), duodenal obstruction (11%), porta block (18%), and disseminated malignancy (11%). Treatment failures were crossed into the other treatment group (stent 3, surgery 1). Proof of malignancy was obtained in 61% and 89% of the endoscopic and surgical groups respectively. Analysis to date (stent n=18, surgery n=19), shows a significant difference in hospital stay between endoscopy and surgery, 6 and 11-5 days respectively, p<0.05. No significant differences were found between endoscopy and surgery (respectively) in relief of icterus (78.9% vs 73.6%), 30 day mortality (5% vs 21%), complications (22% vs 36%), overall survival (md 176 vs 128 days), and total hospital stay (172 vs 286 days). Readmissions only occurred in the endoscopy group (n=7) and were for cholangitis with blocked stents. Endoscopic prosthesis compares favourably with surgical bypass.

F3
Occupationally related angiosarcoma of the liver (ASL) in the United Kingdom

F I LEE AND P M SMITH (Departments of Gastroenterology, Victoria Hospital, Blackpool and Llandough Hospital, Cardiff) Twelve men have developed angiosarcoma of the liver (ASL) in association with occupational exposure to vinyl chloride monomer (VCM) in two factories in the UK. Presenting clinical features included abdominal pain (six), malaise (five), jaundice (two), haemorrhage from oesophageal varices (two), ascites (five) and hepatomegaly (10). The men were aged 37-71 years at the time of diagnosis. In two, non-cirrhotic portal hypertension had been recognised 13 and 5 years previously. Hypercalcaemia was a persistent feature in one case. In general, disease progressed rapidly without remission, death occurring in a few weeks due to hepatic coma in association with gastrointestinal or intrahepatic haemorrhage. One man showed limited response after intermittent chemotherapy and survived longest – seven months. Clinical, laboratory and angiographic features may be typical but open liver biopsy is the safest and most certain method of proving the diagnosis. At necropsy the livers of these patients showed considerable, sometimes massive, replacement by tumour, apparently multifocal, with necrosis and haemorrhage. Only one man, who died from a cerebrovascular accident due to a cerebral deposit, had evidence of metastases. In view of the long latency period observed in some cases world wide, the full extent of ASL occurrence may not be known for 20 years or so. In summary, ASL is a rare, highly malignant tumour seen after several years exposure to medium/high concentrations of VCM. Metastases are uncommon.

F4
Can the mucus bicarbonate barrier withstand low intraluminal pH – studies in health and gastroduodenal mucosal disease

E M M QUIGLEY AND L A TURNERG (Department of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford) Recent studies show the ability of a gastroduodenal mucosa to protect itself from acid-peptic digestion by maintaining a zone of near neutral pH immediately adjacent to the mucosa. In vitro, this zone is dissipated at very low luminal pH. Our aim was to assess, in vivo, the integrity of the juxtamucosal neutral zone in the face of low luminal pH in health and disease. Luminal and mucosal pH were measured in lower oesophagus, fundus, corpus, antrum, duodenal cap and duodenal loop using a flexible microelectrode passed through the biopsy channel of an endoscope. Studies were done in 23 normal subjects, and in patients with reflux oesophagitis (n=10), antral gastritis (n=10), duodenitis (n=6) and duodenal ulceration (n=10).

In normal subjects mucosal pH in the fundus, corpus and duodenum remained stable above pH 4 over a range of intraluminal pH from 1 to 7.4. In the lower oesophagus and antrum, however, mucosal pH dropped sharply when intraluminal pH levels fell below 2.5. In comparison with both controls and the other disease groups patients with duodenitis and DU demonstrated significant deficits in mucosal pH in the duodenal cap once luminal pH fell below 3. At other sites the mucosal pH response to low luminal pH was similar in all patients groups.

While the juxtamucosal neutral zone lining fundus, corpus and duodenum in normal man can resist low luminal pH that lining lower oesophagus and antrum is more easily dissipated. Duodenal ulcer patients have a specific deficit in mucosal pH in the duodenal cap.

F5
‘Real’ cancer risk in ulcerative colitis

S N GYDE, A STEVENS, P PRIOR, J A H WATERHOUSE, D P JEWELL, O BROSTROM, R LOBBERG, G HELLERS, AND R N ALLAN (Gastroenterology Unit, General Hospital, Birmingham) While there is conclusive evidence that ulcerative colitis carries an increased cancer risk, estimates of the apparent cancer risk vary widely between series probably because of selection bias and small sample sizes.

The ideal study would identify a large representative group of patients at the onset of their disease (inception cohort) with complete long term follow up.

We report the results of such a collaborative study between Birmingham, Oxford, and Stockholm. Patients were diagnosed at the referral centre within five years of onset of disease between 1945-65 drawn from a defined geographical area and followed for a minimum of 20 years.

The series comprised 822 patients of whom 485 had extensive colitis. The relative risk of developing colorectal cancer was 7.7 in the whole series and 17.1 for those with extensive colitis. The cumulative colorectal cancer risk in patients with extensive colitis was 0.6±0.1-3.2% at 10 years from onset.
Abnormal expression of C-MYC oncogene product in dysplasia and neoplasia associated with ulcerative colitis

I C Forgacs, V Sundaresan, G Evan, D G D Wight, G Neale, J O Hunter, and J V Watson (Departments of Gastroenterology and Pathology, Addenbrooke’s Hospital, Cambridge and MRC Centre and Ludwig Institute for Cancer Research, Cambridge)

Cellular oncogenes occur both in normal tissue and in tumour cells and, although they may induce cellular transformation in vitro, the importance of their expression in human cancers is unclear. We have studied c-myc oncogene expression in the development of colorectal cancer by immunohistological detection (using monoclonal antibody: 6E-10) of the abundance and distribution of the protein product of c-myc, p62c-myc, in archival histopathological samples of normal colonic tissue (n=21), quiescent ulcerative colitis (UC) (n=10), UC with dysplasia (n=17) and UC with invasive carcinoma (n=8). In normal tissue there was light-to-moderate exclusive (13/21) or predominant (8/21) nuclear p62c-myc staining at the crypt base with moderate exclusive (17/21) or predominant (four of 21) cytoplasmic staining at the mucosal surface. Staining was similar in quiescent UC. By contrast, in the cancers, while intense predominantly nuclear staining was seen at the crypt base, in six of eight tumours there was heavy mixed nuclear and cytoplasmic staining at the surface. Although no consistent pattern emerged in mild dysplasia, in the seven most severely dysplastic tissues, the distribution and intensity of staining paralleled that of the carcinomas.

Thus in the transition from chronic UC to malignancy, there is evidence of abnormal expression of the protein product of the c-myc oncogene.