The British Society of Gastroenterology

The Spring Meeting of the British Society of Gastroenterology was held at the Institute of Education, London on 20–22 April 1983, under the Presidency of Professor J Lennard-Jones. Abstracts and posters presented at the meeting are printed below. A fuller account of the meeting appears on p. 458.

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**TECHNICAL ENDOSCOPY**

**T1**

Assessment of gastro-oesophageal collateral veins in portal hypertension by means of endoscopic ultrasonography

G Caletti, L Bolondi, V Arienti, E Brocchi, S Testa, M Ferrentino, L Zani, A Passaniti, and G Labo (Department of Medicine and Gastroenterology, University of Bologna, Polyclinico S Orsola, 40138 Bologna, Italy)

Gastro-oesophageal varices impinging on the lumen are easily recognised by conventional endoscopy. Abdominal ultrasonography has recently proved useful in the assessment of portal venous system, but fails in detecting collateral veins, particularly perioesophageal and short gastric veins. Angiography is still the most effective tool in this field, but its invasiveness prevents a widespread utilisation and repeated examinations. By means of a newly developed ultrasonic endoscope (Olympus GF UM1/EUM1) we examined 10 patients (seven men, three women, aged 29–70 years, mean 56 years) affected by portal hypertension due to liver cirrhosis. In all cases the presence of oesophageal (and in 2/10 of gastric) varices was established by a previous endoscopy. Endoscopic ultrasonography of the oesophagus was carried out with the ultrasonic probe covered with a water inflated balloon in order to facilitate the ultrasound transmission and the focusing of the oesophageal and gastric wall. Submucosal oesophageal varices, already visualised by endoscopy, have been always displayed in transverse sections as roundish echo-free structures, immediately below the mucosal layer. Enlarged extrinsic perioesophageal veins were easily visualised in all cases and in 9/10 cases their calibre was correlated with the size of oesophageal varices; in one case with minimal sub-mucosal varices we found large collateral veins. In 6/10 cases we succeeded in following the course of these collateral vessels from the splenic hilum to the oesophageal wall. One patient was examined before and after endoscopic injection sclerotherapy, when variceal eradication was achieved; a complete disappearance of the submucosal veins and patency of extrinsic collateral vessel was observed. This technique seems to be useful for a complete, non-invasive and easily repeatable evaluation of gastro-oesophageal collateral veins in portal hypertension.

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**T2**

Blood flow patterns in oesophageal varices measured by Doppler ultrasound

T McCormack, T Martin, R H Smallwood, P Robinson, L Walton, and A G Johnson (University Department of Surgery and Department of Medical Physics, Royal Hallamshire Hospital, Sheffield)

There have been few studies on blood flow in oesophageal varices because of their inaccessibility. We have devised a Doppler ultrasound probe located near the tip of a catheter which passes down the biopsy channel of a gastroscope. This is connected to a bidirectional Doppler Volumeter. The Doppler signal is amplified over a loudspeaker and gives a simultaneous trace on a chart recorder.

Recordings were made in 10 patients during diagnostic upper alimentary endoscopy and subsequently under general anaesthetic before injection of their oesophageal varices. The expected cephalad direction of blood flow was confirmed in some unthrombosed varices in the lightly sedated patient. Flow velocity was increased by inspiration and decreased by expiration. Absence of flow confirmed a varix was thrombosed and further sclerotherapy was unnecessary. During positive pressure ventilation under general anaesthetic, the flow may be reversed and completely stopped in full inspiration. Unexpectedly, in some varices in lightly sedated patient flow occurred in both directions. In one varix the flow was cephalad above 31 cm and caudal below 33 cm. This suggests that a perforating vein from the deep oesophageal veins joined the varix at 32 cm. Inspiration decreased and expiration increased flow through the perforator. These findings have important implications for the theory of formation of varices and the technique of sclerotherapy.

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**T3**

Are gastric varices supplied from the oesophagus?

J D R Rose and P M Smith (Department of Gastroenterology, Llandough Hospital, Penarth, Glam) It is usually held that blood flows from gastric into oesophageal varices. It has therefore been argued that sclerosis of oesophageal varices will lead to the development or enlargement of gastric varices. Observations made during a radiological study of variceal injection challenge the view that blood flow is uniformly cephalad.

Since April 1981 we have performed injection sclerotherapy under radiological control using a sclerosant-contrast mixture without variceal compression. Twenty-five patients have received 103 intravariceal injections. In all patients contrast streamed towards the head, but in nine contrast also flowed caudally into gastric veins when the site of injection was just proximal to the cardia. Gastric varices diagnosed endoscopically before treatment were present in six. All patients with fundal varices showed this pattern. Although the sclerosant (sodium tetradecyl sulphate) can be injected through the flexible needle at pressures up to 100 cm H2O, the small volume used (2 ml) and low flow rate (16 ml/min) make a reversal of the natural direction of flow unlikely.

These observations are consistent with blood from the oesophageal submucosal
plexus flowing into oesophageal varices via a perforator above the cardia. Distal to the perforator blood flows back towards the stomach into subepithelial veins, which may be varicose. We conclude that oesophageal sclerotherapy will not lead to the formation of gastric varices, but to their obliteration.

T4 Injection sclerotherapy of oesophageal varices: a comparison of one and three weekly intervals

D WESTABY, W M MELIA, B R D MACDOUGALL, J E HEGARTY, AND ROGER WILLIAMS (The Liver Unit, King's College Hospital, Denmark Hill, London) A prospective randomised study comparing the efficacy and complication of injection sclerotherapy performed at one and three weekly intervals was undertaken in 55 patients (48 cirrhosis, six portal vein thrombosis, one modular regenerative hyperplasia) presenting with recent variceal haemorrhage. The number of courses of injections required for variceal obliteration was similar in the one and three weekly interval groups (mean 4.1 and 4.2 respectively), although total duration of the treatment period was significantly shorter in the one week interval group (mean five and nine weeks respectively; p<0.05). Significant episodes of rebleeding (requiring 1 unit blood transfusion) occurred in 11 of 28 patients in the one week interval group compared with 14 of 27 in the three week interval group. In 80% and 30% of the patients in the one and three weekly groups respectively, mucosal ulceration was observed during the period of treatment (p<0.05). On 19 occasions, all in the one weekly interval group, the presence of this ulceration led to delay in further injection (on four occasions after two courses, 15 after three). The frequency of post-injection pain (30%) was similar in both groups and there were no instances of stricture formation or oesophageal perforation.

In conclusion, injection sclerotherapy at weekly intervals may offer an advantage to the patient in terms of earlier obliteration of varices and despite the greater frequency of mucosal ulceration, symptomatic complications were not increased by injecting at the shorter interval.

T5 'Hot squeeze' bipolar forceps. A more effective endoscopic method for stopping bleeding from large vessels in the gastrointestinal tract

C P SWAIN, T N MILLS, JULIA M DARK, S MORRISON, AND P R SALMON (Departments of Gastroenterology and Medical Physics, University College Hospital, London) A new bipolar endoscopic electrode has been designed and built by us which can occlude larger diameter arteries than can be occluded by other thermal methods. The hypothesis was tested that if the walls of a bleeding artery are squeezed together and then exposed to bipolar electrocoagulation, more effective occlusion of arteries of 1-3 mm can be achieved than with any laser or probe-type electrode where coagulation without effective compression becomes progressively less effective as vessel size increases. Isolated fresh human and canine arteries (1-3 mm) were treated with NdYAG, Argon and CO₂ lasers, dry monopolar (M), liquid monopolar (L), bipolar 'Bicap' (B), heater probe (H), and the UCH 'hot squeeze' bipolar forceps (HS). 'Hot squeeze' produced bond strengths (mean bursting pressure 800 mm Hg) significantly greater than any other method. New animal models of large vessel bleeding were developed to assess the efficacy and safety of the devices. Mesenteric canine veins were lased over exposed jejunal mucosa and treated with M, L, B, H, and HS at optimal settings. Only HS could seal vessels 1.2-3 mm in this model. 'Hot squeezes' caused less histological damage than other modalities. By compressing a bleeding vessel in its juxta, thus terminating bleeding, it is possible to check that haemostasis will be achieved before energy is deposited. Although less easy to use at endoscopy than other devices, the 'hot squeeze' bipolar forceps appear capable of sealing larger bleeding vessels than any other endoscopic thermal method.

T6 Endoscopic laser treatment of vascular anomalies of the upper gastrointestinal tract

S G BOWN, C P SWAIN, D W STOREY, AND P R SALMON (University College Hospital, London) We report the successful use of Argon and NdYAG lasers in the endoscopic treatment of six patients with documented recurrent haemorrhage from vascular anomalies of the upper GI tract. Treatment was carried out to ablate the lesion visible endoscopically. Three patients had angiodyplasias and three had hereditary haemorrhagic telangiectasia (HHT). Of those with angiodyplasias, two with single gastric lesions required 16 and 35 units of blood in five months before treatment but nil since (follow-up 28 and seven months). The third, with several lesions, bled 24 units in one month, but none after therapy for 18 months. The three patients with HHT bled with increasing severity over five to 20 years culminating in transfusion requirements of 3, 2, and 4 units per week. After laser therapy the first required no transfusion for 20 weeks and then increasing amounts suppressed by further treatment of new or recurrent lesions after 14 and 28 months. The second patient has required no blood in 30 weeks' follow-up. The third was well for eight weeks but then had increased blood loss necessitating a partial gastrectomy six months after initial treatment. Angiography of the resected specimen revealed several discrete vascular ectasias in the submucosa fed by arterioles (diameter up to 0.3 mm). Histology showed destruction of the abnormal mucosa by the Argon laser used in this patient although the more extensive submucosal lesions were unaffected and may have contributed to the early recurrence of bleeding. The greater penetration of the NdYAG laser used in the three patients may treat these more effectively. This pilot study suggests that laser therapy has reduced blood loss in these patients who are difficult to treat by other means.

T7 Is bile reflux gastritis a meaningful endoscopic diagnosis?

I A EYRE-BROOK, A M HOLROYD, AND A G JOHNSON (Departments of Surgery and Medical Physics, Royal Hallamshire Hospital, Sheffield) Postprandial duodenogastric reflux (DGR) was assessed scintigraphically in patients with an endoscopic diagnosis of 'bile reflux gastritis' (BRG) without previous gastric surgery to determine whether these patients have increased postprandial reflux. Results in seven patients with postprandial dyspepsia and BRG were compared with seven dyspeptic patients without BR and with 10 normal controls. BRG was diagnosed endoscopically when macroscopic gastritis was associated with lakes of bile lying in the stomach. Cases were selected from over 700 endoscopies performed on one unit. Post-
prandial biliary secretion of butyl iminodiacetic acid (IDA) was studied dynamically (one-minute frames). Gastric position was established with intravenous technetium-99m pertechnetate (100 μCi) before administration of IDA (3 mCi). A Lundh meal (250 ml) was administered when IDA was first seen in the common bile duct and DGR recorded as the percentage of IDA secreted by the liver which appeared in the gastric region.

Duodenogastric reflux varied from 0-5% in normal controls and from 0-6% in dyspeptics without BRG. Duodenogastric reflux in patients with BRG varied from 0-16% but only one of seven had DGR outside the control range (0-5%).

These findings suggest that ‘abnormal’ postprandial reflux is found in only a minority of those with BRG. This excess gastric bile observed during the invasive procedure of endoscopy need not implicate bile reflux in the aetiology of those patients’ Postprandial dyspepsia.

**T8**

Normal zinc absorption in coeliac disease?

R W CROFTON, S GVOZDANOVIC, D GVOZDANOVIC, P J AGGETT, N A G MOWAT, and P W BRUNT (Departments of Medicine and Biomedical Physics and Bioengineering, University of Aberdeen, Aberdeen) Zinc absorption would be expected to be impaired in malabsorptive states such as coeliac disease. 65Zn was used to investigate the absorption of exogenous zinc and the turnover of the endogenous metal in nine patients with coeliac disease, six before and after the institution of a gluten-free diet and three already on treatment.

Subjects were injected intravenously with 0.25 mg Zn labelled with 18.5 kBq (0.5 μCi) 65Zn and then monitored for two months using a whole body counter. Zinc turnover was calculated. They were then given a standard meal extrinsically labelled with 92.5 kBq (2.5 μCi) 65Zn and followed similarly.

The absorption of 65Zn was calculated, allowing for endogenous loss. The healthy volunteers absorbed 32.5 ± 12.4% (mean ± ISD) of the dose whereas five untreated patients absorbed 30.4 ± 14.5%. This difference is not significant. Two partially treated patients absorbed 30.8 ± 2.2%.

The half-life of 65Zn was significantly less in untreated coeliac disease (volunteers 219-0 ± 21.8 days; coeliacs 150.0 ± 12.5 days, p<0.001) but after starting on a gluten-free diet the half-life improved to 235.8 ± 85.5 days (p<0.05).

It is concluded that at the zinc intake used in this study true zinc absorption is unimpaired in untreated coeliac disease. There is, however, an increased whole body loss of zinc in coeliac disease which rapidly reverses after starting a gluten-free diet.

**T9**

Sodium ion concentration in the unstirred layer of rat small intestine in vivo and in vitro

L M LUCAS AND M J CANNON (Institute of Physiology, University of Edinburgh, and The Food Research Institute, Norwich) Much solute absorption is associated with [Na+] gradients across enterocyte brush border membranes. Yet in vivo, absorption will persist when luminal [Na+] is reduced apparently showing minimal dependence on Δ[Na+]. For this reason, [Na+] at the rat intestinal surface was measured in vivo and in vitro by polymer [Na+] electrodes. With tissue incubated in vitro in Krebs-bicarbonate buffer, jejunal [Na+] was 40 mM when the luminal [Na+] was lowered to 25 mM; it increased to 60 mM in the presence of 10 mM glucose and was lower in the ileum in vitro (35 mM) with and without added glucose. Ouabain, desoxicocholic acid, and dithiothreitol (DTT) at 1 mM all reduced [Na+] in vitro. In vivo, [Na+] was studied in a preparation which allowed access to mucosa held within a Ussing-type chamber but with intact vasculature and which showed active glucose absorption. In vivo, [Na+] was 80 mM when [Na+] was 25 mM, indicating accumulation near the brush border. Omission of glucose from the luminal perfusate reduced [Na+] to 58 mM and Mg2+ ion instead of choline ion substitution further reduced the concentration to 45 mM. Consequently, an appropriately aligned [Na+] gradient persists despite diverse lumen to tissue gradients and may account for solute absorption continuing when [Na+] is low. The action of DTT, Cleland’s mucolytic agent, in reducing [Na+] indicates that extracellular layers are not exclusively aqueous as the term unstirred water layer implies but involves surface mucus for their integrity. The further reduction in Δ[Na+] by Mg2+ substitution may account for the apparently sodium-independent Mg2+-sensitive glucose transport system seen in vivo.

**T10**

Discrepancies in determinations of unstirred layer depth in small intestine

L M LUCAS, L SOOD, J M GEE, AND T JOHNSON (Institute of Physiology, University of Glasgow, and The Food Research Institute, Norwich) The intestinal unstirred water layer (UWL) can be rate-limiting for solute permeation if the membrane transport step is rapid. A widely used technique for determining δ, the UWL ‘depth’, is to monitor the time course for the establishment of an osmotically induced transmural potential. This method is based on a special solution of the diffusion equation, which assumes zero membrane-permeability for the probe solute, an assumption which may be wrong for rapidly absorbing tissues. This can be tested by measuring the half-time for a potential transient induced by solute diffusing into and out from the UWL. If the method is valid the half-times should be identical. The time course for osmotically induced potential transients was measured in perfused loops and everted sacs of rat intestine exposed alternatively to mannitol-loaded and mannitol-free mucosal media.

In both preparation the half-time following ‘wash-in’ was shorter than for ‘wash-out’. Everted sacs of jejunum showed longer half-times than ileal sacs and were more permeable to 14C-mannitol. These results show that the commonly used solution of the diffusion equation is not wholly satisfactory for modelling unstirred layer effects in rat intestine. One possible explanation for this is the occurrence of significant permeation of the solute probe, as has been shown here for mannitol.

**T11**

Acute and short term effects of intestinal alpha-glucosidase inhibition on gut hormone responses in man

L O UTENTHAL, O O UKPONMWAN, M A GHATEI, AND S R BLOOM (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) The competitive alpha-glucosidase inhibitor acarbose has been used to treat dumping syndrome and to reduce post-
prandial glycaemia in diabetics. It may also provide an experimental model for disaccharidase deficiency diseases. We have studied the effects of different doses of acarbose on postprandial plasma gut hormone responses in man. Five healthy volunteers were given 2-2 ml mixed test meals with placebo, 50 mg, 100 mg, 200 mg, and 400 mg doses of acarbose according to a double-blind, latin square protocol. A further test meal with acarbose 100 mg was performed after one week of thrice daily acarbose administration at the highest regularly tolerated dose. Acarbose reduced the postprandial increments of glucose, insulin and GIP to minima of 24%, 33%, and 32% of control values respectively, and increased that of enteroglucagon to a maximum of 11-fold, in a dose-related manner. The effect of acarbose 100 mg on these responses was potentiated 1-5 to 2-fold after one week of regular administration. Motilin responses were significantly increased by all acute doses of acarbose, but showed no dose-dependency over the range tested. A minor (50%) increase in the CCK response was only significant (p<0.025) at the 200 mg dose. There were no significant effects on gastrin, neurotensin, pancreatic polypeptide, and somatostatin responses. Thus acarbose may be used to study the endocrine and intestinal adaptive responses to carbohydrate intolerance. The effects of GIP and enteroglucagon may reflect the degree of shift of carbohydrate digestion and absorption from the upper towards the lower small intestine.

T12
Preparation and initial screening of a complementary DNA (cDNA) clone bank to guinea-pig small gut mucosal RNA

D S BAILEY, D O ROBINSON, J C WALL, G MCALLISTER, AND J HERMON-TAYLOR
(Department of Surgery, St George's Hospital Medical School, London) The developmental programme of small intestinal epithelium culminates in the production of highly differentiated mature enterocytes whose expression of brush-border enzymes comes under adaptive control. Further understanding of these processes and their disorders requires an investigation of the patterns of gene activation. As an essential first step in such a study we have prepared a cDNA clone bank to guinea-pig duodenal mucosal RNA and screened it for enterocyte specific nucleotide sequences. Total mucosal RNA was extracted with guanidium thiocyanate or LiCl/urea; cDNA was prepared using an oligo-dT primer and reverse transcriptase. Removal of the RNA with alkali was followed by double stranding (ds) with DNA polymerase I (Klenow) and treatment with S1 nuclease. ds-DNA was annealed into the Psi I site of the plasmid pAT 153 using homopolymer tailing and used to transform competent E coli HB101. Recombinants were selected by their sensitivity to ampicillin and resistance to tetracycline. Individual colonies were picked from agar into multwell microtitre plates and screened using enterocyte and other guinea-pig tissue-specific 32P-cDNA probes to obtain a set of enterocyte-specific cDNA clones; these are further characterised by hybrid-selection translation to identify those corresponding to mRNAs encoding specific brush-border components.

T13
The kinetics of lactose absorption by human jejunal biopsies

D J DAWSON, R W LOBLEY, AND R HOLMES
(University Department of Gastroenterology, Manchester Royal Infirmary, Manchester) Perfusion studies using lactose have variously indicated that lactose hydrolysis either is or is not rate limiting to lactose absorption in man. We have studied the relationship between lactose hydrolysis and uptake of released glucose by human jejunal biopsies in vitro, using a technique previously described. Multiple biopsies from five subjects (normal histology, lactase activity 4-6-10-2 U/g wet wt) incubated in 0-56-56 mM lactose displayed Michaelis Menten kinetics for both lactose hydrolysis (Km=33-9±14-3 mM; Vmax=26-5±9-2 nmol/min/mg, mean ± 1 SE) and glucose absorption (Kt=47-2±2-1; Jmax=14-12±0-5). Efficiency of glucose capture rose to a maximum of 53% at 5-6 mM lactose and thereafter remained constant. In biopsies from 29 patients (lactase activity 0-04-10-4 U/g wet wt) incubated in 28 mM lactose, absorption of released glucose was proportional to the lactase activity (y=0-4x+0-86, r=0-77). These results confirm the in vivo findings of Gray and Santiago that even in tissue with normal lactase activity, lactose hydrolysis rather than glucose transport rate limiting to overall monosaccharide absorption.

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T14
Improved tests of ileal function using SeHCAT

R FERRARIS, R JAZRAWI, C BRIDGES, AND T C NORTHFIELD (Departments of Medicine and Nuclear Medicine, St George's Hospital Medical School, London) A γ-labelled bile acid (75Se taurohomocholic acid – SeHCAT) is under investigation as a test of ileal function, using both faecal (a) and abdominal (b) counting after oral administration. Problems are incompleteness of colonic emptying and of stool collection. To overcome these, we used 51CrCl3 as non-absorbable marker for (a) and (b), and have also carried out gall-bladder SeHCAT scans (c). We compared these three techniques in four groups of six subjects each: (1) normal controls; (2) ulcerative colitis; (3) ileal Crohn's disease; and (4) ileal resection. Results of faecal study, expressed as absorption index =75Se/51Cr% recovered, gave mean values of 0-83, 0-86, 0-61, and 0-24 for the four groups respectively. Absorption coefficient, derived from slope of total abdominal disappearance curve of 75Se and 51Cr, was 0-76, 0-75, 0-54, and 0-25 respectively. 75Se gall-bladder count decayed exponentially, giving t1/2 values for SeHCAT of 2-3, 3-5, 2-1, and 0-6 days. Group 4 gave significantly different results from 1 and 2 for all three tests. Evaluation of SeHCAT absorption by means of the three different techniques correlated well (faecal count vs total abdominal count r=0-94, p<0-01; gall-bladder count vs total abdominal count r=0-75, p<0-01), providing an internal check on the validity of all three methods. In subjects with complete colonic emptying (persistent 51Cr on abdominal counting), total abdominal SeHCAT results coincided with gall-bladder results only after correction for 51Cr. We conclude that these modifications of the SeHCAT test of ileal function are valid, and have advantages over previous SeHCAT methods.

CROHN'S DISEASE
T15-T22

T15
Colitis in early infancy and childhood: a prospective study

S K F CHONG, J A WALKER-SMITH, A J
Blackshaw, and B C Morson (St Bartholomew's and St Mark's Hospitals, London) Ten children aged 3 months to 4 years with chronic bloody diarrhoea and colitis were studied. All had colonoscopic examination and mucosal biopsies performed. The children were followed up prospectively one to two years after treatment.

Allergic colitis owing to cow’s milk protein intolerance was diagnosed in two, ulcerative colitis in two, probable Crohn’s disease in two, and indeterminate colitis in the remaining four children. The two breast-fed infants with allergic colitis who were treated with a cow’s milk-free diet in baby and mother showed clinical, endoscopic, and histological resolution. The four children with ulcerative colitis and probable Crohn’s disease on treatment with Salazopyrin alone were asymptomatic six months after initial therapy. Of the remaining four children with indeterminate colitis while on treatment with Salazopyrin and prednisolone, three are clinically well with minimal symptoms; one child continued to have frequent relapses and subsequently had a subtotal colectomy performed with clinical improvement. Histopathology showed intestinal Behçet’s disease of the large bowel.

The precise diagnosis of colitis in early infancy and childhood is frequently difficult to establish. In our experience, this syndrome appears to be a heterogeneous group of conditions and should be followed up with multiple mucosal biopsies for further categorisation.

Granulomas were identified in the resected specimen in 143 patients; the incidence in the 60 patients with small bowel disease was 52%, in the 44 patients with ileocolitis disease it was 61% and in the 39 patients with large bowel disease it was 78%. Of the 143 patients with granulomas, 41 (28-7%) subsequently developed recurrence compared with 19 of 93 patients (20-4%) in whom granulomas were not seen (NS). The recurrence rates in the subgroup of patients with small bowel disease, ileocolic disease, and large bowel disease were not significantly greater in patients with granulomas when compared with those without granulomas.

The presence of granulomas in the resected specimen was not associated with a lower incidence of recurrence after resection for Crohn’s disease.

T17 Tissue zinc depletion in Crohn’s disease
C C Ainley, P W N Keeling, and R P H Thompson (The Gastrointestinal Laboratory, The Rayne Institute, St Thomas’ Hospital, London) Zinc depletion has been reported in Crohn’s disease (CD) but principally based on low plasma zinc levels. This measurement is unlikely accurately to reflect body zinc status in CD as: (1) zinc is chiefly intracellular; (2) 60% of the tiny plasma pool is bound to albumin, so plasma zinc levels reflect albumin concentrations, which are often low; (3) zinc, like iron, is displaced from plasma into tissues in inflammatory conditions. We have shown that plasma zinc measurements in chronic liver disease and pregnancy are inadequate, while the zinc content of mixed leucocytes is a good measure of tissue zinc status. To assess tissue status in CD, we have measured the zinc content of peripheral blood leucocytes and muscle.

Mixed leucocytes separated by sedimentation of whole blood, and muscle obtained at laparotomy were dried, the zinc acid-extracted and measured by atomic absorption spectrophotometry.

In CD, the zinc contents of leucocytes and muscle were correlated (n=15, r=0.77, p<0.01), but not those of muscle and plasma (n=15, r=0.17, p=NS) or leucocytes and plasma (n=15, r=0.10, p=NS). Leucocyte zinc concentrations in CD (n=58, 50±2.5 ng Zn/mg dry weight, mean ± SD) were lower than in normal and patient controls (n=48, 56±5.5, p<0.001). Low levels were more frequent in patients with a short small bowel. There was no relation to disease activity.

In conclusion, we have shown that tissue zinc depletion occurs in CD, that the zinc content of leucocytes is a good measure of this, and that plasma zinc measurements are inadequate.

T18 Differentiation between abscess formation and active Crohn’s disease using 111Indium labelled leucocyte gamma imaging
N S Ambrose, M Goldman, R J Hawker, Z Drolc, M R B Keighley, and C N McCollum (Departments of Surgery and Nuclear Medicine, The General and Queen Elizabeth Hospitals, Birmingham) The ability to distinguish an intra-abdominal abscess from severe active Crohn’s disease is clinically very difficult. The treatment may require operation or additional medical therapy and so the differentiation between the two conditions is important.

111Indium labelled leucocytes provide a means of scanning the abdomen and distinguishing between abscess and active disease.

Twenty-two patients with severe Crohn’s disease have undergone 111Indium leucocyte scanning to detect the presence of abscess formation. (The mean values for their indices were Hb 12.8 g/dl; WCC 11.6; albumin 29 g/l; alk phos 295; α₂ GTP 2.4.) Six patients were shown to have abscesses present (but only two of these were clinically obvious), three had only inflammatory lesions confined to the bowel, while 13 had no evidence of inflammation on scanning. All six abscesses were proven at laparotomy. Two of the three patients with inflammatory lesions only were shown at laparotomy to have no abscess. The third recovered without operation after additional medical therapy.

These early results indicate that 111Indium leucocyte scanning has proved a useful means of determining the presence of even small abscesses in patients with Crohn’s disease.

T19 Colonic Crohn’s disease and the contraceptive pill – a causative link?
J M Rhodes, P C Hawker, J Dawson, R Allan, R Cockel, and E Elias (Departments of Medicine, General, Selly Oak, and Queen Elizabeth Hospitals, Birmingham) There have been several reports of women with colitis similar to Crohn’s colitis which
clefts on stopping oral contraceptives and several consecutive cases of ours with colitis on 'the pill' prompted us to look for a causal association. Ninety-seven consecutive women attending follow up with previously diagnosed ulcerative colitis or Crohn's disease were asked about contraceptive pill usage. (The index cases were excluded.)

Twelve out of 16 (75%) women with isolated Crohn's colitis had taken oral contraceptives before developing symptoms. Six of these 12 started oral contraceptives within the year of onset, six had granulomata on biopsy and none had atypical histology. Only 13/48 (27%) women with ileal or ileo-colonic Crohn's disease and 5/33 (15%) women with ulcerative colitis had taken oral contraceptives while symptomatic. The incidence of oral contraception at time of presentation in women with Crohn's colitis <41 years old, 9/12 (75%), was markedly greater than expected from DHSS figures for the general population (30% of women <41 in 1975, p<0.005 by exact binomial test. The prevalence of presymptomatic oral contraception in women with ulcerative colitis was, however, as expected for the general population, when matched for age and year of onset. Records search of Crohn's disease patients showed that isolated colonic Crohn's disease is twice as common in women (30% of 165) than men (15% of 141), p<0.005.

Crohn's colitis without ileal involvement is commoner in women. A significantly high proportion of these women have taken oral contraceptives before developing symptoms. Oral contraception may be a causative factor in Crohn's colitis.

**T20 Causes of persistence of intestinal fistulas**

P J SHOULER, R P GRIMLEY, AND J ALEXANDER WILLIAMS (The General Hospital, Steelhouse Lane, Birmingham) Intestinal fistulas usually heal provided there is no organic or functional obstruction distally or unless the track becomes totally covered with epithelium. Most fistulas arise after operations and most that will heal have done so by six weeks. In a unit specialising in stoma and nutritional problems we have analysed the search for the cause of distal obstruction in 40 patients, mostly referred from outside our district or county. In 33 the cause was known to be persistent active Crohn's disease and so was resected often with intervening radiographic investigation. In some patients with Crohn's disease, however, there was no apparent distal obstruction radiologically. In one of these six, stricturoplasties were performed because of proximal and distal stenosion with no resection. The fistula recurred, again with no radiological evidence of distal organic obstruction, but was cured by further operative relief of a distal stricture. In two the cause of the distal functional (but not radiologically diagnosed) obstruction were small abscesses around non-absorbable suture material. In another two the obstruction was previously unsuspected malignant disease. The duration of the fistulas ranged from four to 200 weeks. All were resolved successfully by surgical treatment but one patient with malignancy died three months later. No enterocutaneous fistulas should be allowed to persist beyond six weeks without a planned surgical approach. The cause of distal obstruction should be sought by every means available but may not be detected till operation.

**T21 Does macroscopic involvement of the jejunum in Crohn's disease present a distinct clinical pattern?**

J H ENTRICAN AND W SIRCUS (Gastro-intestinal Unit, University of Edinburgh, Western General Hospital, Edinburgh) A review of 300 patients with Crohn's disease seen over the last 30 years has revealed a frequency of macroscopic jejunal involvement of one in six cases. The clinical features, complications, and outcome of the jejunal group was compared with the non-jejunal group. Whereas there were no significant differences in the male:female ratio, the occurrence of weight loss, liver disease, erythema nodosum arthropathy, or fistulae between groups, finger clubbing and oedema were significantly commoner in the jejunal group. Hypoalbuminaemia, anaemia, and steatorrhoea characterised the laboratory findings in the jejunal group.

The occurrence of perianal disease was not different between groups, but the distribution of lesions from ileum to rectum varied significantly. The operation rate and type varied significantly between groups.

The jejunal cases required greater attention to maintenance of nutrition and, although apparently more severely ill at presentation as assessed clinically and by serum albumin concentration (mean serum albumin jejunal cases 29 gle, non-jejunal cases 34 gle, p<0.001), the overall mortality between groups was similar.

This large series of cases of jejunal Crohn's disease shows certain distinct features in clinical pattern and treatment. Outcome is surprisingly favourable and is probably similar to those without jejunal involvement.

**T22 Late onset Crohn's disease**

P FABRICIUS, P SHOULER, S N GYDE, D P HART, AND R N ALLAN (Gastroenterology Unit, The General Hospital, Birmingham) Epidemiological studies of Crohn's disease suggest a bimodal distribution for age at diagnosis with a secondary peak between 60 and 75 years although there have been few studies of late onset disease.

Twenty-five patients among a series of 676 with Crohn's disease were more than 60 years of age at diagnosis (mean 69 years). The mean duration of follow up was 10 years (range one to 32 years). Of the 14 patients with small bowel disease 12 were confined to the distal ileum and 10 of the 11 with large bowel disease had disease confined to the distal colon. There was one case of extensive colitis but no cases of diffuse small bowel disease.

Patients with distal ileal disease presented acutely and nine were treated by resection within two months. After a mean interval of 11 years no patient has required further resection.

The patients with distal colitis had severe and persistent symptoms, five with associated diverticular disease. Seven patients needed intensive medical treatment including corticosteroids and four required resection. Three patients in this distal colitis group died of peritonitis after local perforation.

Late onset Crohn's disease usually presents either as acute disease of the distal ileum which runs a benign course after resection or as a distal colitis with high morbidity and mortality particularly when associated with diverticular disease.
The false negative rate for neoplastic lesions of the bowel using Haemoccult occult blood test may be as high as 30%; a symptomatic questionnaire may be more discriminating when used in population screening. To evaluate the benefit of a symptomatic questionnaire, 1533 individuals 45–74 years were sent a five-question self-completion questionnaire and a Haemoccult test to be performed over three days.

Four hundred and eighty-three (31·5%) completed both the questionnaire and the Haemoccult test; 119 (24·6%) of the completed questionnaires were positive (listed one or more symptoms), 42 (8·7%) had had diarrhoea, 60 (12·4%) a change in their bowel action, and 35 (7·2%) rectal bleeding.

Four out of the 119 patients with a positive questionnaire, and eight out of 364 with a negative questionnaire had a positive Haemoccult test (total of 12 or 2·5%).

Examination of the 119 positive questionnaire individuals by flexible sigmoidoscopy, and where indicated barium enema, revealed one adenomatous polyp (0·5–1 cm) (positive on Haemoccult testing). None had cancer. Of the 35 persons complaining of rectal bleeding, 71·4% had piles.

Examination of the eight positive Haemoccult patients out of the 364 with a negative questionnaire revealed two to have cancer (one Dukes' Stage A, one Dukes' Stage B) and three adenomatous polyps (>0·5 cm in size).

A self-completion questionnaire is inaccurate and has an unacceptably high false positive rate.

**T24**

**Colorectal screening by a self-completion symptomatic questionnaire**

P A FARRANDS and J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) The false negative rate for neoplastic lesions of the bowel using Haemoccult occult blood test may be as high as 30%; a symptomatic questionnaire may be more discriminating when used in population screening. To evaluate the benefit of a symptomatic questionnaire, 1533 individuals 45–74 years were sent a five-question self-completion questionnaire and a Haemoccult test to be performed over three days.

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A self-completion questionnaire is inaccurate and has an unacceptably high false positive rate.

**T25**

**Comparison of brush cytology with biopsy in the diagnosis of colonic strictures**

N J MCC MORTENSEN, J D LEVER, W K ELTRINGHAM, AND R A MOUNTFORD (Departments of Surgery, Pathology and Medicine, Bristol Royal Infirmary, Bristol) Endoscopic brush cytology has an accepted place in the diagnosis of upper gastrointestinal lesions. Most colonic lesions, however, can be accurately diagnosed by radiology and colonoscopy with biopsy, and the place of cytology in this situation is unclear. We have assessed colonoscopic brush cytology (BC) in the diagnosis of 43 colonic strictures. Two slides were made from each brushing and read by a cytologist without knowledge of the endoscopic or biopsy diagnosis. Smears were read as benign or malignant and the results compared with colonoscopic biopsies and histology from resected specimens.

There were 26 carcinomas (four recurrent), three villous adenomas, three ischaemic, and 11 inflammatory strictures. Brush cytology was correct in 23 (90%) carcinomas, compared with 13 (50%) correct biopsies, and tumour differentiation was accurately predicted in 14. Biopsy was correct in all 17 benign lesions

but although cytology did not give any incorrect diagnoses there were two technical failures, where slides were overrun with organisms after simple air drying. With alcohol fixation the problem has not recurred.

While we could not recommend routine BC, it has a particular application in the diagnosis of tight colonic strictures, anastomotic recurrences, and villous tumours which may have areas of early malignant change.

**T26**

**Endoscopic polypectomy for malignant polyps of the colorectum**

JANET WHITENAY, E A JONES, F A MACRAE, C B WILLIAMS, AND B C MORSON (St Mark's Hospital, City Road, London) The histopathological criteria and prognosis of malignant polyps of the colorectum treated by polypectomy alone, previously described from this hospital, have been reviewed in the light of recent dissent. Sixty patients, followed up for a minimum of five years, were available for study. Forty-five of these were treated by polypectomy alone. Thirty-six of the polypectomy alone group are alive and well after five years, three have died from unrelated causes after five years, and five from unrelated causes from six months to four years: none of these 44 patients had any evidence of recurrence. The one remaining patient died 18 months after polypectomy at the age of 81 but the cause of death was obscure. Fifteen patients, who had polypectomy followed by a further major surgical procedure, provide a useful control group. Among these, no residual growth was found in 13; in two, residual carcinoma was found at the primary site but not in the regional lymph nodes. In both these cases, however, polypectomy was known to be incomplete. These results vindicate the policy of polypectomy alone for those malignant polyps in which the carcinoma is not poorly differentiated and in which local excision appears complete as judged by both endoscopic and histological assessment.

**T27**

**Pre-neoplastic changes in experimental colorectal carcinoma**

N KIRKHAM, T COOKE, N HUMPHRIES, D STAINTHORPE, AND I TAYLOR (University Surgical Unit, Southampton General
Hospital, Southampton) As part of a study of preneoplastic changes in the colon we have investigated morphological changes in the mucosa during the induction of carcinoma. An experimentally induced colonic carcinoma was used which has many similarities to human colorectal cancer.

Tumours were induced in female Wistar rats by 12 weeks subcutaneous injections of azoxymethane 1 mg/kg. Animals were killed five, 10, 15, 20, and 25 weeks after the induction of carcinogenesis. Five standard biopsies were taken from along the length of the colons and prepared for scanning electron microscopy (SEM) and light microscopy.

The most notable morphological change detected by SEM was the appearance of microadenoma present by five weeks. The adenomatous characteristics of these lesions was confirmed by light microscopy. These microadenomas were found almost exclusively in the distal bowel and increased in size (mean 1.2±0.3×10^-2 mm to 2.3±0.5×10^-2 mm) and number (mean 5–8/lower field) with time after tumour induction.

The distribution of microadenomas was found to be similar to that of established carcinomas present at two to five weeks. These findings support the hypothesis of an adenoma-carcinoma sequence in the development of colorectal cancer.

Using SEM we have shown early neoplastic changes in the colon which would have been difficult to detect by conventional histology. Scanning electron microscopy may therefore be a useful tool in investigation of patients at high risk of developing colonic cancer.

T28 Effect of non-anticoagulating warfarin on induced colorectal cancer in the rat

N Goeting, T Cooke, and I Taylor (University Surgical Unit, Southampton General Hospital, Southampton) Previous studies have suggested that the incidence of metastases and possibly primary tumour growth are reduced by warfarin in azoxymethane-induced colorectal cancer in the rat. In this study the effect of warfarin on the incidence of primary tumours at concentrations below that necessary for therapeutic anticoagulation has been assessed.

Two groups of Wistar rats were studied; group 1 represented the control group and received azoxymethane by weekly subcutaneous injection; group 2 received in addition warfarin (0.2–0.6 mg/l) in their drinking water for eight weeks. Clotting times were monitored using the thrombostest method.

Rats were killed at 10, 15, 20, and 25 weeks after initial injection and stathmo-kinetic studies performed using vincristine. The number of primary tumours and the crypt cell production rate (CCPR) was calculated for each group at each time interval. The CCPR was obtained for each of five areas of the colon. The number of colon tumours was statistically significantly reduced in the group receiving warfarin (29 in group 1, 17 in group 2, p<0.05). There was no statistically significant change in CCPR (caecum group 1–12-0, caecum group 2–12-07; rectum group 1–11-3, rectum group 2–9-0). The incidence of distal metastases was also similar in the two groups.

This study suggests that warfarin acts on local tumour production by means other than metaphase arrest.

T29 Pathogenesis of colonic sodium and water malabsorption in tropical sprue

V I Mathan, M Mathan, and B S Ramakrishna (introduced by C C Booth) (Wellcome Research Unit, Christian Medical College Hospital, Vellore, India) Ten patients with tropical sprue and nine age matched controls were studied by perfusion of the colon with isotonic saline with a non-absorbable marker, after peroral intubation of the caecum. The controls absorbed a mean of 2.5 ml/min (SD 1-2) of water while the absorption in patients was significantly lower (0-24 ml/min. SD 2-11). The colonic absorption of sodium was also significantly decreased in sprue patients. Biochemical and microbiological analysis of faecal collections for three days before perfusion showed that faecal unsaturated fatty acids, correlated significantly with decreased colonic absorption. There was no correlation between faecal hydroxy fatty acids, faecal total and aqueous phase bile acids, aerobic and anaerobic bacterial flora or enterotoxin producing bacteria and colonic absorption. Damaged colonocytes were seen by electron microscopy in sprue rectal biopsies. Unsaturated fatty acids are known to inhibit colonocyte basolateral membrane Na"^k^-ATPase. The functional abnormality of the colon in tropical sprue is likely to be potentiated by the effect of unsaturated fatty acids on damaged colonocytes.

T30 Collagenase inhibition in colonic mucosa

A P Jayaraj, P B Boulos, M R Lewin, J G C Araujo, and C G Clark (Department of Surgery, School of Medicine, University College London, The Rayne Institute, University Street, London) The colonic mucosa produces collagenase demonstrable by collagen substrate lysis, which is responsible for the breakdown of colonic anastomoses. It has been shown that collagenolytic activity can be inhibited by proteinase inhibitors and this study investigates the effect of their administration by different routes.

Equal groups of six New Zealand rabbits were treated with a single dose of soy bean trypsin inhibitor (SBTI—Sigma) 1 ng/kg, given either intramuscularly, or by gastric or rectal instillation. An untreated group served as controls. Biopsies via a paediatric proctoscope were taken at four, 24, 48, and 72 hours after treatment. Each biopsy provided six explants which were incubated on collagen plates for 72 hours. Areas of lysis were traced onto paper, cut, weighed, and expressed in milligrams.

The area of lysis in the controls was 152.0±12, and comparison made with the treated groups.

Lysis was significantly less (p<0.001) in all treated groups. Inhibition was evident immediately after treatment, though delayed until 24 hours on intramuscular administration. Soy bean trypsin inhibitor administered orally or rectally showed significantly greater (p<0.001) inhibition than when given intramuscularly.

The results suggest a direct intraluminal effect and offers options for administration if such inhibitors become of practical use in colorectal surgery.

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After partial gastrectomy for peptic ulcer there is probably an increased risk of gastric carcinoma. We have been unable to show any significant rise in N-nitrosocompounds in patients after gastric resection and so have looked for other aetiological factors.

Nine patients who had previously undergone gastric resection (Bilroth I, n=7; Polya gastrectomy, n=2) were studied over 24 hours while taking the same diet. Hourly nasogastric aspirates were collected and analysed for pH, total bacteria, total and free bile acid concentration.

Total bile acid concentration in 164 aspirates ranged from 0-36-7 mmol/l. Free bile acids were detected in at least two aspirates in every patient (n=74) but many were below the detection limits of our method. The incidence of free bile acids increased with pH, reaching a maximum between pH 6-7 (n=35) and this correlated well with the presence of bacteria known to deconjugate and degrade primary to secondary bile acids (especially Streptococcus faecalis and Veillonella spp, n=27).

The free bile acids isolated with cholic acid (n=74, range 0-1-88 mmol/l), chenodeoxycholic and deoxycholic acid (n=46, range 0-2-14 mmol/l), and lithocholic acid (n=11, range 0-0-6 mmol/l). The presence of free bile acids and bacteria capable of deconjugating bile in the gastric remnant may be an important factor in the aetiology of gastric carcinoma after gastric resection.

Enterokinase (EK) activity in human bile

D A W Grant, R W Talbot, and J Hermont-Taylor (Department of Surgery, St George’s Hospital Medical School, London) Experimental evidence implicates EK in the initiation of some types of acute necrotising pancreatitis (ANP). The pathway appears to be displacement of EK from proximal intestine into portal blood, carbohydrate dependent uptake by hepatocytes, transfer to bile in active form especially by a damaged liver, and the admixture of EK-containing bile with pancreatic juice in the duct system of the gland. To determine whether this pathway might operate in man, bile was obtained from 16 patients, 14 after operation with intubation of the extrahepatic biliary tree and two with percutaneous intrahepatic catheters. Bile was collected resting as well as after 2 mg intravenous glucagon and up to 700 ml of oral Lucozade with a 14C PEG luminal marker. Enterokinase was recovered from bile, concentrated by 2 cycles of ion-exchange chromatography and assayed by quantifying the specific release of tritiated activation peptides from α-N-[3H]acetyl-tryptosyn. Enterokinase was found in the bile of all 16 patients, the majority in the range 0-2-2 ng/ml; inhibition by specific anti-human EK antibody was complete. Duodenobiliary reflux occurred in only two patients, each after biliary sphincterplasty. Highest EK activity, 6 and 35 ng/ml bile, both occurred in the patients with intrahepatic catheters and total extrahepatic biliary obstruction. The findings suggest that EK may indeed follow this pathway in man and, in appropriate pathophysiological circumstances, may be available to participate in initiating acute necrotising pancreatitis.

Specific chemoprophylaxis against acute gastric erosions using pepstatin and its water-soluble analogues

T F Ford, D A W Grant, B M Austen, and J Hermont-Taylor (Department of Surgery, St George’s Hospital Medical School, London) Work in our department has established that in biopsy homogenates of gastric mucosa bearing acute gastric erosions, 42% of the total available pepsinogen is in the form of free active enzyme compared with only 10% in homogenates of normal mucosa between erosions. Such a finding would suggest that the intramusosal activation of pepsinogen to pepsin may be a causative factor in mucosal destruction and that inhibitors of pepsin (pepstatins) may be of value in its prevention. Acute gastric erosions were induced in rats by controlled haemorrhagic shock in the presence of luminal 100 mM HCl either alone or containing 1-5 mM pepstatin (water insoluble; inhibitory constant: $K_I=5\times 10^{-8}M$), 50 mM acetyl statine (water soluble; $K_I=2\times 10^{-4}M$), or pepstatinyl-glyclyl-lysyl-lysine (P-GKK; water soluble; $K_I=3\times 10^{-6}M$). Erosions were quantified according to their number and size and expressed as an erosion index. The erosion index in the presence of native pepstatin (42±29) and its water soluble derivative acetyl statine (44±17) was not significantly less than in the presence of HCl alone (50±29). Pepstatinyl-GKK did significantly reduce erosion formation (index=6±5, p<0.02). The gastric mucosal uptake of the amphipathic pepstatinyl-GKK molecule has been shown, using radiolabelled derivatives, to produce tissue levels substantially in excess of its $K_I$, unlike either the hydrophobic pepstatin or hydrophilic acetyl statine molecules. Potent water soluble derivatives of pepstatin thus, may be of value in the prevention of this lethal syndrome.

Reflex induced cricopharyngeal dysphagia - pathologic change in muscle biopsies

Robert D Henderson, Hanna Wedad, G V Marryatt, and Maria Kando (Women’s College Hospital, Toronto, Ontario, Canada) There is controversy as to whether reflux induced cricopharyngeal dysphagia is reflex motor incoordination secondary to irritation in the oesophageal body or whether it is because of local inflammation produced by the refluxed bolus. This has been investigated by cricopharyngeal muscle biopsies taken at the time of myotomy and examined by electron microscopy and light microscopy. It was hypothesised that, if local muscle irritation was the cause, then muscle degenerative changes would be present. Twenty-four patients were treated by cricopharyngeal myotomy for dysphagia. All had severe symptoms unresponsive to conservative management and all had been investigated by radiology, manometry, pH, and endoscopy. Muscle biopsy was obtained after completion of a cricopharyngeal myotomy under local anaesthesia. Preoperative studies showed radiologic reflux in all patients. Manometrically, cricopharyngeal incoordination was present in 17 of 22 patients. Ultrastructure examination showed increased mitochondria with aberrant forms. The most striking feature was the presence of Nemeline rods in 19 biopsies. Other abnormalities included deposition of fat and glycojen and multinucleation of fibres. The five patients without Nemeline rods were clinically atypical; one with distal obstruction, two with dense scar, and one with scleroderma.

Pathology in the cricopharyngeus accounts for patient symptoms and for the motor changes of incoordination. These changes are compatible with local inflammation, secondary to reflux irritation. These findings are the first clear indication that the cricopharyngeal muscle may be irritated directly by reflux and the symptoms and manometric changes may be due to an inflamed cricopharyngeus muscle.
T35
Computerised system for 24 hour oesophageal pH recording in the ambulatory patient

G C VITALE, A R RIMMER, B HUNTER, J PHELAN, F M TULLEY, J CLARK, AND A CUSCieri
(Department of Surgery and Medical Physics, Ninewells Hospital and Medical School, Dundee, Scotland) A system for ambulatory oesophageal pH monitoring under microprocessor control has been developed. Oesophageal pH is measured continuously by either a radiotelemetric pH capsule or a thin direct pH probe. These data are entered directly into the digital memory of a portable microprocessor throughout a 24 hour test period during which time the patient may be at home, work, or in hospital. On completion of testing, the data are transferred to an Apple computer for immediate printout, plotting and analysis of results; an initial 24 hour graph is obtained showing time of day vs actual pH.

Oesophageal pH testing under microprocessor control allows continuous evaluation of the quality and range of incoming data. Changes in recording format can be programmed to occur with observed pH trends. Communication to the patient of signal loss or system failure is possible through interactive liquid crystal display.

Twenty-four hour oesophageal pH recording has been performed using asymptomatic volunteers and known oesophageal reflux patients. Differences have been noted in frequency and duration of reflux events and their relationship to sleep/position, work, and meals. A subset of patients with possible alkaline reflux pathology has been identified. The technique has wide application for clinical, veterinary, and industrial use on a small, portable device for prolonged pH monitoring.

T36
Dysphagia complicating hiatal hernia repair

R D HENDERSON AND G V MARRYATT (Women's College Hospital, Toronto, Ontario, Canada) After surgical management of reflux, dysphagia may be a continuing or added problem. Radiology alone may not diagnose the problem and only by careful evaluation can a cause be found. In a series of 208 patients treated surgically for a recurrent hiatal hernia, 34 (16.3%) presented with dominant dysphagia.

Before their original operation, 29 had been correctly diagnosed as reflux; however, five were incorrectly diagnosed (four DES and one achalasia) and treated by myotomy and hernia repair. The original operation was Nissen (14); total fundoplication gastroplasty (TFG) (3); Belsey (7); partial fundoplication gastroplasty (PFG) (4); myotomy (5); and unnamed hernia repair (1).

Evaluation by history indicated that dysphagia resulted from the operation (17) and preceded but was worsened by surgery (17). Radiology showed reflux, recurrent hernias, diverticulae or stasis in 14 (41.2%); more importantly, however, 20 patients were called normal. Positive manometric and pH findings of reflux, hernia recurrence, intact HPZ with myotomy, increased wrap length, and scleroderma were present in 23 (68%). Endoscopic stasis, reflux, ulceration, or stricture were present in 17 (51.5%).

The aetiology of dysphagia was diagnosed in all patients reflux stenosis (9); tight or long Nissen (15); muscle injury (3); inappropriate myotomy with reflux (3); myotomy with over competent repair (2); and early Nissen intussusception (2).

Surgical correction was by TFG (32), Nissen (1), and colon interposition (1). In four, the myotomy was closed. Complete follow up averages 3-9 years. There is one anatomic recurrence, 28 were asymptomatic, and five are much improved but have minor persistent dysphagia. Only by complete investigation can the cause of the dysphagia be recognised and treated.

T37
Impaired vagal responses in reflux oesophagitis

A L OGLVIE AND M ATKINSON (University Hospital, Queens Medical Centre, Nottingham) The lower oesophageal sphincter response to increased intragastric pressure is mediated by a vagovagal reflex. In 62 of 83 patients with reflux oesophagitis this response was impaired. Fifty-seven of the 83 patients underwent a standard acid perfusion test. The time to the onset of pain was shorter in those patients who had a normal sphincter response than in those who had an impaired response (p<0.001).

The time to the onset of disordered motility was similar in the two groups suggesting a defect in vagal afferent function in the impaired sphincter response group. Vagal efferent function was assessed by the gastric secretory response to insulin induced hypoglycaemia in a combined insulin/pentagastrin test using a phenol red marker. The ratio of the acid output after insulin to that after pentagastrin was used as a measure of the percentage of parietal cells with an intact vagal supply. The ratio was greater than 70% in all 10 patients with an unoperated duodenal ulcer, but was less than 70% in 15 of 32 patients with reflux oesophagitis.

There was no correlation between impairment of the sphincter response and a low insulin/pentagastrin ratio. These findings suggest that in reflux oesophagitis, impairment of either afferent or efferent vagal fibres may occur, and that dysfunction of either may lead to loss of lower oesophageal sphincter control.

T38
Management of gastroesophageal reflux after gastric surgery

R D HENDERSON AND G V MARRYATT (Women's College Hospital, Toronto, Ontario, Canada) Previous gastric surgery complicates the surgical management of gastroesophageal reflex. Bile gastritis may be an associated problem and some authors have recommended bile diversion as the sole operative approach in patients with Billroth II gastrectomy. In the present study of 125 patients, all had surgical reflux control and bile diversion was added only in those with significant bile gastritis. Previous surgery included 66 hernia repairs; 20 Billroth I; 44 Billroth II (four with Roux-en-Y); 60 vagotomy and drainage; and one oesophagogastronomy. Preoperative investigation included radiology, manometry with pH, and endoscopy. Ninety had a hernia repair only. Further gastrectomy was added in eight patients, four had a pyloroplasty, and 19 required bile diversion because of bile gastritis. Hernia repair by Belsey (18) and partial fundoplication gastroplasty (PFG) (42) was used initially; however, 27 had continued reflux. Four had continued gastritis, including two with bile diversion (follow up seven to nine years). Total fundoplication gastroplasty (TFG) was used in 65 patients. None has clinical or radiological reflux; three have moderate dysphagia, and four persistent gastritis. The four with gastritis include one Billroth I, two Billroth II with bile drainage, and one vagotomy and pyloroplasty. Reflux control is more difficult to achieve in patients with previous

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gastric surgery and a total fundoplication is necessary. Of the eight with continued gastritis, four had had bile diversion. In the majority of patients bile diversion was not necessary.

This approach of hernia repair and selected bile diversion has proved effective in surgical management of reflux after gastric surgery.

COST BENEFITS
T39–T42

T39

Incompletely and completely healed duodenal ulcers outcome in maintenance treatment: a double blind controlled study

P PAOLUZI, G RICOTTA, F RIPOLI, F PROIETTI, R CARRATU, AND A TORSOLI (GI Unit, University of Rome, Italy) After eight weeks’ treatment with cimetidine (CMT 1-2 g/day), up to 30% of uncomplicated duodenal ulcer (DU) patients show incomplete lesion healing at endoscopy with residual linear, irregular or macular (salami) erosions. The aim of this study was to investigate the clinical and anatomical outcome of incompletely vs completely healed DU. A six months double blind controlled study was performed in 107 asymptomatic DU patients after endoscopic assessment of complete (CH) or incomplete (IH) healing on CMT treatment. Patients were stratified according to healing and randomly allocated to CMT (200 mg at lunch, 400 mg at bedtime) or placebo (PL). Endoscopic examinations were performed after six months or when symptoms recurred. Twenty patients dropped out, nine on CMT and 11 on PL. Eighty-seven patients completed the trial. Fifty-six patients showed complete healing at initial endoscopy, 30 of whom belonged to the CMT group. Of the 31 patients with incomplete healing, 15 were undergoing CMT treatment. Ulcers recurred in six of 30 CMT (CH) patients (16-6%) and in eight out of 15 CMT (IH) patients (53-3%). In the placebo group, ulcers recurred in 14 out of 26 CH patients (53-8%) and in 14 out of 16 IH patients (87-5%). Irrespective of treatment, patients with IH ulcers show a significantly higher recurrence — that is, ulcer crater — in comparison with patients with CH ulcers (p=0-005, 71-% vs 33-9%). Irrespective of healing, ulcer recurrence in patients treated with CMT is less frequent than those on PL (p<0-001, 28-9% vs 66-7%). We conclude that in order to avoid a high DU recurrence rate maintenance treatment should start only after the assessment of a complete endoscopic healing of duodenal lesions.

T40

Failure of increased use of endoscopy to influence the complication rate of peptic ulcer disease

G E HOLDSTOCK AND S COLLEY (Southampton General Hospital, Southampton) In order to assess the effects of the increased use of endoscopy on the complication rate of peptic ulcer disease, we have compared the hospital admission rates for peptic ulcer in three District General Hospitals in Wessex with differing endoscopic practices. In Centre A there is an open access GP endoscopy service, in Centre B a freely available hospital-based service, and in Centre C a limited hospital service only. The annual number of endoscopies performed in these centres was 1130, 540, and 150 per 100 000 population served. The mean admission rate per year for peptic ulcer (total with perforation or with haemorrhage) was obtained from the Hospital Activity Index for five years before the increased use of endoscopy (1968–72) and for five years after (1976–80). Admission rates for DU (total) over these two periods was 45-6 vs 49-4 for Centre A, 64-6 vs 64-7 for Centre B, and 47-4 vs 42-6 for Centre C. The equivalent values for perforated DUs were 9-1 vs 11-2, 9-0 vs 7-5, and 6-8 vs 7-1 respectively and those for bleeding DUs 8-9 vs 12-5, 8-0 vs 7-7, and 5-0 vs 5-6. Similar results were obtained for gastric ulcer and its complications. Thus, there was no evidence that the increased numbers of endoscopies performed consequent to the introduction of a GP open access service influenced the complication rate of peptic ulcer disease. The reason for this failure became evident on review of patients admitted with these complications, as only a small proportion had visited their GPs in the three months before hospital admission. These findings suggest that more critical studies on the benefits of the increased use of endoscopy are required.

T41

Improving the cost-effectiveness of open access endoscopy

J MANN, M HARMAN, D MACHIN, AND G HOLDSTOCK (Department of Medicine and Medical Statistics, Southampton General Hospital, Southampton) We have previously suggested that the introduction of an open access GP endoscopy service results in many unnecessary examinations being performed. This study investigates possible means of preventing this. Two hundred and thirty-five patients referred by their GP were interviewed and 77 variables recorded. These were analysed by computer, using several different methods, to see which best discriminated between those with major pathology (ulcers, cancers, oesophageal strictures, n=48) and those without. The only features which discriminated between these two groups were increasing age, history of vomiting, sex, smoking, and a history of peptic ulcer. Other features, notably the nature and duration of pain, response to drugs, and weight loss did not. From the positive variables a scoring system was devised and using it a 60% reduction in investigation results would still result in 79% of the pathology being detected and a 30% reduction in 98%. This system, which can be simplified for easy use, was compared with simply dividing patients into those with the positive discriminating factors — for example, by excluding patients under 55 a 54% reduction in examination results in 70% of pathology being found and excluding non-smokers under 55 resulted in 92% of pathology being discovered with a 29% reduction in endoscopies. If these observations are confirmed in further prospective studies it will be possible, by using either system, to make optimum use of limited resources and to more accurately assess individual priority. Further studies on these lines would improve cost-effectiveness of endoscopy in general and make an open access system more feasible.

T42

Cost analysis of outpatient follow up of ulcerative colitis, Crohn’s disease, uncomplicated gall stones, and chronic active liver disease

A MARTIN, G GURRIERI, G C STURNIOLO, AND R NACCARATO (Cattedra di Gastroenterologia, Clinica Medica I, Policlinico Universitario, Padova, Italy) In recent years, the costs of medical care have grown enormously. The critical economic crises of many European countries will require, in the near future, a reduction in the costs of medical care. If our standards are to be
improved, or even only kept at the present level, our resources will have to be used in a more rational manner. The first step, therefore, is to collect data on the various components of the total cost of medical care. We studied prospectively for one year four groups of 20 patients each, randomly selected from our list of outpatients with ulcerative colitis (UC), Crohn’s disease (CD), uncomplicated gall stones on bile acid treatment (gall), and chronic active liver disease (CALD). The total cost of one year’s follow up in pounds sterling (2288 lire = £1.00) was 358-39 (UC), 802-88 (CD), 627-18 (gall) and 146-85 (CALD). The cost analysis of the various components showed that in UC and CD the cost of hospital stays accounted for 55 and 87% of the total cost, respectively, while in gall drug therapy accounted for over 86% of the total cost. Of the various serum biochemical tests 75 to 93% gave consistently negative results. ‘Indirect’ costs were assessed only approximately but may be as high as the double of the ‘direct’ costs we calculated. Our study provides data on which calculations on the economic cost of outpatient medical care of four digestive diseases can be attempted. It also indicates areas (serum-biochemical tests and bile acid treatment) where costs can be reduced.

DUODENAL ULCER

T43-T46

T43

Duodenal mucosal prostanoids in duodenal ulceration

C L Smith, K Hillier, S J Colley, and R Jewell (Departments of Medicine and Clinical Pharmacology, Southampton University Medical School, Southampton)

Previous work into the changes in mucosal prostaglandin concentrations in peptic ulceration has been mainly on gastric ulceration and has been in general restricted to either prostaglandin E₂ in tissue or secreted into gastric juice and using bioassay. Prostaglandin analogues have been shown to accelerate ulcer healing and thus a defect in prostanooid production may be present in active ulceration. We have therefore studied the changes in prostaglandins E₂, F₃α, and 6-keto-F₂α synthesising capacity as measured by radioimmunoassay in duodenal mucosa from eight subjects with duodenal ulceration compared with seven controls. The concentrations of prostaglandin E₂ in duodenal ulceration (mean ± SE pg/mg protein 32-4±4-6) were not significantly different from the controls (mean 30-1±6-08). The levels of F₃α in ulceration (mean 8-1±1-06) were significantly (p<0-01) lower than controls (mean 14-4±1-48) as were the concentrations of 6-keto F₂α (mean 12-5±2-3 in ulceration compared with 28-2±4-6 in controls) (p<0-05). These findings show a significant defect in the capacity of duodenal mucosa associated with active duodenal ulceration to synthesise cytoprotective prostanoids.

T44

Do the suprarenals play a role in duodenal ulcer disease?

Anna Athow, Anna Sewernjak, and M R Lewin (Department of Surgery, Faculty of Clinical Sciences, University College, London, The Rayne Institute, London)

Vagal drive during insulin testing has been shown to be significantly higher in patients with duodenal ulcer (DU) when compared to patients with duodenal ulcer not receiving therapy (ATHOW, JEWELL and M R WORMSLY, 1982). This increased sensitivity (r=0.537, p<0.001) and DU patients than the standard insulin test is a new finding. Further investigation is required to elucidate whether it has a bearing on the formation of the ulcer itself.

T45

Natural history of asymptomatic duodenal ulcers

E J S Boyd, J A Wilson, and K G Wormsley (Department of Therapeutics, Ninewells Hospital, Dundee)

Asymptomatic duodenal ulcer recurrences are commonly found during endoscopic follow up of patients receiving long term maintenance therapy, and, occasionally, in patients who are receiving no active therapy. We monitored the clinical and endoscopic progress of 35 patients in whom an asymptomatic duodenal ulcer had been found during routine endoscopic follow up. Nine of the patients were receiving no treatment, or placebo; 15 were receiving ranitidine 150 mg nocte; and 11 were receiving cimetidine 400 mg nocte. Treatment was left unchanged when the ulcer was diagnosed. All patients were endoscoped at least once (and in seven cases twice) during subsequent follow up of the asymptomatic ulcer.

Seven of the nine ulcers on placebo remained endoscopically unchanged (median duration of follow up 10 weeks; range four to 44 weeks) and two healed spontaneously. Four of the seven became asymptomatic four to six weeks after diagnosis. Twelve of the 15 ulcers on ranitidine remained unchanged (median follow up 11-5 weeks; range four to 52 weeks) and three healed spontaneously. Four of the 12 became symptomatic four to 20 weeks after diagnosis. Eight of the 11 ulcers on cimetidine remained unchanged (median follow up 27 weeks; range four to 52 weeks) and three healed spontaneously. Three of the eight became symptomatic 16-28 weeks after diagnosis.

We conclude that asymptomatic ulcers are persistent and rarely undergo spontaneous healing. Symptoms only occurred in about one third of patients and were more common in patients receiving no therapy (44%) than in those on active maintenance therapy (27%). Median time to development of symptoms after diagnosis is also shorter in patients receiving no therapy (four weeks) than on active treatment (16 weeks). As they are persistent, asymptomatic ulcers present a clinical problem, the most satisfactory management of which is not clear.
T46 Duodenal ulcer (DU) in Bengali immigrants in East London

D Levine, S Evans, K Woods, and M Beer (Departments of Medicine and Epidemiology, The London Hospital Medical College, Whitechapel, London) Although many reports suggest geographic variations in occurrence of DU, few have compared ethnic groups in one locality. Distribution of DU by age and sex may be a better guide to ethnic differences than crude incidence or prevalence, and could help to identify aetiological factors. We have compared Caucasian and Bengali DU patients in an inner London Borough. Population structures were calculated from the 1981 Census. Duodenal ulcer in Bengali women seems to be rare. For endoscopically or radiologically diagnosed DU the population-adjusted male:female ratios were 19:1 and 2:9:1 for Bengalis and Caucasians respectively. To compare gastric secretory function in healthy Bengali and Caucasian women we have measured plasma pepsinogen I (PGI) by radioimmunoassay, having shown this to correlate well with pentagastrin-stimulated maximal acid output (MAO) in 30 unselected patients (r=0.716, p<0.002). There was no significant difference in PGI between Bengali (n=19) and Caucasian women (n=27). Antenatal questionnaires showed that only 1-1% of Bengali women smoked cigarettes compared with 20-6% of Caucasian women. Mean parity of Bengali women was 2.5 times that of Caucasians. Duodenal ulcer in Bengali men was, however, common, and over a two year period, 56% of all DUs diagnosed below the age of 30 were in Bengali men, who comprise only 11% of the male population of the borough. Mean MAO, corrected for age, height, and weight was lower in Bengali than Caucasian men with DU (28.1±2.25 g/24 h) vs 35.6±0.71 g/24 h (n=199) mmol/l (±SE), p<0.002). We conclude the rarity of DU in Bengali women may be related to non-smoking and multiparity. The apparent excess of DU in young Bengali men is so far unexplained.

F Shahan, A D Befu, J A Denburg, and J Bienenstock (introduced by R Hunt Departments of Medicine and Pathology, McMaster University, Hamilton, Ontario, Canada) Recent reports suggesting that the actions of certain neuroenteric peptides may be mediated in part by mast cell secretion could have important implications for gastrointestinal motility and secretion. Evidence for a mast cell-hormonal interaction, however, is based on studies using peritoneal or cutaneous mast cells. As intestinal mucosal mast cells (MMC) are functionally distinct from peritoneal mast cells (PMC) we compared the effects of several gut hormones on histamine secretion from the two mast cell types in the rat. Mucosal mast cell hyperplasia was induced in rats infected with the nematode, Nippostrongylus brasiliensis and were isolated by collagenase digestion from the small intestine. Peritoneal mast cells were obtained by lavage. Somatostatin, vasoactive intestinal polypeptide, substance P, and neurotensin had a potent secretagogue effect (10^{-7} - 10^{-4} M) on PMC which was temperature-, energy-, and calcium-dependent. Mucosal mast cells from the same animal were also responsive to substance P but were refractory to the other agents. The differential effect was not an artefact generated by the MMC isolation procedure as PMC treated similarly retained their hormonal responsiveness. Furthermore, disodium cromoglycate inhibited substance P-induced secretion from PMC but had no effect on MMC. This study supports the concept of neurocrine control of mast cell function and provides further characterisation of the functional differences between PMC and MMC.

T47 Intestinal mucosal mast cell and its response to gut hormones

D F Evans, G E Foster, and J D Hardcastle (Department of Surgery, University Hospital, Nottingham) In man the fasting migrating motor complex (MMC) is disrupted by feeding for a much more variable period (200-700 minutes) than that seen in laboratory animals, a fact that may be because of the varying nature of meals fed by different workers. Having previously described a relationship between the fat content of a meal and disruption of the MMC we now report a study of the calorific value of a meal on the MMC in 20 volunteers. Linked radio-telemetry capsules were used as previously described to record pressure in the gastric antrum and proximal jejunum. After positioning the capsules fasting patterns were confirmed. Twenty minutes after a phase III activity front had propagated past the recording sites a meal of either 100, 250, 450, or 800 kcal was given and recording continued until fasting patterns were seen again. The MMC was disrupted by all the meals, the period of disruption being significantly greater for each increase up to 450 kcal. (Median disruption 216, 292, and 396 minutes for 100, 250, and 450 kcal, p=0.01 and 0.05 between 100 and 250 kcal and 250 and 450 kcal.) The further increase to 800 kcal showed no significant change. (Median 434 minutes, p=NS.) The period of disruption of the MMC by food is dependent on the calorific value of the meal. The size and composition of test meals, therefore, must be considered when comparing results of motility studies in man.

T48 Disruption of the human migrating motor complex by meals of varying calorific values

D J Evans, G E Foster, and J D Hardcastle (Department of Surgery, University Hospital, Nottingham) In man the fasting migrating motor complex (MMC) is disrupted by feeding for a much more variable period (200-700 minutes) than that seen in laboratory animals, a fact that may be because of the varying nature of meals fed by different workers. Having previously described a relationship between the fat content of a meal and disruption of the MMC we now report a study of the calorific value of a meal on the MMC in 20 volunteers. Linked radio-telemetry capsules were used as previously described to record pressure in the gastric antrum and proximal jejunum. After positioning the capsules fasting patterns were confirmed. Twenty minutes after a phase III activity front had propagated past the recording sites a meal of either 100, 250, 450, or 800 kcal was given and recording continued until fasting patterns were seen again. The MMC was disrupted by all the meals, the period of disruption being significantly greater for each increase up to 450 kcal. (Median disruption 216, 292, and 396 minutes for 100, 250, and 450 kcal, p=0.01 and 0.05 between 100 and 250 kcal and 250 and 450 kcal.) The further increase to 800 kcal showed no significant change. (Median 434 minutes, p=NS.) The period of disruption of the MMC by food is dependent on the calorific value of the meal. The size and composition of test meals, therefore, must be considered when comparing results of motility studies in man.

T49 The ileal brake: ileal fat slows small bowel transit and gastric emptying in man

A Macfarlane, R Kinsman, N W Read, and S R Bloom (Clinical Research Unit, Royal Hallamshire Hospital, Sheffield) Recent studies have suggested that the absorption of a meal may be limited by small bowel transit time. We now report experiments which indicate that the presence of unabsorbed fat in the ileum may help to maximise absorption by delaying the passage of food material through the stomach and small intestine. The small bowel transit time (SBTT) of 100 ml of 10% lactose infused at the ligament of Trietz was measured by breath hydrogen excretion in paired studies performed in eight healthy volunteers, during infusion at a rate of 1 ml/min of 100 ml fat emulsion (Intralipid) or the same volume of isotonic saline into the ileum (205 cm from the teeth). Ileal infusion of fat significantly delayed SBTT (136±23 min) compared with infusion of saline (50±3 min, p<0.001). This delay was not associated with any significant alteration in plasma concentrations of neurotensin or enteroglucagon. Infusion of fat into the jejunum or colon had no effect on small bowel transit time. In a separate series of paired experiments carried out in five volunteers, infusion of intralipid into the ileum of five volunteers significantly delayed the passage of a solid test meal (mashed potato, baked.
beans, and Frankfurter sausages) labelled with 25 μCi 99mTc sulphur colloid through the stomach (t gastric emptying: 184±33 (fat) vs 79±10 min (saline); p<0.02), and small intestine (SBTT: 456±29 (fat) vs 245±32 min (saline); p<0.02). The results support the existence of an ileal brake regulating small bowel transit and possibly absorption.

T50
Inhibition of jejunal motility by ileal fat infusion in man

R C SPILLER, I F TROTMAN, B E HIGGINS, M A GHATEI, Y C LEES, S R BLOOM, J J MISIEWICZ, and D B A SILK (Central Middlesex Hospital and Royal Postgraduate Medical School, London) Delayed small bowel transit and exaggerated postprandial release of the gut hormones entero-glucagon (EG) and neurotensin (NT) have been separately described in fat malabsorption. We have tested the possibility that malabsorbed fat in the ileum exerts a feedback inhibitory control on jejunal motility by studying the effect of ileal infusion of an isotonic, partially digested fat emulsion (10 g in 150 ml over 30 minutes). Fifteen healthy volunteers were intubated with a 5-lumen tube incorporating a 30 cm jejunal study segment AB, and an ileal infusion port which was 170 cm from the mouth. The study segment was perfused with isotonic saline (10 ml/min) and mean transit time from A to B was measured by the dye dilution technique. Preliminary studies (n=5) showed that jejunal transit was stable over a five hour period. Ileal fat infusion significantly prolonged jejunal transit which rose from a control value of 7.0±0.7 min to 14.0±1.1 min (mean ± SEM), n=10, p<0.001. Further studies in which jejunal motor activity was measured manometrically have shown that ileal fat markedly inhibits percent motor activity, which fell to 14.9±2.8% (control 42.0±2.8%). Simultaneously plasma NT concentrations rose, peaking at 58.3±14.5 pmol/l (basal 10±4±2.5) 30 minutes after ileal fat infusion began. Enteroglucagon concentrations rose more slowly plateauing after one hour to 218±37 pmol/l (basal 40±9). Thus the presence of unabsorbed, partially digested fat in the human ileum slows jejunal transit by inhibiting motor activity and this is associated with a gut hormone response similar to that seen postprandially in untreated coeliac disease.

INTESTINAL SECRETION
T51–T54

T51
Effect of prostacyclin on water and electrolyte transport in human jejunum

K J MORTIARY, J O'GRADY, D D ROLSTON, M J KELLY, P D FAIRCLOUGH, M L CLARK, and A M DAWSON (Department of Gastroenterology, St Bartholomew's Hospital, London, and Wellcome Research Laboratories, Beckenham, Kent) Prostacyclin (PGI2) is an arachidonic acid metabolite having many similar properties to prostaglandins. It causes fluid secretion in guinea pig gall bladder, but actually inhibits fluid accumulation and cholera toxin – and prostaglandin - induced secretion in rat small intestine. We report the effect of PGI2 on water and electrolyte transport in human jejunum.

Using a standard technique, 11 subjects were perfused for 210 minutes with a glucose electrolyte solution. In five subjects, the sodium salt of PGI2, reconstituted in glycerine buffer (pH 10.5), was infused intravenously (4 kg/cm/min) from 70 to 150 minutes, causing flushing in all subjects. During the rest of the study period buffer alone was infused. In the other six subjects, buffer was infused throughout the 210 minutes.

PGI2 inhibited jejunal absorption of sodium (p<0.02) and water (p<0.02) by 33% and of chloride (p<0.001) by 50%. Salt and water absorption were still significantly inhibited to a similar degree (all p<0.02) 60 minutes after PGI2 infusion. Glucose, potassium, and bicarbonate transport were unchanged. Thus the jejunum of man behaves differently from rat intestine and resembles guinea pig gall bladder in that PGI2 causes prolonged inhibition of salt and water absorption.

T52
Peptide histidine isoleucine: a secretagogue in human intestine

A A ANAGNOSTIDES, N D CHRISTOFIDES, S R BLOOM, and V S CHADWICK (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Peptide histidine isoleucine (PHI) is a recently discovered peptide from porcine intestine which has sequence homologies with VIP, an established intestinal secretagogue. To study the effects of PHI in human intestine, natural porcine PHI was infused intravenously at 10-7±1.7 pmol/kg/min (mean ± SEM) in normal volunteers during steady state perfusions of the jejunum with an isotonic bicarbonate-electrolyte solution. Plasma PHI concentrations rose to 279±26 pmol/l at 20 minutes, 417±45 at 40 minutes (n=6), and 500±144 at 60 minutes (n=3). After discontinuation of infusion PHI concentrations returned to 114±64 pmol/l at 20 minutes and to undetectable limits thereafter. At these concentrations PHI induced a reversible net secretion of sodium (+18.3±28 vs -117±23 μmol/cm/10 min control; p<0.05) and chloride (+27.5±2 vs -103±15 μmol/cm/10 min; p<0.005) between 20 and 40 minutes. Reduced net absorption or net secretion of fluid (-0.09±0.2 μl/cm/10 min at 40 minutes (n=6) and +0.39 μl/cm/10 min at 60 minutes (n=3) vs -2.0±0.6 μl/cm/10 min in the control period; p<0.05) and potassium were observed during PHI infusion while bicarbonate transport was unaffected (-49±6±21.5 vs -21±5±5 μmol/cm/10 min).

It is concluded that PHI is a potent secretagogue in human jejunum.

T53
Nufenoxole, a new anti-diarrhoeal drug, inhibits water and electrolyte secretion in human jejunum

K J MORTIARY, D D ROLSTON, M J KELLY, P D FAIRCLOUGH, M L CLARK, and A M DAWSON (Department of Gastroenterology, St Bartholomew’s Hospital, London) There is considerable interest in the antisecretory actions of anti-diarrhoeal drugs. Loperamide inhibits secretagogue induced fluid secretion in animal intestine, the effect being blocked by the opiate antagonist, naloxone. Nufenoxole, an isoquinuclidine, is a new orally active drug with an anti-diarrhoeal effect in man at a dose free from cerebral side effects. This study investigates its effect on fluid transport in human jejunum. Six healthy volunteers were perfused with a glucose electrolyte solution containing 0-5 mM dioctyl sodium sulphosuccinate (DSS) to induce jejunal water and electrolyte secretion. After this perfusion, nufenoxole was administered intrajejunally (0-5 mg/kg bolus) to achieve therapeutic plasma concentration. After an interval of 40 minutes, repeat DSS perfusion was performed. Nufenoxole significantly inhibited DSS induced secretion of water (-62.7±26.5 vs +101±8±12.9 ml/30 cm/hour, p<0.005).
sodium ($-8.88 \pm 4.18$ vs. $+16.01 \pm 1.66$ mmol/30 cm/hour, p<0.005), chloride ($-13.11 \pm 3.02$ vs. $+7.23 \pm 0.81$ mmol/30 cm/hour, p<0.005), and potassium ($-1.96 \pm 0.16$ vs. $-1.38 \pm 0.09$ mmol/30 cm/hour, p<0.001). Nufenoxole inhibits DSS induced water and electrolyte secretion in human jejunum, the effect being partially antagonised by high dose naltrexone. These antiseratory properties may contribute to the anti-diarrhoeal action of nufenoxole.

**TS4**

**Peptide histidine isoleucine (PHI) and the Verner-Morrison syndrome**

H DANCYGER, U KLEIN, AND M CLASSEN (Center of Internal Medicine, Department of Gastroenterology, University Clinics, Frankfurt/Main, FR Germany) Peptide histidine isoleucine is a 27 amino acid peptide that has recently been isolated in large quantities from the porcine intestine. Peptide histidine isoleucine has sequence homology to VIP and a similar spectrum of actions and potency (including the stimulation of intestinal secretion). The possibility that PHI is present in tumours producing VIP was therefore investigated. The PHI content of tumour extracts (0.05M acetic acid) was estimated using a previously described radioimmunoassay that was able to detect changes of 2 fmol/tube with 95% confidence. Peptide histidine isoleucine was found to be produced only in those 24 tumours that also produced VIP, while 125 other endocrine tumours produced neither peptide. Twenty-two of the 24 tumours coproducing PHI and VIP were pancreatic in origin (Verner-Morrison syndrome), containing considerable quantities of PHI (105±20 pmol/g, mean ± SEM), whereas the remaining two were ganglioneuromatous (120 and 130 pmol/g). A screen of current plasma samples from patients with endocrine tumours showed that the plasma from all seven patients with increased VIP also contained increased PHI (mean 55±10 pmol/l, controls 6±2 l pmol/l). Fractionation of tumour extracts by high performance liquid chromatography (C18 Bondapak) resulted in the complete separation of VIP and PHI immunoreactivities (VIP eluting much earlier than PHI). Clearly the pathophysiology of the watery diarrhoea syndrome is more complicated than previously thought.

**IMMUNOLOGY**

T55-T58

**TS5**

**Extrahepatic biliary tract is an integral part of the common mucosal immune system in man**

H DANCYGER, U KLEIN, AND M CLASSEN (Center of Internal Medicine, Department of Gastroenterology, University Clinics, Frankfurt/Main, FR Germany) The mucosal lining of the extrahepatic biliary tract contains among other cell types so called basal wandering cells whose nature has remained undetermined up to now. We have characterised these cells by using immunocytochemical techniques.

Acetone fixed cryostat sections of tissue specimens of 10 gall bladders and two bile ducts obtained respectively at operation for cholelithiasis and during Whipple's procedure for pancreatic carcinoma were investigated by applying the Avidin-Biotin-Peroxidase method. Monoclonal antisera to lymphocyte subsets (Ortho: OKT3, OKT4, OKT8, OKIa1) were used at a 1:40 dilution. Appropriate controls were performed. All gall bladders and bile ducts contained lymphocytes in their walls as well as in the surface and glandular epithelium. Whereas the lamina propria lymphocytes were B and T cells (OKT4>OKT8) more than 90% of the basal intraepithelial cells were OKT8+ and only occasional OKT4+ cells were observed. No intraepithelial B cells were found. Analogous to known data in the small intestine we have shown that the human biliary tract contains intraepithelial lymphocytes as well, mainly of the suppressor/cytotoxic phenotype, and should be regarded as an integral part of the common mucosal immune system.

**T57**

**Cytotoxicity of mononuclear cells for autologous colonic epithelial cells in human colonic diseases**

R G SHORTER (Mayo Medical School, Rochester, MN, USA) Using a microcytotoxicity assay, macrophage depleted isolates of mononuclear cells from the colonic mucosa of 25 patients with chronic ulcerative colitis or Crohn's colitis were tested for their cytotoxicity for autologous colonic epithelial cells (ACEC), as were macrophage depleted isolates of MC from the peripheral blood (PBMC). The mean percent cytotoxicity shown by the colonic MC (CMC) was 46.40±2.9 (SEM) at an effector:target of 100:1. Trypsinisation (0-25% for 45 minutes) of aliquots of the CMC reduced the percent cytotoxicity for ACEC to 31-6±0.72 but this was restored by incubating trypsinised CMC in 25% vol/vol heat-inactivated autologous plasma (AP) for one hour at 22°C (mean percent
cytotoxicity = 41.33±5.4). The mean cytotoxicity for ACEC shown by PBMC was 49.63±5.68%; using trypsinised PBMC it was only 4.08±0.96 and became 56.33±3.05% when trypsinised cells had been treated with AP. The effectors in the CMC and PBMC possessed receptors for the Fc portion of IgG. Macrophage depleted CMC from 40 patients with colorectal cancer showed a mean cytotoxicity for ACEC of 19.55±1.83% (E:T, 100:1) which was reduced to 2.30±0.56 after trypsinising the CMC but was not restored by their treatment with AP. The effectors possessed Fc receptors for IgG. PBMC from these cancer patients were not cytotoxic for ACEC (1.44±0.72%) and CMC and PBMC from six patients with other colonic diseases, including three with active chronic diverticulitis, also showed no cytotoxicity for ACEC. Perhaps the cytotoxicity in IBD has pathogenetic significance but a role for that in the cancer group, which seems to involve different mechanisms, is elusive.

T58 Identification of the hepatic asialglycoprotein receptor (hepatic lectin) as a component of liver specific membrane lipoprotein (LSP)

I G MCFARLANE, B M MCFARLANE, G N MAJOR, AND ROGER WILLIAMS (The Liver Unit, King's College Hospital, Denmark Hill, London) The liver specific membrane lipoprotein (LSP) is a target for antibodies in the sera of patients with a variety of liver conditions in which hepatic parenchymal inflammation is a factor. Previous studies have shown that LSP is a large, lipid associated complex related to the plasma-membrane (PM) and containing at least two liver specific antigens (one of which is species cross reactive) but its relationship to the PM and the identity of its constituent antigens has not been established. The present study examined whether LSP contains the hepatic receptor for asialoglycoprotein as this receptor (hepatic lectin) is specific to the liver, is present on the hepatocyte plasma membrane, and is found in several mammalian species. Eight guinea-pig anti-LSP antisera (four antihuman and four antirabbit LSP) were found to react by enzyme-linked immuno sorbent assay (ELISA) and/or radioimmunoassay (RIA) against affinity purified human and rabbit hepatic lectin. Binding of the antisera to 125I-lectin in the RIA was inhibited by unlabelled lectin and by LSP but not by a 20 000 fold excess of whole kidney homogenate. The results indicate that hepatic lectin is a liver specific, species cross reactive antigen that comprises about 0.25% of the protein in LSP. If anti-LSP in patient's sera includes antibodies reacting with the lectin then, by analogy with the ACR-antibodies in myasthenia gravis, these might be important in pathogenesis.

The British Society of Gastroenterology

T59 Practical problems of oesophageal sclerotherapy

J D R ROSE (Department of Gastroenterology, Llandough Hospital, Penarth, S Glam) Despite the accepted value of oesophageal sclerotherapy little practical guidance is available on the site and frequency of injection, the effect of sclerosant on blood, the likelihood of variceal recurrence, and the frequency of follow up. From studies on 53 patients treated by sclerotherapy and in vitro work on sclerocants, guidelines are proposed.

A radiologically controlled trial of intravariceal vs paravariceal injection showed intravariceal to be more effective and, by ensuring intravariceal injection for all treatments in 10 patients, sclerosis of varices was achieved more rapidly than by free hand injection. Rebleeding was related to the number of large varices, which required more injections. Multiple large varices, therefore, require frequent treatment. Should extravasation of sclerosant occur, ulceration may develop over several days, and injections should, therefore, be no more often than every three to four days.

Modern sclerosants are detergents whose activity is well preserved in blood. Haemolysis, increased blood viscosity and inhibition of clotting factors can be demonstrated in vitro: but after 8–12 ml of intravariceal sclerosant there was only a transient fall of haptoglobins, rarely exceeding 1 gm/l.

After successful sclerosis, approximately half the patients can be expected to have a recurrence of varices within the first year: none have relapsed thereafter. Three monthly endoscopic follow up is sufficient in the first year and can then be reduced.

T60 Serum anti-colon antibodies, ulcerative colitis, and sclerosing cholangitis

R W CHAPMAN, W SELBY, H SHEPHERD, S SHERLOCK, AND D P JEWELL (Department of Gastroenterology, John Radcliffe Hospital, Oxford, and Department of Medicine, Royal Free Hospital, Hampstead, London) The aetiology of primary sclerosing cholangitis (PSC) is unknown, but it is closely associated with ulcerative colitis (UC). Serum anti-colon antibodies (SACA), cross reacting with proliferating bile ducts, have been reported in some patients with UC but no studies have been performed in PSC.

The frequency of SACA has been measured in 20 patients with PSC and UC; 77 patients with UC without PSc; 15 patients with PSC without UC; and 20 normal controls. Serum anti-colon antibodies were detected using indirect immunofluorescence and immunoperoxidase techniques on normal human colon. Antibodies to bile duct epithelium were detected using obstructed human liver. Tissue typing of PSC patients was performed using a microcytotoxicity assay.

The frequency of SACA was markedly increased in PSC patients with UC, 12/20 (60%) compared with UC patients 13/77 (17%) and PSC patients without UC 1/15 (7%) (x²=17.9; p<0.001). SACA were almost entirely of IgG and IgA classes in all groups. SACA were not found in control sera. Eighty per cent of patients with PSC and UC who had SACA were HLA-B8 positive, whereas only 50% with negative antibodies had this phenotype.

Serum from some patients with PSC and SACA reacted with bile duct epithelium. Results of absorption experiments will be reported. Cross reacting anti-colon antibodies in susceptible patients with UC may play an important role in the pathogenesis of PSC.

T61 Which electrode? A consumer's guide to endoscopic electrocoagulation of upper gastrointestinal bleeding

C P SWAIN, T N MILLS, E SHEMESH, JULIA M DARK, S G BOWN, T C NORTHFIELD, P B COTTON, AND P R SALMON (Departments of Gastroenterology, University College Hospital, St James' Hospital, and The Middlesex Hospital, London) Several inexpensive endoscopic methods of electrocoagulation appear to promise...
effective control of upper gastrointestinal haemorrhage. We compared four types of electrode: dry monopolar – Cameron-Miller (M), liquid monopolar – Storz (L), bipolar – Bicap ACMI (B), and Heater Probe – Seattle (H). The physics and engineering performance of these electrodes was studied using computerised monitoring of energy deposition and their efficacy and safety was tested in a randomised study in 140 experimental canine gastric ulcers.

At optimal pulse settings 20J (M), 70J (L), 17J (B), 15J (H), effective haemostasis was achieved in all ulcers, the mean number of pulses being M5, L6, H6, B11, the first three requiring significantly (p<0.01) less pulse than B. Relative safety of the electrodes was assessed by comparing the incidence of full thickness damage at histology, B24%, H26%, L58%, M69%, B and H proving significantly (p<0.01) safer than L and M. Sticking was assessed as H>B>M>L. Reproducibility of energy deposition and its insensitivity to extreme angulation was assessed as L>B>M (H is preset). The bipolar probe appeared safe but required an excessive mean number of shots to achieve haemostasis. The heater probe was almost as effective as monopolar electrocoagulation used dry or with conducting film of liquid but caused significantly less full thickness damage. Despite its greater tendency to stick than the other devices, the heater probe appeared the most promising of the endoscopic electrodes tested.

T62 Does the gall bladder function as a pump or as a bellows?

A LANZINI, R JAZRAWI, AND T C NORTHFIELD (Department of Medicine, St George’s Hospital Medical School, London) The gall bladder (GB) is conventionally thought of as a pump which contracts progressively after meals. Gamma camera studies using 99mTcHIDA show continuous ejection, but simultaneous use of an absorbable γ-labelled bile acid suggests that refilling occurs with emptying. To elucidate this process quantitatively, we have modified an intestinal perfusion method which includes intravenous infusion of ICG (hepatic bile marker), adding intravenous bolus of 99mTcHIDA (GB bile marker) to obtain quantitative measurements of absolute GB filling and emptying, in addition to semi-quantitative net measurements. We studied five gall-stone patients with radiologically functioning GBs after an evening meal, sampling every 10 minutes for one hour and hourly overnight. In all 10 minute postprandial samples there was absolute emptying of GB (range 2–20%, with mean cumulative emptying of 49% over one hour); in 70% of the 10 minute samples net filling occurred, as 48±10% of hepatic bile was diverted into GB. Absolute GB filling was measured in two patients, and indicated that 86% and 100% hepatic bile was diverted into GB postprandially. In the overnight hourly samples, absolute GB emptying (5±2%) occurred in 46% of the samples, in spite of net GB filling (62±24%). We conclude that postprandially GB acts as a bellows with alternating filling and emptying, and that all hepatic bile may have to enter GB before reaching duodenum. During overnight fasting, net GB filling occurs all the time, and slight emptying half the time.

T63 Gluten sensitivity in rats seen as defects in intestinal permeability to labelled sugars

D R FRASER AND J S SANDHU (introduced by G Neale) (Dunn Nutritional Laboratory, University of Cambridge, and Medical Research Council, Cambridge) As niacin-deficient rats show disturbed intestinal function with an increased absorption of non-digestible dietary macromolecules, a permeability assay was devised to investigate this phenomenon. The differential absorption of 3H-cellobiotol and 14C-mannitol was determined by measuring their urinary excretion over five hours after dosing the labelled sugars to rats by gastric intubation. Increased absorption of cellobiotol and decreased absorption of mannitol were found in niacin-deficient rats compared with controls. This altered absorption pattern, however, occurred only if niacin-deficiency developed while feeding a cereal-containing diet.

To test whether this sensitivity to dietary cereal was specific to niacin deficiency, the intestinal permeability assay was performed on rats with enteropathy caused by other procedures. These included treatment with the cholesterol-synthesis inhibitor, Triparanol, the cytostatic drug methotrexate, and the detergent cetrizime. Although all three treatments modified absorption of the labelled sugars, only the Triparanol-treated rats showed increased uptake of cellobiotol and decreased uptake of mannitol. As with niacin deficiency this change was dependent on feeding dietary cereal. The noxious effect of cereal was most severe with wheat, followed by rye, barley, and oats, while maize was the least effective. Rice, and the non-cereal, soya-bean, were inactive.

Gluten fed in a non-cereal diet caused the greatest change in permeability to the labelled sugars. It is concluded that with mucosal cell dysfunction in rats, the intestinal mucosa is susceptible to an interaction with dietary gluten resulting in increased permeability to ‘non-absorbed’ molecules such as cellobiotol.

T64 Beneficial effect of moderate alcohol intake on high-density lipoprotein cholesterol and the cholesterol saturation of bile

J R THORNTON AND K W HEATON (University of Bristol Department of Medicine, Bristol Royal Infirmary, Bristol) Bile which is supersaturated with cholesterol is the fundamental prerequisite for cholesterol gall-stone formation. High density lipoprotein (HDL) cholesterol is strongly protective against coronary artery disease. We have previously shown an inverse relation between bile cholesterol saturation and plasma HDL cholesterol. This suggests that factors which affect one of these parameters might affect the other in the opposite way. Alcohol probably raises HDL cholesterol but its effects on bile are unknown. We predicted that it would reduce bile cholesterol saturation. To test this hypothesis, 13 healthy volunteers with a low initial alcohol consumption (mean assessed intake = 2.6 g/day) drank a half bottle of white wine (39 g alcohol) daily for six weeks, followed by six weeks’ abstention from alcohol. Bile and blood were sampled initially and after each six week period. Dietary intakes were monitored by a dietitian and did not change significantly.

Plasma HDL cholesterol rose from 1.05±0.06 to 1.24±0.08 mmol/l after alcohol (p<0.01) and fell to 1.04±0.06 after abstention (p<0.005). Conversely, the cholesterol saturation index of bile fell from 1.31±0.06 to 1.08±0.06 after alcohol (p<0.001) and rose to 1.27±0.09 after abstention (p<0.01). Bile saturation index and HDL cholesterol were inversely correlated (r=-0.558, p<0.001).
The data confirm a biochemical link between coronary artery disease and cholesterol gallstones and suggest that moderate alcohol intake has a protective effect against both diseases.

T65
Restorative proctocolectomy with ileal reservoir for ulcerative colitis and familial adenomatosis: clinical results in 62 patients followed for up to six years

R W MOTSON, M PESCATORI, R J NICHOLLS, AND THE LATE A G PARKS (St Mark's Hospital and the London Hospital, London) Few patients relish the prospect of a permanent incontinent ileostomy. A variety of techniques have been developed to avoid ileostomy including ileorectal anastomosis, continent ileostomy and, more recently, ileal reservoir with ileoanal anastomosis. With this procedure there is no abdominal stoma and all colonic and rectal mucosa is removed. Sixty-two patients (38 men, 24 women, age 31±11 years, 40 with ulcerative colitis, 11 with familial adenomatosis) have had a reservoir operation with no operative death. Fifty-five had their ileostomy closed and have been followed for a mean of 22 months (one month to six years). Three patients have had their reservoir removed. General operative complications were similar to other major colorectal procedures except for pelvic sepsis, which occurred in 12 cases (19%) and was associated with some breakdown of the ileoanal anastomosis in 11. There was no sexual dysfunction related to operation in any of 38 male patients. Two women patients had disturbed menstruation. Bowel frequency was 3-6±1/day, similar to patients with ileorectal anastomosis. Nine patients (17%) experienced some urgency. Eighteen (35%) evacuated spontaneously, 19 always used a catheter, and 16 (31%) sometimes used a catheter and sometimes evacuated spontaneously. Thirty-three patients had completely normal continence, nine noticed occasional staining, seven had troublesome incontinence but six of these were only symptomatic at night. Thirteen patients had perianal soreness. All 52 patients, including those with leakage, preferred their present state to an ileostomy.

It is concluded, therefore, that ileal reservoir with ileoanal anastomosis provides a satisfactory alternative to proctocolectomy and avoids a permanent stoma.

GASTRODUODENAL
F1–F8

F1
Role of endogenous opiates in mediating the antral motor response to solid food in man

G R SHARPE, W D W REES, S R BLOOM, AND L A TURNBERG (Departments of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford, and Hammersmith Hospital, London) The gastric antrum regulates solid particle emptying from the stomach and the physical nature of ingested food determines the postprandial antral motor response in man. Antral myenteric plexus contains enkephalin-like immunoreactivity and we have studied the role of endogenous opiates in mediating the antral contractile response to solid food.

Antral and duodenal motor activity was recorded in eight healthy subjects using perfused tubes connected to strain gauge transducers. In each subject, motor activity was recorded during a three-hour fasting period and for two and a half hours after ingestion of a solid meal, on two separate days. Intravenous saline was administered on one day and naloxone, an opiate antagonist (40 μg/kg/day), on the other, in random order. Ingestion of food disrupted the interdigestive cycle (phase 1) resulting in increased antral and duodenal motor activity lasting 90 to 120 minutes. Intravenous naloxone markedly reduced the antral contractile response to food (motility index: control=1975±226; naloxone=228±107 mm², p<0.001, n=8) but did not alter duodenal motor activity. This effect of naloxone was because of a decrease in both the amplitude (control=35±4; naloxone=10±4 mm Hg, p<0.001, n=8) and frequency (control=2.6±0.1; naloxone=0.6±0.3 contractions/min, p<0.01, n=8) of antral contractions. Naloxone did not modify the serum gastrin response to the meal.

In conclusion, naloxone inhibits the antral motor response to solid food and this suggests that endogenous opiates regulate postprandial antral contractile activity in man.

F2
Electrogastrographic findings in patients with nausea and vomiting

H GELDOF, E J VAN DER SCHEE, M VAN BLANKENSTEIN, J L GRASHUIS (Departments of Internal Medicine II and Medical Technology, Erasmus University, Rotterdam, The Netherlands) Unexplained nausea and/or vomiting is a challenging diagnostic problem. In the gastrointestinal tract myoelectric activity is the basis of motility, and abnormalities in gastric myoelectric activity could be a cause of nausea and vomiting. Gastric myoelectric activity can be recorded by cutaneous electrodes. This is called electrogastrography (EGG). The aim of this study was to investigate whether running spectrum analysis of the EGG could reveal abnormalities of the gastric myoelectric activity in patients with nausea and vomiting. In a control group of 25 healthy subjects abnormalities were not observed. From 53 patients a total of 76 recordings was made of sufficient quality to apply running spectrum analysis. An abnormal EGG was found in 11 out of 28 endoscopically normal patients with unexplained nausea and/or vomiting, who had not responded to medication. Unstable frequency and/or a decrease in amplitude after a test meal was seen in 10 patients, two of whom also had tachyarrhythmia in the fasting state. One patient showed an abnormal pattern only in the fasting state. Preliminary results in a group of 25 gastric ulcer patients revealed an abnormal postprandial frequency pattern in the 11 ulcer patients with nausea and/or vomiting. Tachyarrhythmia was not seen in this group.

This study indicates that EGG with running spectrum analysis is a suitable technique for recording and interpreting gastric myoelectric activity. The results strongly suggest that there is a relation between nausea and/or vomiting and postprandial EGG abnormalities in endoscopically normal and gastric ulcer patients.

F3
Positive correlation between duodenogastric reflux and gastric dysplasia

W E G THOMAS, M J COOPER, N J MCC MORTENSEN, P BURTON, AND E R DAVIES (Departments of Surgery, Radiodiagnosis and Histopathology, Bristol Royal Infirmary, Bristol) Severe gastric mucosal changes can often be seen in patients who have undergone gastric resection. The role that duodenogastric reflux plays in the production of such changes is unknown. Fifty-seven patients undergoing routine gastroscopy had multiple gastric biopsies taken and assessed blind by a pathologist.
Duodenogastric reflux was then determined by milk/CKC BID A scanning and graded 0-4 by a radiologist.

Patients who had dysplastic changes in the gastric mucosa (n=33) had a significantly higher mean grade of reflux of 2-1±0-21 (mean ± SEM) than patients with no dysplasia (1-1±0-24, p<0.0025). Sixty-nine per cent of patients who refluxed had dysplastic changes compared with 35% of patients who had no reflux (p<0.02).

Similarly, patients with metaplasia (n=33) had an increased mean grade of reflux of 2-0±0-19 compared with patients without metaplasia (1-3±0-29, p<0.05) but there was no significant difference in degree of reflux between patients with and without gastritis.

When the degree of reflux was plotted against increasing degrees of mucosal abnormalities, however, from normal mucosa through gastritis, metaplasia and mild, moderate and severe dysplasia, then a positive regression line can be drawn with significant correlation (r=0.99, p<0.001).

These findings suggest that duodenogastric reflux plays a significant role in producing gastric mucosal changes, and that the degree of reflux correlates well with the degree of mucosal abnormality.

F4 Diurnal variation in bile acid reflux in polya gastrectomy patients

C N HALL, N VINYE, J S KIRKHAM, AND T C NORTHFIELD (Norman Tanner Gastroenterology Unit, St James’ Hospital, and Department of Medicine, St George’s Hospital Medical School, London) Polya gastrectomy (PG) and pernicious anaemia (PA) are precancerous conditions, and bile acid reflux has been postulated as a causative factor in PG. Increased bile acid (BA) concentrations have been reported in gastric aspirate in PG before and after a liquid test meal. The extent of reflux during normal activities and the proportion of BA in solution are unknown. Bile aci reflux in PA has not been investigated. We have studied hourly gastric aspirations over 24 hours in nine PG patients, eight PA patients (disease controls) and nine matched healthy controls. During the day patients were up and about and ate three standardised solid meals. BAs were estimated enzymatically in the whole sample and in supernatant after centrifugation. Total BA concentration (mean ± SEM) was 0-14±0-04 mM/l in controls, 3-84±0-41 mM/l in PG (p<0.005), and 0-24±0-10 mM/l in PA (NS). In PG a higher concentration of total BA occurred at night (5-63±0-42 mM/l) compared with the day (3-34±0-42 mM/l; p<0.025), but in the other two groups there was no significant difference. Mean percentage BA in solution in PG was 50±3%, and BA solubility was related to increasing pH (r=0.39, p<0.01).

We conclude that BA reflux is increased in PG but not PA; that this increase reaches a maximum at night because PG subjects show a diurnal variation in BA concentration; and that half the BA is in solution on average, solubility being dependent on pH.

F5 Relationship of gastric and gall bladder emptying to a solid meal: a double isotope study in normal subjects

J N BAXTER, J S GRIME, M CRITCHLEY, AND R SHIELDS (Departments of Nuclear Medicine and Surgery, Royal Liverpool Hospital and University of Liverpool, Liverpool) Very little is known about the normal quantitative relationship between gall bladder emptying (GBE) and gastric emptying (GE). Using a double isotope technique we decided to investigate this relationship in 22 normal adults. 74 MBq of 99mTc-HIDA was given intravenously after which gall bladder filling was monitored with a gamma camera-computer system. After counts over the gall bladder reached a plateau (52±1 min), the subject ate a solid meal containing 9-2 MBq of 113mInm and GBE were simultaneously monitored until the end of the study at 120 minutes. Results: GE was monoeponential (tI=40±3 min), whereas GBE was double exponential. In 15 subjects GBE started within 1-4±0-8 min after the commencement of eating and they subsequently went on to empty 15-2±1-7% of gall bladder contents before GE began. These 15 subjects could be further divided into two subsets according to two parameters of the first exponential (tI and ejection fraction) – that is, type I (n=9) and type II (n=6) (p<0.001). The remaining seven subjects spontaneously emptied their gall bladders unrelated to eating a meal of 33-5 minutes after the HIDA injection.

It is concluded that (1) the gall bladder empties according to a double exponential function; (2) the results suggest a cephalic phase to GBE; (3) variations in matching between GE and GBE have been described – the physiological significance of which has yet to be shown.

F6 Gastric emptying after anterior lesser curve myotomy and posterior truncal vagotomy

T V TAYLOR, S HOLT, AND R C HEADING (Departments of Surgical Gastroenterology, Manchester Royal Infirmary, Manchester, and Clinical Pharmacology and Therapeutics, Edinburgh Royal Infirmary, Edinburgh) Anterior lesser curve seromyotomy with posterior truncal vagotomy (AMPT) has recently been described as a simple, safe, and expeditiously performed method of denervating the parietal cell mass, whilst preserving the pylorus. Dumping and diarrhoea are uncommon after this procedure. Gastric emptying has been assessed after AMPT and other elective operations for duodenal ulcer. Fourteen patients after AMPT were compared with 17 control subjects, 14 after vagotomy and pyloroplasty, 11 vagotomy and gastroenterostomy, and six Polya gastrectomy. Liquid and solid phase emptying studies were performed after a minimum period of three months. There was no delay in emptying time for liquids or solids between AMPT patients and controls (0.5±0.5 vs 0.4±0.4); early emptying of liquids (p<0.001) but not of solids (p>0.1) was increased after this procedure. All parameters of gastric emptying were significantly increased when truncal vagotomy and drainage was compared with AMPT (p<0.01), with the exception of early emptying of liquids. After Polya gastrectomy both early and late emptying of liquids and solids were markedly increased (p<0.001). With the exception of an increase in the early emptying of liquids after AMPT gastric emptying does not depart from normal and is less affected by this operation than either vagotomy and drainage or Polya gastrectomy.

F7 Assessment of anatomical and functional vagal regeneration

W A BROUGH, T V TAYLOR, J B ELDER, AND I E GILLESPIE (Department of Surgery, Manchester Royal Infirmary, Manchester) Incomplete vagotomy is the major cause of recurrent peptic ulceration after vagotomy. Both the ability of the vagus nerve to undergo spontaneous regeneration and the reason for the reversal of postoperative
insulin status from negative to positive remain controversial.

The problem has been assessed from a structural and functional standpoint under conditions considered optimal for vagal regeneration.

Three dogs underwent complete truncal vagotomy and three hemivagotomy. The divided nerves with their ends approximated were sutured in a silastic sheath. Serial insulin and pentagastrin tests were performed preoperatively and for 18 months after vagotomy to assess functional regeneration.

When the dogs were killed the vagi were removed along with the sheath and sectioned longitudinally. Morphological connection occurred in none of the three dogs submitted to complete vagotomy nor was there any evidence of functional regeneration. Dogs having undergone incomplete vagotomy showed a temporary marked reduction of acid and pepsin output which returned to the preoperative level by six months. The study suggests that morphological regeneration does not occur and this is reflected in the functional studies performed. Incomplete vagotomy may result in total functional reinnervation from one intact vagal trunk.

F8
Duodenal ulceration (DU): a fresh look at an old problem

S N JOFFE, K TABATA, M CHEN, R F MURPHY, AND E D JACOBSON (Departments of Surgery and Physiology, University of Cincinnati Medical Center, Cincinnati, Ohio, USA.) Mepirizole, a potent non-steroidal anti-inflammatory agent, produces duodenal ulcers unrelated to acid hypersecretion. This study examines other factors which may be involved in the pathogenesis of DU. Mepirizole (200 mg/kg), either orally or subcutaneously as a single dose, was given to male Sprague-Dawley rats after a 17 hour fast. Duodenal ulcers were produced in 83% of the rats at 24 hours (n=50). Using in vivo duodenal perfusion, a maximum decrease in alkaline output occurred at three hours from 71 (+9) to 39 (+6) μEq/h (<0-01) after treatment.

Gastric acid output in both control and mepirizole treated groups were similar. Plasma hormone concentrations (pg/ml) at 0, 6, and 24 hours for gastrin (51±10, 69±11, 97±49); VIP (240±56, 196±39, 222±36); PP (23±2, 32±1, 27±2) and secretin (44±5, 37±6-6, 26±3) were unchanged after mepirizole treatment and compared with control rats. The secretin content in homogenised extracts of duodenal mucosa were unchanged in control rats but fell from a mean basal value of 754 (±87) pg/mg wet weight to 144 (±25) at six hours (p<0-001) and to 303±71) at 24 hours (p<0-01) after mepirizole and VIP content increased from 158 (±59) pg/mg wet weight to 271 (±36) at 24 hours (p<0-01). Exogenous secretin (1 CU/kg/h) had no effect on either gastric acid secretion or duodenal alkaline output although secretin in pharmacological doses (10 CU/kg/h) significantly inhibited gastric acid output (p<0-01).

These results indicate that changes in the acid disposal mechanism related to duodenal alkali hyposecretion and paracrine hormone modulation may play a role in the pathogenesis of duodenal ulceration.

F9
Identification and characterisation of a novel gastrointestinal peptide which causes acute oedematous pancreatitis in mice

H J R EVANS, D A W GRANT, D BAINBRIDGE, V MUTT, AND J HERMON-TAYLOR (St George's Medical School, London, and Karolinska Institute, Stockholm, Sweden) We have identified a novel gastrointestinal peptide from porcine small intestine, copurifying with CCK-PZ (Karolinska Institute). This peptide specifically causes acute oedematous pancreatitis when infused intravenously into conscious mice for 20 hours. The pancreatitis, characterised by oedema, white cell infiltrate, acinar cell disruption, and high serum amylase appears similar to that reported in the rat after supramaximal stimulation by caerulein. Intravenous caerulein, CCK-PZ 33, and Pancreozymin (Boots) do not cause pancreatitis in the mouse nor do VIP or GIP. During the purification of CCK-PZ the pancreatitis-inducing component is separated by chromatography on Amberlite XE 64. The component does not bind to thiopropyl sepharose indicating the absence of an available sulphhydril group. H2O2 oxidation destroys its pancreatitis-inducing activity which is restored by subsequent reduction with cysteine but not by 'adding-back' CCK-PZ; this suggests the presence of an essential methionine residue. Pancreatitis-inducing activity is unaffected by trypsin hydrolysis but is destroyed by chymotrypsin. Further chromatography of this component will be reported. The induced pancreatitis is unaffected by somatostatin, glucagon, and trasyal but is profoundly modified by simultaneous intravenous Leupetin which reduces oedema and abolishes the leucocyte infiltrate without reduction in hyperamylaseaemia suggesting a direct action of the pancreatitis-inducing peptide on the acinar cell.

F10
Gastrin and somatostatin release in man – are they functionally linked?

M R LUCEY, P D FAIRCLOUGH, J A H WASS, J WEBB, G M BESSER, AND L H REES (Department of Gastroenterology, Endocrinology, and Chemical Endocrinology, St Bartholomew's Hospital, London) It is postulated that somatostatin exerts a continuous restraints on antral gastrin secretion and that stimulation of gastrin secretion is in part mediated through inhibition of somatostatin secretion. Our aim was to study this possible 'functional linkage' by use of cholinergic blockade of postprandial release of plasma gastrin and somatostatin in man. Five healthy male volunteers were given (a) a mixed meal followed at 15 minutes by atropine (0-04 mg/kg im), (b) a meal plus saline im, (c) atropine alone. Plasma gastrin and somatostatin were estimated by radioimmunoassay. There was an immediate and sustained rise in plasma gastrin, basal (mean ± SEM) 18±6 pg/ml, peak 35±5 pg/ml at 30 minutes (p<0-02); and plasma somatostatin, basal 11±2 pg/ml, peak 27±3 pg/ml (p<0-01) after the meal plus saline im. The peak postprandial gastrin level was higher and later after atropine, 54±12 pg/ml at 180 minutes (p<0-02, vs meal + saline). Atropine arrested the postprandial rise in plasma somatostatin. Atropine alone did not alter either plasma gastrin or somatostatin. To limit the effect of gastric factors, a further five subjects were given an intraduodenal infusion of fat both alone and after atropine im. Plasma gastrin concentrations were unchanged on either occasion, but plasma somatostatin rose significantly after intraduodenal fat alone. This rise was also abolished by atropine. These data suggest that (a) cholinergic mechanisms modulate postprandial release
of gastrin and somatostatin in man, (b) atropine abolishes plasma somatostatin release independently of its effects on gastric function, and (c) are consistent with the hypothesis that atropine potentiates postprandial gastrin release through reduction of somatostatin mediated inhibition.

F11
Low dose PYY inhibits gastric secretion in man

T E ADRIAN, G R SAGOR, A P SAVAGE, J M ALLEN, A J BACARESE-HAMILTON, K TATEMOTO, J M POLAK, AND S R BLOOM (Department of Medicine, RPMS, Hammersmith Hospital, London, Department of Surgery, St Albans Hospital, Herts) PYY is a newly discovered peptide localised to endocrine cells in the intestinal mucosa. PYY is found throughout the intestine, with very high concentrations in the human colon. The physiological role of PYY is now being investigated. The effects of this candidate gut hormone on gastric and pancreatic function have therefore been assessed.

PYY is infused in 12 healthy subjects for a period of one hour (PYY 1 pmol kg/min). In six subjects PYY was superimposed on a background infusion of pentagastrin (3 pmol kg/min). In six other subjects PYY was superimposed on a background infusion of secretin (0-25 pmol kg/min) and CCK-8 (0-15 pmol kg/min). Intraduodenal phenol red and PEG 4000 acted as recovery markers for gastric and pancreatic secretion respectively. Plateau gastric acid output during pentagastrin alone was 345±62 pmol/min. By the end of the PYY infusion this had fallen by 52±6% to 165±30 pmol/min (p<0.005).

PYY had no significant effect on duodenal juice volume or output of trypsin, bicarbonate, or bilirubin during secretin/CCK stimulation. Thus a low dose of PYY inhibits gastric acid secretion in man but has no significant effect on pancreatic or biliary secretion. In view of the large concentrations of PYY in the human colon this peptide should now be considered as a possible candidate for the classical entero gastrone.

F12
Effect of alcohol on pancreatic regeneration in the rat

J G R CUMMING, R A B WOOD, A CUSCHIERI, E E MCGUINNESS, AND K G WORMSLEY (Departments of Surgery, and Pharmacology and Therapeutics, Ninewells Hospital and Medical School, Dundee) Pancreatic regeneration has been assessed after 80% partial pancreatectomy in rats, using anatomic (pancreatic weight) and functional (output of trypsin and amylase in response to 60 Ivy DU cholecystokinin (CCK)/kg/h) criteria. Pancreatic weights had reverted to near control (non-resected) values 12 weeks after surgery. Secretion of enzymes in response to the maximal stimulation with CCK was linearly related to pancreatic weight. Output of enzymes was significantly less than control immediately and one week after resection but had returned to values not significantly different from control (non-resected) values 12 weeks after resection. Administration of a diet in which 33% of the calories consisted of ethanol resulted in pancreatic weights at 12 weeks post-resection which were significantly less than the pancreatic weights of rats with resection 12 weeks previously and fed a normal diet, but not significantly different from normally fed rats one week after resection. Similarly, the enzyme outputs in alcohol treated rats were significantly less than control (non-resected) and normally fed rats 12 weeks after resection. We conclude that an alcohol containing diet inhibits functional and anatomic regeneration of the rat pancreas. We propose that a similar mechanism, inhibition of pancreatic regeneration, may be responsible for the development of chronic pancreatitis in alcoholic individuals.

F13
Interference with co-translational processing of pancreatic secretory pre-proteins limits the biosynthesis of enzymes which can contribute to pancreatic pathology

B M AUSTEN, D H RIDD, M A KADERBHAI, S CAWTHORN, AND J HERMON-TAYLOR (Department of Surgery, St George's Hospital Medical School, London) The nascent chains of many secreted proteins are biosynthesised with amino-terminal extensions (signal sequences) the function of which is to aid translocation of the proteins across the endoplasmic reticulum membrane on the first part of the secretory pathway. The preforms of canine, rat, and human pancreatic secretory proteins have been characterised by translation of the corresponding oligo-dT purified mRNAs in rabbit reticulocyte lysates in the presence of 35S-methionine and electrophoresis on polyacrylamide gels and fluorography. Secreted proteins have been radioactively labelled by incubating pancreatic lobules in physiological media in the presence of 35S-methionine. The secreted proteins have been identified by electrophoresis in two dimensional gels. Many of the preforms are found to be slightly larger than their secreted counterparts; cleavage of signal sequences occurs when nuclease treated rough microsomes from canine pancreas are present during translation of mRNAs. Pretrypsinogens have different properties to their maturezymogens; they are not readily activated by entero kinase, and are themselves more susceptible to proteolytic degradation. Thus, short term interference with the cotranslational conversion of nascent pretrypsinogens, as well as with the conversion of other secretory zymogens, would lead to the production of a population of enzymes with a limited ability to contribute to pancreatic pathology.

F14
(Asp)4-Lys sequence of trypsinogen activation peptides is resistant to pancreatic and small intestinal proteolysis

A COOK, S CLIFFE, B M AUSTEN, D A W GRANT, AND J HERMON-TAYLOR (Department of Surgery, St George's Hospital Medical School, London) (Asp)4-Lys containing trypsinogen activation peptides are released into the duodenal lumen during digestion in quantities equimolar to the substantial amounts of trypsin. Little is known of their potential functions or fate. Human trypsinogen activation peptides Ala-Pro-4-C-Phe-(Asp)4-Lys and (Asp)4-Lys were synthesised on solid phase supports and purified by ion exchange and silica gel chromatography. Absence of racemisation or α to β rearrangement was confirmed by NMR spectroscopy. Pancreatic exocrine secretion and duodenal aspirate were obtained after secretin/CCK-PZ stimulation and the concentrations of trypsin, aminopeptidase and dipeptidylpeptidase IV determined. Fifteen milligrams of the (Asp)4-Lys octapeptide were incubated in 0-1M NaHCO3/4 mM Ca2+ buffer in the presence of 160 µl aliquots of enterokinase activated pancreatic juice or 200 µl of duodenal aspirate. Samples were withdrawn at intervals up to 20 hours, deproteinated through an octadecane
derivatised silica cartridge, lyophilised and analysed by high voltage paper electrophoresis pH 6-5 using (Asp)₄-Lys and aspartic acid standards. Cleavage of the N-terminal tripeptide was rapid and complete in four hours in both systems; the (Asp)₄-Lys sequence itself was resistant and quantitatively identified after 20 hours. Autoradiographic studies following the intraduodenal instillation of α-H-[³H]acetyl(Asp)₄-Lys in rats showed that the α-N substituted peptide was poorly absorbed from the intestine. Taken together the results suggest that (Asp)₄-Lys sequences are likely to persist intact in the small gut lumen after a meal and could therefore act as a physiological signal.

F15 Carbonoxalone inhibits thromboxane B₂ synthesis by human gastric mucosa

B M Peskar and H Weiler (Department of Gastroenterology, Medical Clinic, University of Essen, FR Germany) Carbonoxalone accelerates peptic ulcer healing by a mechanism not involving inhibition of acid secretion. It has, therefore, been proposed that effects strengthening mucosal defensive mechanisms might mediate its ulcer healing properties. We have shown previously that carbonoxalone inhibits the prostaglandin (PG) metabolising enzymes 15-hydroxy-PG-dehydrogenase and PG-Δ₁₃-reductase and had suggested that reduced inactivation of mucosal PG might contribute to the beneficial activity of the drug. We now report that in addition to increasing release of PGE₂, carbonoxalone inhibits formation of thromboxane (TX) B₂ during incubation of human gastric mucosa in vitro. Mucosal biopsies obtained endoscopically were incubated in Tris-HCl buffer (0.5 mmol/l, pH 7.4-7) at 37°C for 10 minutes in the absence or presence of carbonoxalone. Release of TXB₂ and PGE₂ into the incubation medium was measured using radioimmunoassays. Human gastric mucosa synthesised considerable amounts (pg/mg wet weight/10 min, mean ± SEM) of TXB₂ (67±106, n=15) which even exceeded formation of PGE₂ (367±40, n=15). Addition of carbonoxalone in concentrations of 0-4 and 1-6 mmol/l to the incubation medium dose dependently reduced mucosal release of TXB₂ to (pg/ mg wet weight/10 min, mean ± SEM) 323±51 (n=15, p<0.01) and 144±15 (n=10, p<0.001), respectively. Simultaneously, release of PGE₂ was increased to (pg/mg wet weight/10 min, mean ± SEM) 710±145 (n=15, p<0.05) and 660±152 (n=10, p<0.05), respectively. TXA₂, the biologically active precursor of TXB₂, has recently been found to produce extensive mucosal damage in the canine stomach, an effect attributed to its potent vasoconstrictor action. Inhibition of gastric mucosal TXA₂ synthesis by carbonoxalone might, therefore, improve mucosal microcirculation. This effect in combination with increased formation of PGE₂, which has vasodilating properties and may stimulate protective processes such as mucus and bicarbonate secretion, could effectively assist mucosal defence and accelerate mucosal repair reactions during carbonoxalone therapy.

F16 Relationship of mast cell degranulation and vascular changes in the stomach of rats

A P Jayaraj, F I Tovey, and C G Clark (Department of Surgery, Faculty of Clinical Sciences, University College, London, The Rayne Institute, London) It is well established that mast cell degranulation is accompanied by the release of histamine, one of the vasoactive substances responsible for increased vascularity and an important factor in peptic ulceration. A new method, to study mast cell populations together with the microvascular changes accompanying ulceration of the stomach in rats, eliminates the artefacts associated with traditional methods.

One group of 10 Wistar rats (220 g) was fed with stock diet and another group of 10 with ulcerogenic South Indian diet. After 24 hours' starvation, the pylorus was ligated and the animals killed after six hours. The stomach was distended with normal saline and the oesophagus ligated. After fixation in 20% formalin, the stomach was cut along the greater curvature and stained with toluidine blue for mast cells. Specimens were also stained with benzidine for vascular pattern.

The diameter of the arterioles and venules was significantly enlarged (p<0.01) in rats fed with ulcerogenic diet at 42 (38-51) and 181 (160-212) compared with controls at 36 (32-40) and 103 (92-122) μm respectively. The total number of mast cells was increased (p<0.05) in rats fed on ulcerogenic diet at 64 (53-73) compared with controls at 59 (53-62). There was significant increase in mast cell degranulation (p<0.01) in rats fed on ulcerogenic diet at 34 (12-42) compared with controls at 0 (0-2) per field.

Results indicate an association between mast cell degranulation and microvascular enlargement. This was accompanied by dense capillary networks around the ulcers in the stomachs of rats fed on ulcerogenic diet.

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Gynaecological disorders and hyperprolactinaemia in chronic constipation

D M Preston, L H Rees, and J E Lennard-Jones (St Mark's Hospital, and St Bartholomew's Hospital Medical College, London) Slow transit constipation appears to affect only women, and symptoms often begin at the menarche. Sixty-four patients (mean age 30 years), seen from 1969–1981, have been compared with age-matched controls to determine the incidence of associated gynaecological problems. Patients with STC were more likely to have irregular periods (p<0.05), to have galactorrhoea (p<0.01), and to find difficulty in becoming pregnant (p<0.05). Many who did become pregnant noticed looser motions in contrast with control subjects who tended to become constipated. Over 70% of both groups complained of dysmenorrhoea but patients with STC were more likely to take time off work, use analgesics and consult their doctor (p<0.001). Excluding minor procedures, such as sterilisation, patients with STC were more likely to undergo gynaecological surgery (p<0.001), 12 having had hysterectomy and 14 ovarian cystectomy compared with two each in the control group.

Study of sex hormones in patients still attending showed that most of those not using the contraceptive pill had a raised serum prolactin. This did not seem to be a stress effect, as concentrations remained high on serial samples and were normal in a group of women with the irritable bowel syndrome and constipation. Controls 176±23 mU/l (SEM), STC 569±78 (p<0.01), IBS 189±26 (NS). (Upper limit of normal 360 mU/l.) Many of the patients with STC also had low urinary oestrogen excretion and low plasma oestradiol. Slow transit constipation in women appears to be a disorder associated with abnormalities of the reproductive system.
F18
Neurotensin stimulates defaecation in man
J CALAM, R J UNWIN, AND W S PEAR (The Medical Unit, St Mary’s Hospital, London)
The gastrocolic reflex occurs normally and is exaggerated in some disease states, but how eating stimulates propulsive colonic motility is not known. Neurotensin (NT) is rapidly released from the small gut after eating, and three normal subjects defaecated within one hour of receiving intravenous neurotensin 12 pmol/kg/min for 15 minutes. We therefore infused NT 13-5 pmol/kg/min, or vehicle only for 30 minutes, double blind, into five healthy men aged 26–34 years and collected stools passed during the following three hours. Studies were performed after lunch, and after any postprandial defaecation had occurred. No subjects defaecated after control infusions, but all did so after NT. Stools were formed in two, sloppy in one, and formed plus sloppy in two. They weighed 94, 11–258 g (median and range) and were 78, 72–88% water by dry weight. Stool water sodium and potassium were 75, 11–109 and 98, 51–133 mmol/l respectively; sodium:potassium ratio 1-0:1, 0-1-2:1. The stools resembled normal colonic contents so NT probably caused propulsive colonic motility but effects on secretion or reabsorption or ileal motility are not excluded. All subjects noticed borborygmus after NT and the two who passed formed stools also had colic. Neurotensin was measured by a radioimmunoassay specific for its C-terminus, after extraction by Sep-pak C18 (Waters). Plasma concentrations before infusions and during control infusions were 14, <14-45 pmol/l (n=20), and peak concentrations during NT infusion were 540, 370–990 pmol/l (n=5); roughly three times the levels reported in normals after steak and chips. Also, raised plasma NT concentrations have been observed in patients with coeliac disease and VIPomas and after peptic ulcer surgery and jejunoileal bypass so NT may be involved in the pathophysiology of diarrhoea.

F19
Impaired gastrin release in chronic constipation
D M PRESTON, T E ADRIAN, J E LENNARD-JONES, AND S R BLOOM (St Mark’s Hospital, and Hammersmith Hospital, London) The possible role of gastrin in regulating gut motility is not clear, though it has been postulated that an abnormal response to circulating gastrin may play a part in the pathogenesis of the irritable bowel syndrome. Serum gastrin concentrations have been measured in 40 patients with functional bowel disease after gastric distension with water (10 ml/kg body weight taken orally) and compared with matched controls. Patients studied were: slow transit constipation with a normal barium enema (12), idiopathic megacolon (10), irritable bowel with pain/constipation (9), and functional diarrhoea (9).

F20
Are raised intraluminal pressures found in diverticular disease?

F21
Canine colonic blood flow measured by clearance of inhaled hydrogen
R J MAXWELL AND T G PARKS (The Queen’s University of Belfast, Department of Surgery, Institute of Clinical Science, Belfast) The Kety-Schmidt principle has been widely applied to the measurement of regional blood flow by external recording of washout of radioactive tracers. Aukland described a more direct adaptation of this method, based on the clearance of hydrogen gas by an electrode inserted in the tissue.

In this study on anaesthetised greyhounds, a 0-2 mm diameter platinum electrode implanted in the colon wall was used to record the washout of inhaled hydrogen. A range of flow rates was obtained by partial occlusion of arterial supply. The mono-exponential clearance curves obtained were plotted semi-logarithmically and blood flows calculated by the Kety method. Simultaneous venous outflow measurements were made from the same segment of colon. Seventy-six recordings were taken in five dogs.

Correlation coefficients for venous outflow and hydrogen clearance estimations in the five animals were 0-88, 0-90, 0-88, 0-78 (all p<0-001) and 0-81 (p<0-01). The mean coefficient of variation for consecutive flow measurements was 5-2%. Analysis of the complete washout curve is
tedious and time consuming. A shorter method of analysis using the first 3-0
minutes of the curve is shown to be accurate.

The hydrogen clearance technique allows repeated determinations of local
blood flow under various experimental conditions. The method is possible using
relatively simple equipment and the handling of radioisotopes is avoided.

F22 Electrically evoked activity in the normal external anal sphincter
A L WRIGHT, J GIBSON, J F B MORRISON, D E NEAL, AND N S WILLIAMS (Departments of
Anaesthesia, Physiology, and Surgery, Leeds General Infirmary, University of
Leeds, Leeds) Electrical stimulation of the perianal skin has recently been shown to
produce a reflex EMG response in the external anal sphincter. The latency of this
reflex was 8-3 milliseconds and its prolongation in patients with faecal inconti-
tenence was interpreted as evidence of pelvic floor denervation.

To establish the nature of the electrically evoked activity in the external anal sphincter we studied eight normal subjects before and during spinal anaesthesia for hernia repair. Stimuli (0-02 msec, 50–150V, 0-2/sec) were applied to the perianal skin while EMG activity of the sphincter was recorded with a concentric needle electrode.

Before anaesthesia an early response (ER) consistently followed the stimulus artefact with a latency of 6-8±SD 0-9
milliseconds and peaks of activity occurred during the subsequent 500 milliseconds –
that is, late response (LR) latency range 50–150 msecs). During anaesthesia ER
remained in each patient whereas IR was abolished. There was no difference in
latency of the ER during anaesthesia (7-5±SD 0-9 msecs) compared with before.

To ascertain that the ER did not have a reflex component twin stimuli were
applied. The ER to both stimuli was the same whereas inhibition of the LR
occurred after the second stimulus, indicative of a reflex response.

Thus, the ER, previously interpreted as
the anal reflex is not reflex in origin and
studies which have interpreted it as such
need reassessment.

F23 Differences in sphincter function in patients

with haemorrhoids and patients with the
descending perineum syndrome
D C C BARTOLO, N W READ, AND A G JOHNSON
(Department of Surgery, Royal Hallam-
shire Hospital, Sheffield) Patients with
haemorrhoids may be confused with patients with the descending perineum syndrome (DPS) because both can present with
staining at stool, incomplete emptying, and rectal bleeding. Moreover, propelling anterior rectal mucosa in DPS
may be mistakes for prolapsing piles. To document the important physiological
differences between the two groups, anorectal manometry was carried out
during station pull through, during balloon
distension of the rectum, and during rectal infusion with saline. Maximum basal and
peak (squeeze) sphincter pressures in patients with DPS were significantly lower
than in patients with haemorrhoids during pull through (basal pressures: 76±6 vs
112±7 cm water, p<0.001; control 83±6; peak pressures: 114±14 vs 160±13,
p<0.05; control 126±16). During rectal infusion with saline, basal and peak
pressures in patients with DPS were lower
than controls (p<0.05) and haemorrhoid patients (p<0.01). A lower rectal distend-
ing volume was required to inhibit anal
tone for more than a minute in patients
with DPS (45±7 ml) compared with
controls (77±12) or haemorrhoid patients
(90±12). Finally, 40% DPS patients leaked
during rectal infusion of 1500 ml of saline
compared with 14% haemorrhoid patients.

Our results suggest that DPS patients have
a weaker anal continence mechanism than
haemorrhoid patients and controls.
Inadvertent anal stretch or haemorrhoid-
exomy in these patients may well lead to
severe and incapacitating incontinence.

F24 Effect of intravenous vasopressin on canine
colic blood flow
R J MAXWELL AND T G PARKS (Department
of Surgery, The Queen’s University of
Belfast, and Institute of Clinical Science,
Belfast) Control of colonic bleeding using
vasopressin in patients with diverticular or
Crohn’s disease has been reported but
there is a paucity of experimental data on
the effect of this agent on the colonic
circulation.

In this study, six anaesthetised adult
greyhounds, mean weight 22±1-6 (SEM)
kg were given 2-5 units of vasopressin
intravenously over a 15 minute period.

Repeted measurements of blood flow in
the colon wall were made by the hydrogen
clearance technique for one hour before
and two hours after the vasopressin
infusion. Heart rate (HR) and mean blood
pressure (BP) were monitored.

Fifteen minutes after commencing
vasopressin, the mean blood flow had fallen to 49±5% of the control recordings
(p<0.001) (Student’s t test for paired data).
At 60 and 120 minutes the values were
64±5% (p<0.001) and 73±6%
(p<0.001). The HR fell from 140±6 per
minute to 118±7 per minute (p<0.01) at
15 minutes and by 60 minutes had returned to
137±7 per minute. Mean BP increased from
137±5 to 155±10 mm Hg (p<0.02)
after 15 minutes and at 60 minutes was
137±4 mm Hg.

It is concluded that intravenous vaso-
pressin produces a significant reduction in
colonic blood flow which is sustained after
heart rate and mean blood pressure have
returned to normal. The intestinal colic
experienced by patients given this agent
may be related to ischaemia.

LIVER I

F25 Low hepatic aldehyde dehydrogenase
activity in alcoholics is not a primary
abnormality
W J JENKINS, K L CAKERREAD, AND K R
PALMER (Department of Medicine, Royal
Free Hospital School of Medicine, London)
Numerous studies have shown that
acetalddehyde is toxic and that its
metabolism is impaired in alcoholics. It was
suggested recently that the low cytosolic
activity of hepatic aldehyde dehydrogenase
(AldDH) in alcoholics persists despite
abstinence, and may represent a primary
abnormality predisposing to alcoholism.
Our aim was to determine whether low
hepatic AldDH activity in alcoholics is a
primary abnormality.

Twenty-nine patients with alcoholic liver
disease each had two liver biopsies six
months apart. Hepatic AldDH activity was
measured on each occasion. The patients
were seen regularly and their alcohol con-
sumption assessed independently.

The results show that hepatic AldDH
activity was unchanged (3-8±1 (SE) vs
3-7±0-9 (SE) mU/mg protein) in 17
patients who continued to drink excess alcohol (>80 g/day); it rose from 4.3±1.2 (SE) to 8.9±1.6 (SE) μM/g protein (p<0.01) in 10 who significantly reduced their alcohol intake (<40 g/day); and it fell in two patients who were virtually abstinent initially, but then began drinking heavily.

Isoelectric focusing showed no evidence of missing hepatic isoforms of ALDH in these patients, but one or two extra cytosolic isoforms when alcohol consumption was excessive.

Our results clearly show that alcohol consumption itself depresses hepatic aldehyde dehydrogenase activity. It is unlikely that the low hepatic AlDH activity reported in alcohols represents a primary abnormality.

F26
Isoenzymes of alcohol and aldehyde dehydrogenase in alcoholic and non-alcoholic patients

KEVIN WARD, J MCCRODDEN, D G WEIR, AND K F TIPTON (Departments of Medicine and Biochemistry, Trinity College, Dublin, and Sir Patrick Dun's Hospital, Dublin) In some patients there is a genetic predisposition to alcoholism. A possible basis might involve alterations of the isoenzymes of alcohol dehydrogenase (ADH) of aldehyde dehydrogenase (ALDH). Liver biopsy samples from 45 patients were assessed for the isoenzymes of ADH and ALDH. Each patient was independently assessed for drinking behaviour. There were five teetotallers, 21 alcoholics, and 19 social drinkers (<40 g ethanol/day). Liver biopsy samples were graded for presence of alcohol related damage. There were 16 normal biopsies, 20 with alcoholic liver disease, and nine with non-alcoholic liver disease. The isoenzymes were separated by isoelectric focusing in the pH range 9-11 for ADH and 3-5-9-5 for ALDH. The presence of individual isoenzymes was assessed by spectrophotometric scanning of the stained gels. The separated isoenzymes were stained for enzyme activity. Alcohol dehydrogenase patterns varied considerably and there were no consistent differences between the alcoholic and non-alcoholic groups. Two alcoholic and two non-alcoholic patients were shown to possess the 'atypical' form of ADH. Aldehyde dehydrogenase also varied in the numbers and forms present. The severity of the liver damage did not affect the number of forms present. The relative intensity of staining of the two major bands of ALDH, at pH 4-9-5-0 and at pH 5-3, however, varied with the degree of liver damage but did not vary between the alcoholic and non-alcoholic liver disease groups. These results suggest that a primary abnormality of ADH or ALDH is not associated with the development of alcoholic liver disease.

F27
Pharmacology of propranolol in patients with cirrhosis and portal hypertension

M J P ARTHUR, A R TANNER, RALPH WRIGHT, A G RENWICK, AND C F GEORGE (Departments of Medicine and Clinical Pharmacology, Southamptom University, Medical School, Southampton) Many patients with cirrhosis and portal hypertension are receiving propranolol as prophylaxis against rebleeding from oesophageal varices. In patients with chronic liver disease the bioavailability, protein binding, half-life, and clearance of a drug may be altered. The aim of this study was to investigate the pharmacokinetics and pharmacodynamics of propranolol in such a group of patients.

Ten patients with cirrhosis and portal hypertension received an initial 20 mg oral test dose of propranolol and subsequently 160 mg of a slow release preparation, orally each day for seven days. Protein binding, serial plasma, propranolol concentrations, and effects on heart rate were studied.

Protein binding was depressed (mean 85%, range 78-9-88-1%). In patients with severe liver disease (serum albumin <30 g/l) propranolol remained detectable in plasma 24 hours after the single 20 mg dose and high steady state levels (mean 265 ng/ml, range 75-406 ng/ml) were observed during regular dosing.

At steady state there was a significant correlation between log plasma propranolol concentrations and the percentage fall in heart rate (r=0.659, p<0.05).

We conclude that dosage modification and individual monitoring are required when administering propranolol to patients with severe chronic liver disease and portal hypertension.

F28
Comparison of oral metoprolol and injection sclerotherapy for long-term management of variceal bleeding in cirrhosis

D WESTABY, B R D MACDOUGALL, W M MELIA, AND ROGER WILLIAMS (Liver Unit, King's College Hospital, Denmark Hill, London) In a prospective randomised clinical trial involving 32 patients with cirrhosis (Child's classification A or B only included) and recent variceal bleeding, the B1 receptor blocker metoprolol, in a dose sufficient to reduce resting pulse rate by 25%, was compared with repeated sclerotherapy for prevention of recurrent variceal haemorrhage. In patients receiving metoprolol, portal pressure was measured before and after four weeks of oral therapy and showed a mean fall of 3.7 mm Hg (17.3±4.5 and 13.6±4.4 mm Hg respectively; p<0.01) although in four patients the pressure fall was less than 10%. Nine of the 15 patients in the metoprolol group had rebleeding with a total of 21 episodes (mean follow up 10 months) compared with six of 17 in the sclerotherapy group with a total of nine episodes (mean follow up 12 months). The risks of rebleeding per patient month follow up was three times higher in the metoprolol group compared with patients receiving sclerotherapy (0.14 and 0.04 respectively; p<0.05).

Six of the nine patients rebleeding in the metoprolol group had shown a fall in portal pressure of 10% or more. In conclusion, long term injection sclerotherapy is significantly more successful than oral metoprolol for the prevention of recurrent variceal bleeding and this applies equally to those patients in whom a significant fall in portal pressure was observed.

F29
Further evidence of idiopathic portal hypertension in Kenya; a study of hepatitis B markers, immunoglobulin levels and enzyme-linked immunosorbent assay for Schistosoma mansoni in patients and controls

K M DE COCK, S AWADH, R S RAJA, B M WANKYA, J E LILLYWHITE, N HODGEN, J BERTRAND, R JUPP, AND S B LUCAS (introduced by J Lennard-Jones) Kenyatta National Hospital, Nairobi, London School of Hygiene and Tropical Medicine, London, and St Thomas' Hospital, London) Previous reports have suggested that idiopathic portal hypertension, a condition quite distinct from tropical splenomegaly syndrome, occurs in Kenya. In the present study patients with oesophageal varices were allocated to diagnostic groups on the basis of liver histology and results of splenportovenography, and
The British Society of Gastroenterology

F31 Prospective study of possible non-A non-B post transfusion hepatitis in Britain

J Collins, M F Bassendine, R Ferner, A A Codd, A Collins, and F W JAMES (Department of Medicine, Freeman Hospital, Public Health Laboratory, and Regional Blood Transfusion Service, Newcastle upon Tyne) We carried out a prospective study of post transfusion hepatitis in 248 patients undergoing cardiac surgery. Each had preoperative LFTs and serum stored for virology. Total blood transfused was 1559 units, total platelets 22 units, total fresh frozen plasma 215 units. Two patients died during operation. Eighteen died within six months. Two hundred and twenty-eight were followed to six months. All had serial LFTs and virology until discharge or death and at six months postoperatively. 44/228 living nearest the hospital had monthly LFTs.

The results show that 27 patients had raised AST and ALT one to four weeks postoperatively. In 25/27 these were normal within six weeks and remained so at six months. One patient with persistently abnormal LFTs had liver biopsy at six months showing very mild chronic persistent hepatitis; the other patient had abnormal preoperative LFTs and full features of alcoholic liver disease but refused biopsy. Of the remaining 203 patients none had abnormal AST or ALT after one or six months postoperatively. In addition, 49 patients developed jaundice within two days postoperatively not associated with other evidence of hepatitis (12 died). This settled within eight days in survivors. In the 18 patients who died, the 27 patients with transient or persistent transaminemia and the 49 with jaundice, there was no serological evidence of fresh infection with HAV (IgM), HBV (new HBsAg or anti-HBc), nor new infection of reactivation of cytomegalovirus, Epstein Barr virus or herpes virus.

The brief rise of transaminases in the one to four week postoperative period in 27 patients was possibly caused by an NANB virus. We cannot exclude a brief transaminemia after this period in other patients. We conclude that post transfusion NANB hepatitis is rarely severe and probably leads to significant chronic liver disease very rarely indeed in Britain.

F32 Non-A non-B hepatitis after factor VIII replacement

M Fletcher, J Trowell, J Craske, and C R Rizza (Oxford Haemophilia Centre and Nuffield Department of Medicine, and Public Health Laboratory, Manchester) Thirty patients with factor VIII deficiency (concentrations 0–30%) who require infrequent treatment were followed for evidence of hepatitis after factor VIII treatment. Patients were assessed clinically and blood was taken before treatment and at intervals for one year. The patients had not received factor VIII in the six months before the study and it was given for trauma or elective operations. The 25 men and five women ages ranged from 12 to 70 years.

Four patients had raised aspartate transaminase (AST) concentrations before this episode of treatment and all had received factor VIII in the past. They continued to have raised AST concentrations and are assumed to have chronic liver disease. Seventeen patients developed hepatitis out of the 26 whose AST levels were normal before treatment. All five patients who received commercial concentrate developed hepatitis. Twelve patients developed hepatitis out of the 21 who received only NHS factor VIII: 10 patients became jaundiced and six patients were actually ill. The incubation period of the hepatitis was either under one month (13 patients), in one instance two weeks or it was between eight and 12 weeks (four patients). The latter had minimal symptoms but their AST concentrations remained over 100 SI units for more than six months. Six out of the eight patients whose AST levels rose at one month had raised levels at six months and four at one year. No evidence was found of current

these groups were then compared for prevalence of hepatitis B markers, immunoglobulin concentrations, and results of enzyme-linked immunosorbant assay (ELISA) for Schistosoma mansoni infection.

Eighty-five patients with oesophageal varices were studied. Of these 29.4% had histological evidence of S mansoni infection, 20% had cirrhosis, and in 25.9% liver histology was non-diagnostic and the portal vein was radiologically shown to be patent. A comparison of clinical findings, serological data, and parasitological investigations suggested that this latter group was a distinct one, and did not result from failure of histological diagnosis of cirrhosis or schistosomiasis. It is likely that these patients had idiopathic portal hypertension.

In 82 normal controls, the carrier rate of hepatitis B surface antigen (HBsAg) was 12.2%, 59.8% had antibody to HBsAg (anti-HBs) and 7.3% showed antibody to core antigen (anti-HBc) as the only viral marker; 58.3% of cirrhotics and 26.7% of patients with probable idiopathic portal hypertension were HBsAg+. The implications of these results, and limited data on hepatitis Be antigen and antibody are discussed.

F30 Analysis of the molecular state of HBV-DNA in the liver of patients with chronic hepatitis or primary liver cell carcinoma

H C Thomas, M J F Fowler, I V D Weller, A S F Lock, and J Moniardino (Royal Free Hospital, London) The duck hepatitis 'B-like' virus replicates by reverse transcription. Using molecular hybridisation the replicative intermediates and the presence of integrated sequences have been examined in liver from patients with HBV induced chronic hepatitis (CH) or hepatocellular carcinomas (HCC).

In the 22 HBs antigen positive patients the pattern of viral DNA was that of free molecules. Replicative intermediates included two smears of HBV-DNA (2.8–1.8 and 1.6–0.2 Kb). The 3.2 Kb band and upper smear were shown by DNase and restriction endonuclease cleavage to be double stranded DNA. The lower smear consisted of single stranded DNA. Fractionation of subcellular organelles showed the replicative intermediates to be present in the nuclei. Only one Turkish patient had integrated HBV sequences. In the eight HBs antibody positive patients the 3.2 Kb and lower molecular weight replicative intermediates were absent. In three, integrated HBV sequences were present. HCC: from two HBsAg-, anti-HBe anti-HBc patients contained integrated HBV sequences, whereas two tumours occurring in patients with autoimmune liver disease without serological markers of past or present HBV infection, did not.

The replicative intermediates of HBV resemble those found with the duck virus. Integrated sequences were found late in the chronic infection usually, during the anti-HBe phase. Integrated sequences were present in HBsAg+, anti-HBc, HCC but not in HCC from patients with autoimmune chronic liver disease.
hepatitis A, B, or EB or CMV during the study which suggests that these were two serotypes of non-A non-B hepatitis. The difference in the incidence of hepatitis after commercial or NHS factor VIII may be related to previous exposure, method of fractionation, pool size, or source of donors.

**P1 Intramural distribution of neuron specific enolase (NSE) in the human gastrointestinal tract**

G-L FERRI, P J MARANGOS, S R BLOOM, AND J M POLAK (Departments of Histochemistry and Medicine, RPMS, Hammersmith Hospital, London, and Laboratory of Clinical Science, NIMH, Bethesda, Maryland, USA) Neuron specific enolase, the neuron specific isoenzyme of enolase, has recently been shown to be present in enteric neurons and in all types of gut endocrine cells. Normal samples of stomach (fundus and antrum, n=5 each) and small and large bowel (n=15) were separated by micro-dissection into mucosa, submucosa, and muscularis externa. The intestinal mucosa was further separated into epithelium and lamina propria by treatment with EDTA. Neuron specific enolase immunoreactivity, measured by radioimmunoassay, showed a fairly similar pattern of distribution at all levels, being most abundant in the external muscle layer (71.0±2.4% of its total content, mean ± SEM). The mucosa and submucosa contained 16.4±1.6% and 12.6±1.4%, respectively, while a smaller but clearly detectable amount was measured in the separated epithelium (1.6±0.2). In conclusion, throughout the human gut NSE immunoreactivity showed an intramural distribution primarily parallel to that of nerve elements. Lower concentrations were found in the separated epithelium, containing the endocrine cells. These observations are in keeping with previous immunocytochemical findings and suggest that the NSE content of endocrine cells may be significantly lower than that of enteric neurons.

**P2 Vasoactive intestinal polypeptide (VIP), substance P (SP), somatostatin (SOM), and PHI in the enteric sphincters of the cat**

G P MCGREGOR, A E BISHOP, M A BLANK, N D CHRISTOFIDES, Y YANGOU, J M POLAK, AND S R BLOOM (Departments of Medicine and Histochemistry, RPMS, Hammersmith Hospital, London) There is no major anatomical feature which distinguishes 'sphincter' from 'non-sphincter' enteric smooth muscle. The gut has an extensive peptidergic innervation which is intrinsic and in which the neuropeptides VIP, SP, SOM, and PHI are major components. The nature of this innervation in respect of the sphincter regions has not been studied in detail. From five cats, 1 cm segments of whole gut wall thickness were dissected out in the region of the cardiac and pyloric sphincters, the ileal caecal valve, and the anal sphincter. Each tissue was extracted in boiling 0.5M acetic acid and 10 μl aliquots were assayed in duplicate using previously described specific radioimmunoassays. Tissue was fixed in bazoquinone and sections immunostained with specific antibodies for each peptide. In the anal sphincter the concentrations of all four peptides (VIP 116±19; SP 5.6±2.0; SOM 22±13; PHI 24±4) were significantly (p<0.01) less than in the 1 cm segment taken immediately proximal (VIP 712±53 pmol/g; SP 17.5±2.5; SOM 163±66; PHI 451±38). Immunocytochemistry indicated peptide nerves in the internal anal sphincter but they were few in number compared with more proximal bowel. The contracted state of the anal sphincter and its reduced intrinsic innervation might be functionally related. Across each of the other sphincter regions there appears to be a 'gradient' of VIP and PHI. Therefore, it is possible that the physiology of gut sphincters might be determined by the nature of their peptidergic innervation, and this may be relevant in certain diseases.

**P3 Ultrasound in the assessment of colonic motility in patients with the irritable bowel syndrome (IBS)**

R D'OLIVEIRA, B TAYLOR, AND H L DUTHIE (Welsh National School of Medicine, Cardiff) Ultrasound has been shown to give similar results to intraluminal pressure measurements in studies on the stomach and small bowel. We have studied the motility of the sigmoid colon in 20 patients with irritable bowel syndrome, before and after administration of the essential oil of citral, either as a local infusion or in an oral preparation. A Doppler ultrasound probe placed on the skin of the left iliac fossa was directed to the same segment of sigmoid as an intraluminal, perfused open-tip catheter, by focusing on a balloon at the end of the catheter. Good correlation was found between the two methods. Compared with a control infusion local administration of citral 0.2 ml in 50 ml saline significantly inhibited motility (p<0.01) in response to 0.5 mg prostigmine intramuscularly. A similar inhibition of motility was seen in four of six patients given an oral citral preparation for a period of one week.

**P4 Gastric emptying in diabetes: relationship to blood glucose levels**

S L GRAINGER, JUDITH I GAUNT, P M BROWN, R P H THOMPSON, AND D N CROFT (Gastrointestinal Laboratory, Rayne Institute, and Department of Nuclear Medicine, St Thomas' Hospital, London) Impaired gastric emptying occurs in patients whose diabetes is complicated by autonomic neuropathy. Studies of gastric motility in diabetics without such complications are lacking. We have studied the relationship between preprandial blood glucose and gastric emptying, and the increment in glucose after the meal, in diabetics with and without autonomic neuropathy. Gastric emptying was measured by a radio-nuclide technique using 99mTc-technetium labelled poached egg white as the meal marker. The test meal contained 35 g carbohydrate. Anterior and posterior images of the stomach were obtained for one hour after the meal and the extent of emptying determined from the area under the geometric mean time-activity curve (AUC).

In diabetics without autonomic neuropathy the AUC correlated significantly with log preprandial blood glucose (n=12, r=0.67, p<0.05). No such relationship existed for patients with autonomic neuropathy. The increment in blood glucose after the meal correlated inversely with the AUC for all subjects (n=23, r=0.58, p<0.01). The dependence of gastric emptying on the preprandial blood glucose has not previously been shown. Thus high blood glucose concentrations may diminish gastric emptying and be a causative factor in acute gastric atony. Also, the daily
variations in blood glucose concentration will alter the time of intestinal absorption of calories after eating and contribute to difficulties in good diabetic control. The dependence of the postprandial rise of glucose on gastric emptying has implications for insulin dependent diabetics. Finally, studies of gastrointestinal motility in diabetics must take into account the prevailing blood glucose concentrations.

P5 Evidence of gastric carcinoma during follow up of apparently benign gastric ulcer

R Farini, F Farinati, F Cardin, F Di Mario, F Vianello, C Arslan Fagnini, and R Naccarato (Istituto Clinica Medica I, Cattedra Malattie Apparato Digerente, Istituto Anatomia Patologica, Università degli Studi di Padova, Italy) One hundred and thirteen patients (74 men, 39 women, aged 30–86 years) with apparently benign gastric ulcer (macroscopic view at endoscopy and gastric biopsies negative for malignancy) were endoscopically followed up (for less than six months in 27 cases, for six months in 43, for 12 months in 43) in order to evaluate the outcome of the lesion. Particular attention was given to detect possible delay in diagnosing gastric cancer and the frequency of association with epithelial dysplasia. Endoscopic check-ups (395), always with at least five gastric biopsies taken from the edge or scar of the ulcer, were carried out after one, three, six, and 12 months from diagnosis. Gastric cancer and gastric epithelial dysplasia were assessed according to the histological classification of Minsky (1973) and Morson et al (1980) respectively.

After the initial diagnosis of benign gastric ulcer, seven out of the 113 patients (6.1%) were subsequently found to present histological evidence of malignancy (within two month follow up in two patients, within four months in three, and after 12 months in two); four of them were also in follow up for moderate or severe dysplastic changes of the mucosa of the edge or scar of the ulcer. Other 14 patients (12.9%), regardless of the outcome of the ulcer (scarred, relapsed) presented moderate or severe epithelial dysplasia.

These data suggest: (1) even in a standardised follow up for gastric ulcer, delay in diagnosing gastric carcinoma may occur; (2) moderate or severe dysplasia may be a useful marker for a more careful follow up of the patients; (3) the macroscopic appearance of gastric cancer may remain virtually unchanged, at least in its early stages, throughout several months.

P6 Non-invasive assessment of small intestinal damage in Crohn's disease and ulcerative colitis

M DE F A Gomes, J Dunne, L H Logan, and R E Pounder (Academic Department of Medicine, Royal Free Hospital, London) The L-rhamnose/lactulose permeability test has been used prospectively to assess small intestinal damage in 71 patients with either Crohn's disease or ulcerative colitis. The test involves swallowing a hypertonic solution of L-rhamnose and lactulose, which is followed by a five hour urine collection. Both sugars are measured quantitatively and quickly in the urine, using a single thin-layer chromatography plate. Inflammatory bowel disease was diagnosed using conventional criteria.

Disease activity was assessed by the combination of a disease activity index, sigmoidoscopy, and c-reactive protein.

Of 30 Crohn's disease patients in remission, four had abnormal intestinal permeability, but three of the four were taking steroids. Eight of the nine patients with active Crohn's disease had abnormal intestinal permeability. Serial studies in Crohn's disease patients show that permeability returns to normal when the disease is in remission. All 31 patients with ulcerative colitis, whether in remission or relapse, had normal permeability to the test sugars.

This study suggests that patients with active Crohn's disease have diffuse small intestinal damage, and that the presence of this damage correlates with disease activity.

P7 Gall stone recurrence after medical dissolution: an overestimated threat?

A Lanzi, R Kupper, A Joseph, and T C Northfield (Departments of Medicine and Nuclear Medicine, St George's Hospital Medical School, London) After medical dissolution of gall stones, overall recurrence rate has been reported as 50% and cumulative recurrence at five years as 100%. These figures might be an overestimate for two reasons: (1) some patients might not have achieved complete dissolution, as diagnosis mainly based on oral cholecystogram; and (2) cumulative figures bias the results in favour of recurrence if the length of follow up varies. We have observed 26 patients for six to 48 months after gall-stone dissolution (mean 21 months, median 24 months). Complete dissolution was confirmed radiographically and by two ultrasounds three months apart, and recurrence was diagnosed by six monthly ultrasound, confirmed radiographically. Ultrasound showed false positive results for complete dissolution by radiography in three patients (12%). Eight patients had gall stone recurrence (31%), all within three years. Cumulative recurrence rate at one, two, three, and four years was 20.35, 80, and 80% respectively. Estimated recurrence rate using an actuarial method was 20, 29, 36, and 36%.

We conclude that previous estimates of cumulative recurrence rate, based mainly on radiographic diagnosis of complete dissolution, have overestimated the risk; but that the risk remains an important one even when complete dissolution is based on ultrasound as well, and when actuarial methods of assessing risk are used.

P8 Thermal vs photoacoustic fragmentation of biliary calculi using continuous wave and giant pulse lasers

C P Swain, T N Mills, G M Watson, S G Bown, H Webster, C Edwards, T Dowst, A Fergusson, H K Wickramasinghe, J Wickham, and P R Salmon (Departments of Gastroenterology and Medical Physics, University College Hospital, London, Academic Department of the Institute of Urology, Department of Electronic and Electrical Engineering, University College, The Royal Signals and Radar Establishment, The Rutherford-Appleton Laboratories, The Clarendon Laboratory, The Royal Institution) This study explores the possible application of laser technology to the endoscopic destruction of cholesterol calculi in the biliary tracts, contrasting thermal vapourisation using continuous wave lasers with fragmentation by photoacoustic stimulation using giant pulse lasers. Thermal vapourisation using continuous wave lasers is effective (CO2, 5 W>1Nd YAG, 80 W>1Ar, 10 W) but disadvantages include strong absorption of CO2 laser light by water, current unavailability of an endoscopic fibre for this wavelength, ignition of some gall stones, recrystallisation during treatment to a more heat resistant form, and the requirement of considerable endoscopic skill to
limit thermal damage to surrounding tissue (CO₂<Ar<Nd YAG). Fragmentation of calculi by direct photoacoustic stimulation has been studied using a variety of single-shot Q-switch lasers (Nd YAG – 10 J/shot, frequency-doubled Nd YAG – 1 J/shot, and Kr F – 2 J/shot). Single 5-5 J pulses of Nd YAG fragmented dark pigmented calculi. To increase greatly the efficiency of stress wave generation a confined film photoacoustic transducer has been constructed. Multiple shots using a 10 Hz repetition rate 500 mJ Q-switch Nd YAG laser successfully fragmented calculi immersed in water in a few minutes and produced little damage to surrounding tissue. We are investigating the possibility of sending calculi into destructive resonance by photoacoustic stimulation with a low power continuous wave laser modulated at resonant frequencies. As heating and consequent damage to surrounding tissue is very small, endoscopic fragmentation of calculi using single or multiple shot giant pulse lasers promises distinct advantages over continuous wave thermal method.

P9 Vitamin A deficiency in Crohn’s disease

A H N MAIN, P R MILLS, J BRONTE-STEWART, L M NELSON, A MCLELLAND, A SHENKIN, AND R J RUSSELL (Gastroenterology Unit and Department of Biochemistry, Royal Infirmary, and Tenet Institute of Ophthalmology, Western Infirmary, Glasgow) Low intake or absorption of vitamin A, or depletion of retinol carrier proteins in plasma, namely retinol-binding protein (RBP) and pre-albumin (PA), can result in clinical signs of vitamin A deficiency (impaired dark adaptation). Such circumstances might occur in Crohn’s disease. We decided therefore to investigate 52 Crohn’s patients for evidence of vitamin A deficiency. Plasma retinol concentration correlated with RBP (r=0.75, p<0.001) and with PA (r=0.71, p<0.001). Eleven patients (21%) had low plasma retinol concentrations (<1.2 µmol/l). In six of these patients, retinol depletion was mild (<1.0 µmol/l) and was associated with no symptoms. All these patients weighed >80% ideal body weight. In contrast, five who had plasma retinol concentrations <1.0 µmol/l weighed <80% ideal; they also had extensive small bowel disease. Three of these, two of whom complained of night blindness, had impaired dark adaptation and plasma retinol concentration <0.8 µmol/l in association with low RBP and PA levels. Triglyceride absorption was very low and faecal fat excretion high in two of these patients. Dark adaptation improved with intravenous feeding in one patient and oral vitamin A supplementation in the other. It is concluded that patients with extensive small bowel Crohn’s disease who weigh <80% of ideal body weight merit measurement of plasma retinol concentration. Those with plasma retinol <0.8 µmol/l (<23 µg/l) run a high risk of developing night blindness. Vitamin A supplements should be given and protein depletion corrected.

P10 Follow up studies on four patients with epidemic hypochlorhydria

T GLEDHILL, R J LEICESTER, N LIGHTFOOT, J BARNARD, D DARWIN, N VINEY, B ADDIS, AND R H HUNT (RN Hospital, Haslar, Gosport, Hants, and Smith Kline and French Research, Welwyn, Herts, and McMaster University, Hamilton, Canada) Further studies on four patients with epidemic hypochlorhydria have included electron microscopy on initial gastric biopsies, analysis of 24 hour intragastric pH, bacteria, nitrate reducing bacteria (NRB), nitrite, and stable and unstable nitrosamine concentrations. At eight months endoscopy and gastric biopsies were obtained in four subjects and acid secretion studies in three.

Electron microscopy did not show any inclusion bodies or any other evidence of viral disease. During hypochlorhydria, of 48 samples of gastric juice examined, 98% had a bacterial growth of >10⁶ organisms/ml and 95% had a growth of NRB of >10⁶ organisms/ml. Mean intragastric nitrite concentrations were 10 times higher than a group of eight healthy volunteers studied previously. Mean values of stable and unstable nitrosamine concentrations were not raised.

During the illness, all biopsies had shown an active superficial gastritis. After eight months, the gastritis was still active but chronic inflammatory cells were also present. One biopsy was noted to have scanty parietal cells.

Acid secretion studies at eight months showed two patients to have a basal pH >6.0. Peak acid output had risen to 10.0 and 15.7 mmol/h in these two subjects. In the third patient, basal acid output was 2.58 mmol/h and peak acid output was 15.6 mmol/h.

We conclude that epidemic hypochlorhydria is associated with a prolonged disturbance of the intragastric milieu.

P11 Acute intermittent porphyria in Chester – a public health problem

M R QADIRI AND G R YOUNGS (Chester Royal Infirmary, Chester) Acute intermittent porphyria affects a large family in Chester and presents an increasing and largely unrecognized community health problem. An 18 year old girl has repeated admissions with abdominal pain and motor neuropathy. Her father, brother, and four other relatives under the age of 50 have died within the last five years from probable porphyric illnesses. The consequent anxiety amongst the relatives prompted us to study the natural history of the disease in the family to decide if a diagnostic and counselling service should be offered.

The family is characterised by its low socioeconomic class, low migration, and high fecundity. It stems from a marriage in 1896 which produced 10 children. About 25 families in Chester with around 90 children and adolescents are currently at risk. The survey shows that the disease has variable penetrance and often presents in an atypical fashion. Porphyric symptoms may mimic those of other acute illnesses so that incorrect or incomplete death certificates have been issued. The condition is poorly understood by hospital and general practitioners and the Department of Community Health has been unaware of the problem. Detection of the asymptomatic carrier is now possible by measuring uroporphyrinogen-1-synthase.

The study shows that an increasing population in Chester is at risk from acute intermittent porphyria. The mode of presentation is variable and the illness may be misdiagnosed. We suggest the families at risk should be offered biochemical screening, education, and genetic counselling and that a central register should be established.

P12 Gluten content of ‘gluten-free’ foods

P J CICLITIRA, H J ELLIS, E S LENNOX, D J EVANS, AND R H DOWLING (Gastroenterology Unit, Guy’s Hospital, Department of Histopathology, RPSMS, MRC Laboratory of Molecular Biology, Cambridge) Wheat flour is a complex mixture
containing substances which are toxic to coeliac patients. We have previously shown in one coeliac patient, biopsied serially, that three hours after commencing a 100 mg intraduodenal gliadin challenge, there were minimal changes in the jejunal mucosa and in two other coeliac patients that six hours after 1000 mg intraduodenal challenges of α, β, γ, or ω gliadin there were gross histological changes. To see if any of these toxic gliadin subfractions were present in supposedly 'gluten-free' foods we wished to develop radioimmunoassays to the gliadin subfractions.

Eight New Zealand white rabbits were injected monthly with 300 μg of unfraccionated gliadin or the individual subfractions. By six months, high titre antisera to the α, β, and γ (but not to ω) gliadins were obtained, but as there was no non-equivalent cross-reactivity, we used an antiserum to unfraccionated gliadin to measure the degree of contamination of wheat gliadin in three commercial gluten-free flours.

The results based on assays of 10 mM acetic acid extracts showed that these nominally gluten-free flour products A, B, and C contained 1.9×10⁻², 2.4×10⁻³, and 1.4×10⁻²% wheat gliadin by weight. Bread from these gluten-free products would therefore be expected to contain approximately 6-4, 0-4, and 0-2 mg gliadin per standard 30 g slice respectively. Following these findings, product A has now been withdrawn.

It is concluded that bread made from nominally gluten-free flours which are based on wheat starch contain small amounts of gliadin. Regular intake of these products may explain why some patients fail to respond to a gluten-reduced rather than a gluten-free diet.

The relative merits of xyl, 3mGlc, lac, and L-rhamnose (rham) for clinical detection of villous atrophy have been assessed by performing absorption tests on 19 adult patients with untreated coeliac disease and 28 healthy adult volunteers. After a fast each subject ingested an iso-osmolar load (xyl 5 g, 3mGlc 2-5 g, lacl 5 g, and rham, 1 g in water to 250 ml: 270 mmol/kg) and, on a different day, a hyper-osmolar load (lac 5 g, rham 1 g, lactose 20 g, and sucrose 20 g in water to 100 ml: 1400 mmol/kg). A five hour urine sample and, for the xyl-3mGlc test, timed blood samples, were collected for sugar analysis by quantitative thin-layer and paper chromatography.

Excretion of xyl, 3mGlc, rham, and lac after the iso-osmolar test fell within the mean ± 2 SD control range for two, eight, eight, and 10 of the 19 coeliac patients, while none came within ± 3 SD of the control mean when results were expressed as lac/rham or lac/xyl ratios. Similarly, plasma xyl and 3mGlc concentrations at 60 minutes fell within the mean ± 3 SD control range in five and eight of the coeliac patients, but only one came within this range when xyl/3mGlc plasma ratios were used. The hyperosmolar test accentuated lactulose excretion in the coeliac group with corresponding improvement in discrimination. The advantage of differential absorption ratios is clearly shown.

P14 Towards a radiological definition of idiopathic megacolon

D M PRESTON AND J E LENNARD-JONES (St Mark's Hospital, London) It has been stated that a barium enema is unhelpful in the evaluation of adults with chronic constipation. To establish a normal range of colonic size we have made measurements of double contrast enemas reported as normal from 50 patients investigated for rectal bleeding without piles or inflammatory bowel disease (selected to give a representative age range in both sexes). The rectal area to pelvic brim was 89±13 cm² (SD) (upper limit 115) and rectal width at the pelvic brim 4.2±0.9 cm (UL 6), sigmoid colon 4.3±0.8 cm (UL 6), descending colon 4.8±0.4 cm (UL 5-6), transverse colon 6.2±0.9 cm (UL 8), ascending colon 6.7±1.0 cm (UL 8-7). All but five of 300 values were below the mean +2 standard deviations suggested as the upper limits of normal. Radiographs of 38 patients with chronic constipation (excluding Hirschsprung's disease) were compared with the normal range. The radiographs of 18 women, all of whom had an increased intestinal transit time, fell within this range. The radiographs of the remaining 20 patients showed an enlarged rectum and sigmoid, and in a few, enlargement of the proximal colon. This latter group had been diagnosed as having idiopathic megacolon, and the sex ratio was equal. The upper limits of normal given above thus correspond with the current qualitative diagnosis of megacolon and establish quantitative values for future research. The findings support the concept that there are two populations of patients with idiopathic constipation and barium enema is useful in distinguishing these two groups.

P15 Nocturnal nasogastric tube feeding at home

P B MCINTYRE, S R WOOD, J POWELL-TUCK, AND J E LENNARD-JONES (St Mark's Hospital, London) Five malnourished patients who consistently failed to gain or maintain weight with oral supplements have been taught to give themselves a nocturnal nasogastric tube feed at home to supplement their daily dietary intake. At the start of treatment all patients were significantly below their ideal weight, mean 29-3% (range 15.5-46.3%). Patients were taught to pass a soft fine-bore nasogastric tube on themselves and to check the tube's position by aspirating gastric juice and testing for acid with litmus paper. The feed to be used was placed in a reusable enteral feeding bag and the rate of infusion regulated using a simple peristaltic pump. Three commercially available feeds, Isocal, Ensure, and Nutraneal were used to give nocturnal suplements of 1000-2000 kals per night. Patients gained weight at a mean rate of 0.54 kg/week (range 0.42-0.61 kg/week). The one patient with hypoalbuminaemia raised his serum albumin from 15 g/l to 35 g/l; all other patients raised or maintained a normal albumin concentration, in one case despite a protein losing enteropathy. No patient suffered regurgitation or aspiration of the nasogastric feed, and there were no metabolic complications. Diarrhoea and abdominal pain in one patient was relieved by decreasing the amount of feed given. Nocturnal nasogastric tube feeding at home can be a safe, effective, and acceptable way of providing nutritional support.
for a small number of patients in whom other dietary measures have failed, and for whom the alternative may be the potentially more hazardous and expensive technique of home parenteral nutrition.

P16 Tissue localisation by whole body autoradiography and scintillation counting of pepstatin and its analogues after oral and intravenous administration

T F FORD, D A W GRANT, R J MCCULLOCH, B M AUSTEN, AND J HERMON-TAYLOR (Department of Surgery, St George’s Hospital Medical School, London, and Glaxo Group Research Ltd, Ware, Herts) Pepstatins are potent inhibitors of acid proteinases including pepsin, renin, and cathepsin D and have been advocated as therapeutic agents in the treatment of gastrointestinal haemorrhage, hypertension, malaria, and malignant ascites. We have used both whole body autoradiography and tissue pulse counting in rats to study the distribution of the insoluble analogue pepstatin-[14C]glycine (including pepstatin-labelled liposomes), the soluble derivative [3H]acetyl statine and the water soluble analogue pepstatin-[14C]glycyl-lysyl-lysine (pepstatinyl-GKK). After intravenous administration of pepstatin-[14C]glycine 95% of the dose is cleared from the bloodstream within 15 minutes by the liver and kidney and excreted unchanged in the bile and urine. After incorporation of the inhibitor into liposomes, a qualitatively similar distribution is seen but blood levels remained high (50% of the dose) for substantially longer (two hours). By contrast, [3H]acetyl statine is widely distributed to most tissues and there was persistence of the compound in the bloodstream at 30 minutes but by 60 minutes most had been excreted in the urine. After oral administration of all analogues, there was virtually no absorption and more than 95% of the radiolabel remained in the alimentary canal. There appeared to be differential uptake of pepstatinyl-GKK by the gastric mucosa, however, as 1–2% of it could be recovered compared with <0.1% for all other isotopes. Such data may provide invaluable information for the targeting of these compounds in the exploitation of their considerable therapeutic potential.

P17 Immunocytochemical localisation of the newly discovered neuropeptide Y (NPY) in extrinsic (nor-adrenergic) and intrinsic gut neurons

G-L FERRI, A ALI-RACHEDI, S R BLOOM, K TATEMOTO, AND J M POLAK (Departments of Histochimistry and Medicine, RPMS, Hammersmith Hospital, London, and Department of Biochemistry, Karolinska Institutet, Stockholm, Sweden) The newly discovered peptide NPY has been isolated from the porcine brain, but has not been so far shown in the gut. By immunocytochemistry, using an antiserum not significantly cross reacting with the closely related peptides PYY (isolated from the porcine gut) and avian pancreatic polypeptide (APP), we have shown the presence of NPY-immunoreactive nerve fibres throughout the human, porcine, and rat gastrointestinal tract. In man, a rich supply was found in the muscularis mucosae, while the rat mucosa and external muscle layer were also heavily innervated. A perivascular NPY-immunoreactive nerve network was prominent in all three species and was the only one to disappear after selective destruction of nor-adrenergic neurons with intraperitoneal 60H-dopamine (four rats). Neuronal perikarya could be clearly identified in the rat submucous plexus after local treatment with colchicine, while no endocrine cells were immunostained. In conclusion, NPY-like immunoreactivity is present in gut nerves, partially co-localised with noradrenalin. The precise chemical nature of NPY-immunoreactive peptide/s in the gut remains to be elucidated.

P18 Mucosal distribution of VIP-, substance P-, and met-enkephalin-containing nerves in the human stomach and duodenum

G-L FERRI, P L BOTTI, G BILITTO, P VEZZADINI, S R BLOOM, G LABO, L TONELLI, AND J M POLAK (Departments of Histochimistry and Medicine, RPMS, Hammersmith Hospital, London, and Departments of Medicine I, University of Bologna, and Surgery I, University of Firenze, Italy) Little detailed information is available concerning the peptidergic innervation of the human gastro-duodenal mucosa. By fluorescence immunocytochemistry, we studied normal samples of stomach (oxyntic area, n=7, and antrum, n=8) and duodenum (n=8). Thin slices of p-benzoquinone-fixed mucosa and duodenal submucosa were microdissected, immunostained, and observed whole. VIP-containing nerve fibres formed a rich network in the muscularis mucosae and around fundic and pyloric glands, but were sparse in the pit region. Substance P-immunoreactive nerve fibres were rare in the fundic mucosa and more numerous in the antrum. Fibres containing either peptide were also seen in close correlation with intramucosal blood vessels in the stomach and formed a very rich network in the duodenal villi. VIP- and substance P-immunostained nerve bundles and perikarya were revealed between the lobules of Brunner's glands, while only few fibres reached the acinar cells. Scattered met-enkephalin-immunoreactive fibres were seen, mainly in the submucous plexus and in the muscularis mucosae. In conclusion, the distribution of the peptidergic nerves in the gastric mucosa is clearly distinct from that shown in the duodenum and, previously, in the distal gut.

P19 Immunocytochemical demonstration of the serotoninergic neuronal system of the human gut

S S KURIAN, G-L FERRI, J DE MEY, AND J M POLAK (Department of Histochimistry, RPMS, Hammersmith Hospital, London, and Laboratory of Oncology, Department of Life Sciences, Janssen Pharmaceutica, Beerze, Belgium) An intrinsic neuronal system containing serotonin, or 5-HT, is known to be present in the human gut and is thought to be involved in the control of postprandial vasodilation, secretion, and peristalsis. Because of the lack of simple techniques for its demonstration, however, this system has been little investigated. Samples of human jejunum, ileum, and colon (obtained fresh at surgery) were incubated with 50 mmol/L L-tryptophan (in order to enhance neuronal concentrations of 5-HT, for which L-tryptophan is the precursor) and fixed in 4% paraformaldehyde. After repeated washings in 70% alcohol, sections were cut with a cryostat and stained by immunofluorescence. At all levels studied, a rich arborisation of thin 5-HT-immunoreactive nerve fibres was seen in the myenteric ganglia, while fibres running across the muscle layer could be occasionally followed for longer courses. In the submucosa, a lower number of varicose fibres was also revealed in proximity of the ganglia. In conclusion, the 5-HT-containing nerves can be shown in the human gut by means of a simple, widely
proven, suspected, Strictureplasty.

P20

Strictureplasty. A useful, effective surgical treatment in Crohn's disease

P C HAWKER, R N ALLAN, P W DYKES, AND J ALEXANDER-WILLIAMS (Gastroenterology Unit, The General Hospital, Birmingham)

Strictureplasty is an accepted surgical technique in management of tuberculous ileal strictures. After an initial encouraging result we have used this operation in a series of patients with Crohn's strictures. This technique is described elsewhere.

Fifteen patients (five men, mean age 38.2 years, range 19-55) had 39 strictures (three duodenal, 13 jejunal, 18 ileal, one rectal, four ileocolonic anastomotic) treated by strictureplasty. The length of stricture: 3 cm (13), 10 cm (three), 10 cm (five).

Indications for surgery were recurrent obstructive symptoms or persistent pain, weight loss, and malaise in patients with either extensive disease or previous resection.

The mean hospital stay was 26 days (range 12-43). Four patients developed symptoms suggesting a suture line leak, one with a small fistula, and all settled conservatively.

Mean follow up of 12 months (range 5-18). Eleven patients have had an excellent result with loss of all symptoms and improvement in nutrition. Mean weight gain 6.6 kg and increase in serum albumin 6-1 g/l.

Four patients had only minor improvement, in three the symptoms are because of persistent extensive gut disease, the fourth developed a recurrent enterocutaneous fistula above an untreated stricture, requiring further strictureplasty.

Strictureplasty is an effective, safe procedure in selected patients with Crohn's disease.

P21

Accuracy of preoperative biopsy in the assessment of the histological grade of rectal carcinoma

M F DIXON, G D H THOMAS, N S SMEETON, N S WILLIAMS (introduced by Professor D Johnston) (University Departments of Pathology, Statistics and Surgery, The General Infirmary, Leeds) As the degree of differentiation of a rectal carcinoma is increasingly being used in making decisions on surgical management – for example, in selecting patients for local excision and in determining the margin of distal clearance in low sphincter-saving resections – we sought to determine the accuracy of preoperative biopsy.

The preoperative biopsy and the corresponding resected tumour from 100 patients were graded independently by two pathologists. The slides were examined randomly on two separate occasions to test intra-observer variation. Fifty of these paired biopsies and main tumours were graded by five pathologists to assess inter-observer variation. The intra-observer agreement between biopsy and tumour varied from 56-69% but as few as 46% of poorly differentiated carcinomas were diagnosed as such in the biopsy. Furthermore, although kappa statistics revealed significant overall agreement between observers, the levels for some observer pairings did not differ significantly from chance.

In an attempt to improve the predictive value of the diagnostic biopsy, multiple biopsies (mean 6-5) were taken from 32 rectal carcinomas under general anaesthesia. The level of agreement, however, with the main tumour (53%, k=0.172) showed no improvement.

We conclude that the histological grade of a rectal carcinoma cannot be accurately assessed by preoperative biopsy, and that studies which utilise histological grade for comparison purposes must be viewed with considerable scepticism.

P22

111Indium autologous leucocyte scanning in acute pancreatitis

J R ANDERSON, R A J SPENCE, J D LAIRD, W R FERGUSON, AND T L KENNEDY (Departments of Surgery, Radiology and Medical Physics, Royal Victoria Hospital, Belfast) 111Indium labelled autologous leucocyte scanning is now an established method for locating sepsis and assessing the extent of inflammatory bowel disease. We have assessed its value in acute pancreatitis.

Thirteen patients (seven women and five men, mean age 55.7 years, range 19-86 years) have been studied shortly after admission. The diagnosis of acute pancreatitis was based on clinical findings and amylase concentrations greater than 100 IU/l. Three patients had severe disease assessed by the presence of three or more of Imrie’s modified criteria. All three had positive 111In scans. A fourth patient, judged on prognostic factors to have mild disease, had a positive 111In scan; he developed a pseudocyst. A positive scan probably indicates severe fat necrosis. The remaining nine patients all had mild pancreatitis, none had a positive leucocyte scan and all settled without complications.

It is important to identify those patients who have severe disease with its high mortality and morbidity. From our initial experience it appears that 111In leucocyte scanning is a simple, non-invasive means of assessment. Its accuracy is similar to that of prognostic factor grading.

F23

Abnormal relationship between sex steroids and SHBG in primary cirrhosis

M L WILKINSON, M J IQBAL, F J JOHNSON, AND ROGER WILLIAMS (Liver Unit, King's College Hospital, Denmark Hill, London) Because of the striking female preponderance in patients with primary biliary cirrhosis (PBC) and the known cholestatic potential of oestrogens, we have measured serum total oestradiol (E2), testosterone (T), and 5α-di-hydrotestosterone (DHT) by radioimmunoassay and sex hormone binding globulin (SHBG) by two-tier column assay in 29 patients with PBC (eight men) and 41 age-matched controls (20 men). Total E2, T, DHT, and SHBG were all significantly raised in PBC women (190 pmol/l, 2.14 nmol/l, 0.744 pmol/l, and 89-8 nmol DHT bound/l respectively) and all but T raised in PBC men (239 pmol/l, 12.9 nmol/l, 1.4 pmol/l, and 69-5 nmol DHT bound/l respectively). In contrast with control subjects where, in agreement with previous experience there was a positive correlation between SHBG and E2 (women r=+0.91, p<0.001; men r=+0.66, p<0.001) and negative correlation between SHBG and T (women r=−0.31, p<0.05; men r=−0.58, p<0.01) and SHBG to DHT (women r=−0.45, p<0.05; men r=−0.52, p<0.05), in women PBC patients relationship was reversed (r=−0.57, p<0.05 for E2, r=+0.56, p<0.01 for T, and r=+0.67, p<0.01 for DHT) and none of the correlations was significant in PBC men. To determine if this was a general feature of cirrhosis or specific to PBC, the same parameters were measured in 25 patients with alcoholic cirrhosis (14 men). The only significant
correlation in this group was between SHBG and E₂ in men (r = +0.63, p<0.025). Raised E₂ concentrations may aggravate cholestasis in PBC and abnormal relationships between SHBG and circulating sex steroids may be due to abnormal steroid binding in the serum of these patients.

**P24**

**Transjugular liver biopsy. Preliminary results**

**NUNO GRIMA, A NUNES DIOGO, F RAMALHO, AMELIA BATISTA, AND J PINTO CORREIA**

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Transjugular liver biopsy (TLB) consists of obtaining a liver specimen, with a needle introduced into the liver parenchyma from the wall of a hepatic vein, through the internal jugular vein. This procedure eliminates the necessity for traversing the peritoneal cavity and puncturing the liver capsule. In this report we describe the results obtained through this process in 22 patients, in which percutaneous liver biopsy was not possible because of bleeding tendency and/or massive ascites. A transjugular liver biopsy was attempted in 20 out of the 22 patients, and liver specimen was obtained in 17 patients (85%). The samples obtained were fragmented and large enough for a histological diagnosis on 14 (82.0%) out of 17, with the following diagnosis: 12 with liver cirrhosis (in seven an information on aetiology was obtained), chronic active hepatitis with cirrhosis in one case, and granulomatous hepatitis in another. In the other three biopsies, the liver specimens were small and/or much fragmented, allowing only an assessment of hepatic cell morphology, and a presumptive diagnosis of liver cirrhosis was possible. In spite of small specimen of liver tissue obtained by TLB, the morphological information is similar to that obtained by percutaneous liver biopsy. Transjugular liver biopsy was followed by no complication in our patients. It seems, therefore, an efficient and innocuous method of obtaining liver tissue, large enough for a correct diagnosis. It should be used in patients when the percutaneous approach is contraindicated or dangerous.

**P25**

**Ulcerative colitis and persistent liver dysfunction**

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Six hundred and eighty-one outpatients with ulcerative colitis were screened for the presence of persistently abnormal liver function tests. Twenty patients (2.9%) with quiescent or mild cirrhosis had abnormal liver function and of these 16 (2.2%) were shown to have primary sclerosing cholangitis (PSC) by cholangiography. Only 56% of patients with PSC were symptomatic and two have died. Although there was wide variation in serum biochemical tests, often to within the normal range, persistent raising of alkaline phosphatase was a common finding. Liver biopsies showed a wide range of histological features and were diagnostic of PSC in only 50% of patients with PSC on cholangiography. The extent of PSC, judged radiologically, did not correlate with the biochemical abnormalities, liver histology, or the clinical features of the colitis. A close association with PSC and histocompatibility antigens HLA B8 and DR3 (eight of 15 patients, p<0.02, and nine of 12 patients, p<0.01, respectively) was found. Two patients with ulcerative colitis had previously been diagnosed as chronic active hepatitis and had been successfully treated with steroids but subsequently cholangiography showed PSC. This study shows that when persistently abnormal liver function tests are found in patients with ulcerative colitis it is likely that PSC will be present (80% of patients). A reliable diagnosis can only be made on cholangiography in addition to liver biopsy.

**P26**

**Are low C4 levels in chronic active hepatitis inherited?**

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Low concentrations of C₃ and C₄ complement components are found in patients with chronic active hepatitis (CAH), a disease associated with a familial predisposition to autoimmunity. These low concentrations have been attributed to immune consumption or defective synthesis secondary to liver damage. As genetic deficiency of complement components predisposes to viral and autoimmune diseases, however, we have performed a family study in children with CAH. C₃, C₄, and C₃d were measured by nephelometry. Low C₄ concentrations (0.11±0.03, normal 0.2±0.6 g/l) were found in 15 (75%) of 20 children with CAH, four of whom also had decreased C₃ (0.38±0.09, normal >0.55 g/l). To evaluate the role of complement consumption C₃d, a fraction derived from C₃ activation was measured in 15 children. Increased C₃d concentrations occurred in three of eight patients with reduced C₄, suggesting that low C₄ is not because of excessive consumption. C₄ was also measured in the healthy parents of six patients. Five children with low C₄ concentrations had one or both parents with similarly low concentrations, while normal concentrations were found in the parents of one child with normal C₄.

Our results suggest that low C₄ concentrations in some patients with CAH are inherited. This may be a factor predisposing to the development of CAH.

**P27**

**Immunglobulin abnormalities in cirrhosis**

PAN BO RONG, J KALSI, AND H J F HODGSON

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To elucidate the mechanism of hyperglobulinaemia in liver disease, we have investigated a group of 18 patients with cirrhosis. We assessed the relationship between immunoglobulin (Ig) synthesis in vitro by peripheral blood mononuclear cells (PBMC), suppressor cell activity in vitro, and in vivo serum concentrations. Suppressor activity was assessed by the short lived suppressor assay, in which activity is expressed as a suppressor index (SI), higher levels indicating greater activity. Peripheral blood mononuclear cells from cirrhotic individuals spontaneously synthesised more Ig than from normal control individuals after seven days in vitro culture (IgG 987±167 (SEM) ng/ml, n=18 vs 323±40 ng/ml, n=11; IgA 768±144 vs 288±48 ng/ml; IgM 113±15 vs 75±14 ng/ml). Enhanced synthetic rates were found both in alcoholic cirrhosis and in patients with chronic active hepatitis. There was a strong linear correlation between IgG synthesised in vitro and the serum concentration (r=0.90, p<0.01) amongst the whole group of cirrhotic patients. The suppressor cell activity in cells from patients was markedly reduced (SI=1.3±0.25 vs 2.37±0.16). Furthermore, for both IgG and IgA, there was a
striking inverse correlation amongst patients with cirrhosis between the amount of Ig synthesised in vitro and the suppressor cell activity in the same cell population (IgG r = -0.85, p<0.01; IgA r = -0.74, p<0.01). These results support the hypothesis that raised IgG concentrations in cirrhosis reflect increased synthesis, permitted by diminished activity of immunoregulatory suppressor cells.

P28 Which gliadin fraction is toxic? 
T S SINCLAIR, A D OHANNESIAN, D JONES, S EMMET, P KUMAR, N WALDRON, M L CLARK, AND M DAWSON Departments of Gastroenterology and Chemistry, St Bartholomew's Hospital, London, and Chelsea and Westminster Hospital, London Electrophoretic separation of gliadin yields four fractions (alpha, beta, gamma, and omega). Doubt remains as to which fraction or fractions is toxic to coeliac jejunal mucosa because of difficulties in separation of a sufficient pure quantity for clinical testing. With improved separation techniques we have been able to separate sufficient pure fractions to challenge tested coeliac volunteers.

Gliadin and its fractions were prepared by the method of Patey et al. Having shown that a 25 g dose of a whole gliadin was toxic, we challenged four patients with a 25 g mixture of beta 4-8, gamma and omega fractions by intraduodenal or intragastric infusion and further challenged one of the four patients with a 4-5 g mixture of alpha and beta 1-3 fraction. Jejunal biopsies were taken before and 24 hours after the challenge. Intraepithelial lymphocytes per 100 epithelial cells (IELs) and lamina propria IgA and IgM containing cells/mm² were measured.

No significant change in IELs or IgA and IgM containing cells were seen after challenge with the beta, gamma, and omega mixture in any of the four patients. The patient who was further challenged with the alpha and beta gliadin mixture, showed a rise in IELs from 35 to 59, a rise in IgA cells/mm² from 435 to 611, and a rise in IgM cells/mm² from 235 to 317.

Toxicity appears to be confined to the alpha and beta 1-3 gliadin mixture and further challenges with its separate components are planned.

P29 Comparison of Eder-Puestow and Celestin technique for dilating benign oesophageal strictures
K R HINE, C J HAWKEY, G K T HOLMES, AND M ATKINSON (University Hospital, Nottingham, and Derbyshire Royal Infirmary, Derby) Endoscopic dilatation is now established as the method of choice in the treatment of peptic oesophageal stricture. We have compared the Eder-Puestow metal olive dilators with the recently introduced Celestin tapered dilators, in a randomised trial.

Ninety-one dilatations were performed on 53 patients with benign strictures, of these 49 were Eder-Puestow and 42 Celestin dilatations. These two groups were comparable in the grade of dysphagia, number of previous dilatations, and characteristics of the stricture.

There were no perforations but pharyngeal bleeding occurred in three patients undergoing Eder-Puestow dilatation. The Celestin technique was significantly quicker and caused damage to only two guide wires, whereas 26 wires were damaged using Eder-Puestow dilators. On three occasions with Celestin dilatation, insufficient guide wire could be passed through the stricture to accommodate the leading part of the Celestin dilator and the Eder-Puestow method had to be substituted. In some patients, the teeth caused resistance to the advance of the large Celestin dilator which could be confused with resistance from the stricture. Reassessment of the patients one month after dilatation showed the methods were equally effective in relieving symptoms.

We conclude that both techniques are safe and effective but that the Celestine method is quicker and less likely to cause pharyngeal trauma. It is not applicable, however, to those patients in whom only a short length of guide wire can be passed through the stricture.

P30 Endoscopic transpapillary biopsy (ETPB) – light and electron microscopic findings, clinical significance
H DANCIYGER, J PHILLIP, F HAGENMULLER, K JESSEN, U KLEIN, K HUBNER, U LESCHNER, AND M CLASSEN (University Medical Centre, Department of Gastroenterology and Centre of Pathology, University Clinics, Frankfurt/Main, FR Germany) Endoscopic transpapillary biopsy has been performed in 53 patients undergoing investigation for bilipancreatic disease or during endoscopic sphincterotomy. One hundred and thirty-seven biopsies from hepatic ducts, the common bile duct, and from the papillary/ampullary region were investigated by light microscopy, transmission and scanning electron microscopy, and by immunocytochemical methods.

Eighty-nine per cent of the biopsies were suited for histological examination whereas 11% yielded only material for cytological evaluation. Various degrees of inflammation were seen in the hepatic ducts, common bile duct, and the ampulla in 14, six, and 24 biopsies respectively. Benign neoplasms were seen in three hepatic duct and in 15 ampullary biopsies. Six ampullary carcinomas were proven histologically. The epithelial cells resemble those of the small intestine showing microvilli, a terminal web, and a prominent Golgi apparatus. In severe cholestasis goblet cell metaplasia occurs. Small basal cells are intraepithelial suppressor T lymphocytes.

Endoscopic transpapillary biopsy is a valuable tool to increase our knowledge of the structure of human bile ducts. While the clinical significance of 'blind' hepatic duct biopsy is not apparent, biopsy of even tiny ampullary lesions is mandatory.

P31 Split overtube for easier colonoscopy
CHRISTOPHER B WILLIAMS (St Mark's Hospital, London) Many of the technical problems of colonoscopy are because of unavoidable looping of the sigmoid colon. The use of overtube (stiffening tube) passed up over the colonoscope prevents this problem but present overtubes must be in place on the instrument before the procedure and require fluoroscopy for safe insertion.

A new soft plastic split overtube is described which can be used or removed at any point in the examination and does not require fluoroscopy. Initial experience shows it to be more comfortable for the patient than conventional overtubes and its construction makes any likelihood of complications inherently unlikely. Many examinations which would previously have been prolonged or painful have proved quick and easy using the split overtube.

GASTRIC CANCER
F33–F36

F33 Effect of ascorbic acid treatment on gastric
juice nitrite and N-nitroso compound concentrations in achlorhydric subjects

P I REED, K SUMMERS, P L R SMITH, C L WALTERS, B A BARTHOLOMEW, M J HILL, S VENNITT, D HORING, AND J-P BOJOUR (Gastrointestinal Unit, Wexham Park Hospital, Slough; Leatherhead Food Research Association, Leatherhead, Surrey; Public Health Laboratory Service, Porton Down, Wilts; Pollards Wood Research Institute, Chalfont St Giles, Bucks; and Hoffman-LaRoche, Basle, Switzerland) N-nitroso compound involvement is increasingly suspected in the development of gastric cancer, an increased risk of which exists in hypochlorhydric conditions including pernicious anaemia (PA), atrophic gastritis with intestinal metaplasia (AG), after partial gastrectomy (PG), and probably vagotomy with drainage. Animal studies have shown that concurrent administration of ascorbic acid (vitamin C), a strong antioxidant, with amine and nitrite could reduce and even prevent tumour production and vitamin C could also block nitrosation of virtually all substrates in vitro. We report the effects of vitamin C treatment on the intragastric milieu, including N-nitroso compound formation, in hypochlorhydric states.

In 51 patients with either PA, AG, or PG, taking vitamin C 1 g qds for four weeks, 226 fasting gastric juice samples were obtained endoscopically before, during, and four weeks after treatment; were cultured for total and nitrate reducing organisms, mutagenicity studies were performed and pH, nitrate, nitrite, and total extractable N-nitroso compound concentrations measured, as were plasma vitamin C concentrations. Mean N-nitroso compound concentration was significantly reduced in the group as a whole, from 6.84 ± 9.39 μmol/l SEM pretreatment to 4.64 ± 10.17 μmol/l after four weeks on vitamin C (p = 0.028), rising to 8.88 ± 14.64 μmol/l four weeks off treatment. A significant reduction (p = 0.027) was seen in the PG group (n = 21) but not in the other two groups. Vitamin C treatment reduced nitrite concentration from 1237 ± 2647 μmol/l to 775 ± 1538 μmol/l (p = 0.08) and also growth of nitrate-reducing organisms. Of the 25% of samples which were mutagenic, 74% were obtained when vitamin C was not taken. The gastric pH was virtually unchanged: 5.63 ± 1.00 before and 5.57 ± 1.03 during vitamin C treatment. Subnormal basal plasma vitamin C concentrations (<2 mg/l) were recorded in 51% patients. No significant side effects were noted during treatment.

Thus, for the first time in man vitamin C treatment has been shown to reduce gastric nitrite and N-nitroso compound formation, the latter significantly, in hypochlorhydric subjects at risk from gastric cancer. Vitamin C treatment might be useful in protecting susceptible individuals from the effects of such carcinogens and further studies in larger patient groups to test this theory are justified.

F35
Endoscopic examination of the gastric remnant 31–39 years after subtotal gastrectomy for peptic ulcer

I R PICKFORD, J L CRAVEN, R HALL, G THOMAS, AND W D STONE (York Pechic Ulcer Trust, York District Hospital, York) Published endoscopic studies of the gastric remnant 15–20 years after partial gastrectomy have revealed unsuspected carcinomas and a high incidence of mucosal abnormalities. The aim of this study was to evaluate the role of routine endoscopy in the long term management of postgastrectomy patients and to determine their risk of gastric cancer.

Three hundred and seven patients have been followed up at least 20 years after subtotal gastrectomy for peptic ulceration. Endoscopy was carried out in 54 patients and multiple biopsies taken from the peristomal gastric mucosa.

There were nine deaths from gastric cancer, three times the expected number. If gastrectomy was performed for gastric ulcer the risk of later development of carcinoma (7%) was significantly greater than that after operation for duodenal ulcer (1.6%) (p = 0.001).

No cancers were diagnosed in the patient endoscoped. Atrophic gastritis was found in 98% of patients and intestinal metaplasia in 44%. Dysplasia was present in 35% but in no case was it severe.

Although we have found that there is an increased risk of cancer developing in the gastric remnant we do not consider routine endoscopic follow up of all post-gastrectomy patients to be a practical proposition.

F36
Staging of gastric cancer by means of endoscopic ultrasonography

G CALETTI, L BOLONDI, E BROCHI, P CASANOVA, L ZANI, S GAJANI, S TESTA, G GIUZZARDI, AND G LABO (Department of Medicine and Gastroenterology, University of Bologna, Bologna, Italy) Endoscopy with brush cytology and multiple biopsies is a technique with high sensitivity and
specificity in the diagnosis of gastric cancer, but gives insufficient information about the real extension of the neoplasm and the involvement of extraluminal tissues. By means of a newly developed ultrasonic endoscope (Olympus GF – UM1/EUM1), filling the stomach with 300–500 ml of distilled water, it is possible to obtain a good visualisation of the normal gastric wall’s layers (1) mucosa and submucosa; (2) muscle coats; (3) serosa; (4) periserosal fat. In order to evaluate the accuracy of this technique in assessing the invasivity of the gastric cancer, we examined 12 patients with a normal stomach and 10 patients (aged 41–75 years, mean 64 years; seven men and three women) affected by gastric cancer (seven ulcerated type on the lesser curve, one fungating type at the cardias, one fungating type and one superelevated early gastric cancer on the posterior wall of the body). In all ulcerated cancers the ultrasonographic findings revealed a large area of localised thickening with a central depression and a complete disappearance of the 1st, 2nd, and 3rd echographic layers. In two of these cases also the 4th layer was not recognisable, and we hypothesised an involvement of the extraluminal tissues. In one case some roundish echo poor masses were seen outside the gastric wall and these were referred to metastatic lymphnodes. In the two cases of fungating neoplasms a large echogenic mass irregularly protruding into the lumen but not involving the 4th layer, was observed. In the case of early gastric cancer, type I, a small circum- scribed thickening of the first layer was seen. The pathological examination of the surgical specimens confirmed in all cases the ultrasonographic diagnosis. This method may be useful for a better definition of the real extension of gastric cancer, so giving important information about resectability.

AND V S CHADWICK (Departments of Medicine and Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, London) There is conflicting evidence about plasma CCKs in coeliac disease and their relation to gall bladder function. To study these aspects further we compared both gall bladder emptying and plasma CCK responses in normal volunteers and patients with coeliac disease.

Studies were performed in six normal volunteers and in 10 patients with coeliac disease: four untreated, four on a gluten free diet, and two non-responsive patients also on a diet. All patients had recently had a jejunal biopsy. Each subject received 100 µCi 99mTc-HIDA intravenously to show the gall bladder and then drank a liquid fat meal. Gall bladder emptying curves were generated using a gamma camera linked to a computer and blood samples taken for plasma CCK estimations and integrated CCK responses (I CCK) calculated.

Gall bladder emptying rates (t½) were 21·6±4·9 (SEM) minutes in normals, 143·6±60·2 minutes in untreated coeliacs, 37·3 and 40·7 minutes in non-responsive coeliacs, and 23·7±4·3 minutes in treated patients with a virtually normal biopsy. Corresponding plasma I CCK responses were 45±4·9–8 pmol/l/30 min in normals, 16·5±10·7 in untreated coeliacs, 20·8±6 and 44±1·8 in non-responsive patients, and 47·2±8·7 in treated patients. In one patient studied before and after nine months on a gluten free diet, the jejunal biopsy improved markedly, gall bladder emptying rate changed from 160·8 to 20·1 minutes.

Impaired biliary responses to meals in coeliac disease are reversed by a gluten free diet, and are probably because of impaired CCK release.

F39
Hyposplenism of coeliac disease is largely reversible
J G O’GRADY, F M STEVENS, T A O’GORMAN, AND C F MCCARTHY (Regional Hospital, and University College, Galway, Ireland)
Hyposplenism in coeliac disease (CD) is considered irreversible and unlikely to be related to the state of the jejunal mucosa. We assessed splenic function in 161 adults with CD – treated and untreated – by evaluating the percentage of ‘pitted’ erythrocytes in peripheral blood. Platelet counts, serum immunoglobulins, and HLA type were studied in these and in 121 normal and in 103 splenecomised controls.

Hyposplenism was found in 76·5% of 81 coeliacs with grade III small bowel biopsies (severe mucosal damage), in 76·9% of 26 coeliacs with grade II biopsies (moderate mucosal damage), but only in 8·7% of 46 coeliacs with grade 0/1 biopsies (normal or minor abnormalities). Coeliacs with severe hyposplenism had higher platelet counts (p<0.001) and lower IgM concentrations (p<0.002) than coeliacs with normal splenic function. Sequential studies were performed in 18 untreated coeliacs with hyposplenism. ‘Pitted’ erythrocyte counts fell in all cases (p<0.01) and after six months on a gluten free diet, splenic function was normal in 83·3%. The platelet counts fell (371×10^12±132×10^12) to withdrawal. Two patients had osteomalacia. On introducing prednisolone 20–30 mg/day, two patients improved symptomatically, but only one improved histologically. We therefore introduced azathioprine 2 mg/kg/day and weaned the patients off prednisolone. All three patients improved symptomatically. Furthermore, the three patients showed a mean surface cell height of 11 µm (range 10–12) before azathioprine, rising almost to the normal range, mean 25 (range 20–30), after azathioprine and in addition a mean intraepithelial lymphocyte count/100 cells of 2 (range 50–70) before azathioprine and dropping to the normal range, mean 16 (range 10–25), after azathioprine, indicating that all had a dramatic histological improvement.

We conclude that azathioprine is a useful alternative therapy for non-responsive villous atrophy, either where prednisolone has failed or where the dose of prednisolone required to maintain remission causes unacceptable side effects.

F38
Azathioprine responsive villous atrophy
T S SINCLAIR, P J KUMAR, AND A M DAWSON (Department of Gastroenterology, St Bartholomew’s Hospital, London) Villous atrophy unresponsive to gluten withdrawal is a morbid disease and can be fatal. Prednisolone may induce remission but large doses may be required with consequent side effects. We have studied three patients all of whom presented with weight loss, diarrhoea or steatorrhoea, and had villous atrophy unresponsive to gluten

SMALL INTESTINE
F37–F40

F37
Reversible defect of gall bladder emptying and plasma cholecystokinin (CCK) release in coeliac disease
N P MATON, A C SELDEN, M L FITZPATRICK,
Loperamide has antisecretory activity in vivo in human jejunum

S HUGHES, N B HIGGS, AND L A TURNBEG (Department of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford The antidiarrhoeal effects of opiates, initially thought to be because of actions of intestinal motility, are now also known to have antisecretory activity in vitro. We examined the possibility that the antidiarrhoeal, loperamide, can influence intestinal secretion in man using a triple lumen tube perfusion technique. Loperamide (4 mg bolus, followed by 3 mg/l of perfusate, intraluminally) failed to alter basal absorption of H2O, Na, K, or Cl from a bicarbonate/saline or bicarbonate free solution (n=5). Loperamide, however, inhibited prostaglandin induced secretion. PGE2 (5 x 10^-6M), intraluminally, induced secretion of Na, Cl, and H2O (H2O secretion 89±1±8.9 ml/h/30 cm) which fell spontaneously during the second of two consecutive study periods (by 51±58.3%, n=6). Loperamide (4 mg bolus + 3 mg/l perfusate) converted secretion to absorption in three of six subjects and reduced mean H2O secretion by 95.1±15.2% (n=6) (significantly greater change than that seen with two consecutive PGE2 alone studies). Mean transit time was markedly shortened by PGE2 (6 minutes control, 2 minutes PGE2) but this was unaffected by loperamide. Pretreatment with loperamide (8 mg bolus) after perfusion with PGE2 plus loperamide (6 mg/l) markedly reduced the secretion of H2O and Cl provoked by prostaglandin alone (H2O secretion after loperamide 36.3±13.3 ml/h/30 cm, n=5) compared with PGE2 alone, 90±3±10.4 ml/h/30 cm (n=12) (p<0.02). Cl secretion after loperamide was 5.74±2.2 mmol/h/30 cm (n=5) compared with PGE2 alone, 12.75±1.4 mmol/h/30 cm (n=12) (p<0.02). Thus loperamide given before or after the secretagogue reduced secretion, suggesting that this antisecretory effect may be important in its antidiarrhoeal activity.

NUTRITION
F41–F44

F41 Prospective controlled study of the significance of catheter tunnelling and a nutrition nurse on TPN catheter sepsis

P F KEOHANE, B J M JONES, H ATTRILL, J NORTHOVER, A CRIBB, AND D B A SILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Despite a lack of controlled data to confirm efficacy of the technique, TPN catheter tunnelling is widely used to prevent catheter sepsis. All patients receiving TPN in this hospital are managed by a nutrition team, augmented for the last year by a nutrition nurse with complete responsibility for catheter care. A three year prospective controlled study of catheter tunnelling is reported. Silicone catheters (Nutricath S, Vygon) were used in all patients, inserted by subclavian (94%) or jugular (6%) approach under sterile conditions by three experienced operators, and used only for nutritional fluids. Patients were randomly allocated to receive tunneled (52) or untunneled (47) catheters. Cultures of skin, blood, and catheter tip were performed on removal of all catheters. Sepsis occurred in 13 of 47 untunneled catheters (28%), inserted in 39 patients for 10.2±7 (range 3–35) days. Significantly less sepsis occurred in the tunneled group (p<0.05) being found in only six of 52 catheters (12%) used for 11.3±8 (range 2–36) days. Additionally, a nutrition nurse significantly (p<0.001) reduced sepsis rate from 33% (tunneled six; untunneled 11) to 4% (tunneled nil; untunneled two) no other changes being made. These results show that sepsis rate in silicone TPN catheters is significantly reduced by both catheter tunnelling (p<0.05) and a nutrition nurse (p<0.001).

F42 Nutritional cost of protracted diarrhoea in young Gambian children

ANDREW TOMKINS Medical Research Council, Fajara, Gambia, W Africa, and Department of Human Nutrition, London School of Hygiene and Tropical Medicine, London Three day measurements of dietary intake and faecal losses during and after recovery from protracted diarrhoea (PD) were made in nine young children eating a traditional diet of rice and millet. Intake (in units/kg body weight/day) was lower during PD than after recovery (energy 67 vs 143 kcal, nitrogen 265 vs 486 mgm). Faecal losses decreased after recovery (energy 13 vs 8 kcal, nitrogen 72 vs 57 mgm). Twenty-one young children with PD received a locally prepared formula feed only (dried skimmed milk, sugar, oil, and water). They achieved better intakes of energy (132 vs 67 kcal) and nitrogen (634 vs 265 mgm) although faecal losses were greater than in the children receiving traditional diet (energy 18 vs 13 kcal, nitrogen 130 vs 72 mgm).

F43 Double blind controlled trial of ‘starter regimes’ in enteral nutrition

P F KEOHANE, H ATTRILL, M LOVE, P FROST, AND D B A SILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Despite lack of supportive evidence, the use of dilute ‘starter regimes’ to increase diet osmolality incrementally during the first three to four days of enteral nutrition is widely advocated to reduce gastrointestinal side effects. This double blind study was performed to investigate influence of both diet osmolality and ‘starter regimes’ on nutrient intake and gastrointestinal complications during enteral nutrition. One hundred and eighteen medical and surgical patients with normal gastrointestinal function were randomised to three groups. Group 1 (40 patients) received a hypertonic diet (Clinifeed 400; 430 mOsmol; 12 gN; 1900 ml/day). Group 2 (39 patients) received the same hypertonic diet with a three day ‘starter regime’ (5 gN day 1 to 12 gN day 3; 1900 ml/day). Group 3 (39 patients) received an isotonic diet (Clinifeed ISO; 300 mOsmol; 12 gN; 2310 ml/day). All diets were aseptically prepared and administered by 24 hour nasogastric infusion via 1-51 bags. Mean daily nitrogen intake in group 1 (11±2±4 gN/day in 8±8±7 days) was significantly greater (p<0.05) than both group 2 (7±5±4 gN/day in 8±4±7 days) and group 3 (5±4±6 gN/day in 10±7±1 days).
days) and group 3 (8.9±3 gN/day in 8.8±8 days). Incidence of hæmæuse, bloating, cramps (10% group 1; 15% groups 2 and 3) and diarrhoea (5% group 1; 21% group 2; 18% group 3) was similar in all groups, but diarrhoea was significantly associated (p<0.001) with antibiotic therapy. These findings suggest that a 'starter regime' is unnecessary and better nitrogen intake and balance result from the use of hypertonic diets administered via constant gravity infusion. Diarrhoea is related to concurrent antibiotic therapy and not to intolerance of hypertonic diet.

F44
Effect of supplemental enteral nutrition on anthropometric measurements, nitrogen balance, and pre-existing oral intake

M J HALL, A P MANNING, AND C SYMES (University Department of Medicine and Department of Dietetics, Bristol Royal Infirmary, Bristol) Enteral nutrition is widely used to restore nutritional status but few studies have shown significant improvement of anthropometric and other nutritional parameters. Continuous infusion of nutrients through a fine bore nasogastric tube facilitates continued oral intake provided there is patient compliance.

Twenty-three patients, 10 with inflammatory bowel disease, received supplemental enteral nutrition which provided 9.8 g nitrogen and 8550 kJ (2040 kcal)/day for a mean of 22 (range nine to 44) days.

There were significant increases after seven days of nutrition in percentage of ideal weight (I) (70.4±2.0 vs 76.3±1.8, mean ± SE), percentage of previous weight (P) (76.2±1.6 vs 82.5±1.2), triceps skinfold thickness (TSF) (44.2±3.2 vs 48.2±3.1% standard), and arm muscle circumference (AMC) (71.8±1.5 vs 74.9±1.6% standard). Further significant increments occurred after 14 days (I, P, TSF, AMC), 21 days (TSF), and greater than 21 days (I, P, TSF).

No significant decrease occurred in pre-nutrition oral non-protein energy and nitrogen intakes throughout the period of the study. Nitrogen balance increased from 0.7±0.1 to 6.1±0.1 g/d (p<0.001) after seven days and remained at this level.

We conclude that supplemental enteral nutrition is an effective method of providing nutritional support and does not suppress existing oral intake when given as a continuous infusion via a fine bore nasogastric tube.

LIVER/BASIC SCIENCE
F45–F48

F45
Pigment gall stones following resection of bypass of the distal ileum

K I BICKERSTAFF AND A R MOOSA (introduced by Professor A Cuschieri) (University Department of Surgery, Ninewells Hospital and Medical School, Dundee, and Department of Surgery, University of Chicago, Illinois, USA) In a previous experiment we unexpectedly observed the formation of bilirubin gall stones after distal ileal resection. To further investigate this hitherto unreported phenomenon the following study was performed. Resection (IR) or bypass (IB) of the distal third of the ileum and sham laparotomies were performed on prairie dogs fed a standard rodent diet (n=10 for each group). Cholecystectomy was performed in all animals eight weeks after operation and the gall bladders examined for stones and the bile cultured. Total bilirubin bile acid, cholesterol, and phospholipid concentrations of gall-bladder bile, haematocrit and serum bilirubin concentrations were determined. The common bile ducts were cannulated and the hepatic bilirubin output calculated over 90 minutes. The main component of the stones (determined by infra-red spectroscopy) was bilirubin. Infected bile occurred in two animals (1S, +IR). The haematocrit, serum bilirubin, and hepatic bilirubin output did not differ significantly between the groups. We conclude that IR and IB in the prairie dog predisposes to the formation of bilirubin gall stones. The aetiology of the stones is unclear, but they are not associated with biliary sepsis or increased haemolysis.

F46
Functionally separate hepatic arterial and portal venous vasculature

P N BENNETT, A B AHMAD, AND M ROWLAND (School of Pharmacy and Pharmacology, Bath University, Royal United Hospital, Bath, and Department of Pharmacy, Manchester University, Manchester) The vascular spaces (V) of the hepatic artery (HA) and portal vein (PV) in isolated in situ Wistar rat livers perfused through both vessels were calculated from the flow rate and mean transit times of 51Cr-labelled red blood cells (RBC). V_HA and V_PV were determined at HA:PV flow ratios ranging from 9:1 to 1:9 with a total flow of 10 ml/min in 25 rats. Analysis of the regression line (r=0.99) for the HA space against fractional HA flow contribution (f_HA) indicated that when f_HA=0, the intercept on the y-axis was 0.11, a value which was significantly different from zero (p<0.05). This implies that when the HA flow is reduced to zero, PV flow can occupy only 89% of the total vascular bed. The intercept on the y-axis when f_HA=1 was 0.94 implying that there are some areas of the liver that are not accessible to the HA stream. The data suggest that the hepatic vascular bed comprises one region which is supplied with blood solely from the HA, one supplied solely with blood from the PV, and a third region representing a very large fraction of the total vascular space, which is capable of being supplied by blood from both sources. These vascular beds may also be functionally separable as the clearance of the highly heptatically extracted drug, lignocaine, administered simultaneously through the HA and PV could always be predicted from the sum of the clearance values determined when the drug was introduced separately into the HA or PV. Furthermore, the perisinusoidal albumin (ALB) space (125I-labelled ALB) calculated as V_ALB−V_RBC correlated with increasing f_HA (r = −0.90) and with systemic availability of lignocaine (r = −0.95).

F47
Effect of portal venous diversion on tumour growth

G JACOB, S C HOWE, AND K E F HOBBS (Academic Department of Surgery, Royal Free Hospital School of Medicine, London) Clinical and experimental studies have shown the regression of established liver tumours after portal venous deprivation. Little is known, however, about initial tumour growth in the absence of portal venous blood. We have studied the growth of implanted hepatic and subcutaneous tumours after portal venous diversion.

Seven groups of male Sprague-Dawley rats (body weight 268±15 g) underwent staged portal diversion (n=10 per group) or sham surgery (n=10). Each experimental group received an inoculum of Walker carcinoma cells (5×10⁴ in suspension) into the median lobe of the liver and axillae at either 0, 1, 2, 3, 4, or 6 days after portal diversion. Ten days after inoculation the liver, tumour, and body weights were recorded. There was a significant increase in the weights of the liver, tumour, and body in every group compared with the sham-operated group.
in both liver tumour weight, axillary tumour weights and tumour/body weight ratios in those groups inoculated between the second and fourth days after diversion (p<0.01, t test). No evidence of hepatocellular dysfunction was noted on serial enzyme assays.

A further seven groups (n=5 per group) underwent hepatic and axillary inoculation at similar intervals after excision of the left lateral lobe (=30% hepatectomy). There was no difference in tumour weights or tumour/body weight ratio between groups or sham operated controls 10 days after inoculation.

We conclude that for a limited period after portal venous diversion there is a systemic stimulus to tumour growth which does not follow 30% hepatectomy.

F48
Acute folate deficiency does not increase the rate of liver folate release: a mechanism for acute megaloblastic anaemia following intensive care therapy
D G WEIR, A MOLLOY, A SMITHWICK, P MCQUIGG, AND J M SCOTT (Departments of Clinical Medicine and Biochemistry, Trinity College and St James’s Hospital, Dublin, Eire) Rapidly proliferating cells of the bone marrow and GI tract are dependent on plasma folate for normal DNA biosynthesis. Megaloblastic marrows have been reported to occur in intensive care units in the presence of normal red cell folate concentrations. The suggested explanation was an inability to mobilise ‘tissue folate stores’ quickly enough. The following experiments were performed to test this hypothesis. (1) Groups of rats were injected with (H³) folate acid to label their liver folate polyglutamates. After 48 hours’ equilibration they were assigned to folate-deplete or supplemented diets and the rate of mobilisation monitored for 23 days. Mobilisation was the same in both groups. (2) Rats maintained on a folate deficient diet for two months were then treated as in (1) above. Again mobilisation rate were identical in both groups, although L-Casei estimation of total liver folate revealed a significant increase in the liver folate of the supplemented group. (3) Rats with liver folate pools equilibrated with (H³) folate acid as in (1) were exposed to either N₂O or air. Again there was no difference in the mobilisation rate of the labelled folate although the total liver folate of the N₂O treated rats was reduced by half. (4) No evidence of any cytosolic folate conjugase activity was found in the liver of either the replete or deplete rats. Furthermore, ethanol did not increase biliary folate excretion in our hands.

In conclusion, folate deficiency does not increase liver folate mobilisation to a rate greater than normal, suggesting that the marrow and other cells depend on the diet and cell death to replenish plasma folate supplies. There is no evidence that the body possesses a tissue folate store capable of being mobilised.
J A Wilson, E J S Boyd, and K G Wormsley
(Department of Therapeutics, Ninewells Hospital and Medical School, Dundee)

Omeprazole is a substituted benzimidazole which inhibits gastric secretion by
inhibiting hydrogen-potassium dependent ATPase. We have examined gastric acid
output on three separate occasions to determine the effect of intraduodenal omeprazole (40
mg, 80 mg, and also placebo).

Basal gastric juice was collected for 30
minutes. Gastric aspiration continued while a pentagastrin infusion (0.25 μg/kg/
hr) was given for three hours. One hour after the start of the infusion the drug or
placebo was given through an intraduodenal tube in randomised double-blind
fashion, together with phenol red as marker to detect duodenogastric reflux.

Mean acid output fell with omeprazole (40 mg) by 56% from 21.9 to 9.7 mmol/
in the first hour after drug administration and to 0.5 mmol (98%) in the second hour.
With 80 mg, acid decreased by 73% from 24.0 to 6.4 mmol in the first hour and to 0
mmol (100%) in the second hour. This fall was paralleled by pepsin; with 40 mg, pepsin
decreased by 65% from 151 to 53 mg in the first hour and to 11 mg (93%) in the
second hour. Respective values with 80 mg were 80% from 132 to 27 mg, and to 0
mg (100%) in the second hour. The degree of gastric inhibition was statistically signifi-
cantly greater during the second hour after administration of the 80 mg compared with
the 40 mg dose. No change in gastric secretion was observed after adminis-
tration of placebo.

We conclude that omeprazole is a highly potent antisecretory agent with a systemic
effect on gastric secretion.

F52
Effect of omeprazole on gastric acid secretion in human volunteers
C W Howden, J L Reid, and J A H Forrest
(University Department of Materia Medica and Gastroenterology Unit, Stobhill
General Hospital, Glasgow) Omeprazole, a substituted benzimidazole, is a new agent
which appears to inhibit gastric acid secretion by selective non-competitive
antagonism of the H⁺/K⁺ ATPase enzyme in the parietal cell.

We have assessed its effects on basal and
stimulated gastric acid secretion, and fasting plasma gastrin concentrations, in 12
healthy male volunteers. Two groups of six
subjects received 30 or 60 mg once daily for
seven days. Basal and stimulated acid secretion (following pentagastrin 1-2 μg/kg
intravenously over one hour), and fasting plasma gastrin concentrations, were
determined after placebo administration and after the first and last dose of
omeprazole.

A single 30 mg dose of omeprazole reduced mean basal acid output (BAO) from
4-30 to 1-53 mmol/h (−66%) and mean peak acid output (PAO) from 35-41
to 10-24 mmol/h (−71.2%). After seven days of treatment the mean BAO was 0-01
(−99-0%) with five out of six subjects being achlorhydric, and the mean PAO 0-56 mmol/h (−98-4%) with three subjects being achlorhydric. A single 60 mg dose
reduced mean BAO from 4-56 to 0-38
mmol/h (−91-7%) and mean PAO from
37-11 to 1-74 mmol/h (−95-3%). After
the seventh dose the mean BAO was 0-04
(−99-1%), with five subjects being achlor-
hydric, and mean PAO 0-37 mmol/h
(−99%) with only one subject achlor-
hydric.

Fasting plasma gastrin concentrations were raised after treatment in those
subjects who received 30 mg/day. Pre-
treatment concentrations were 64±5-17-3
ng/l (mean ± SD), and post-treatment values were 149±5-54-1 ng/l (p<0-05). No
clinical or laboratory side effects were noted.

F53
Sucralfate in refractory duodenal ulcers
M Guslandi, E Ballarin, and A Tittobello
(3rd Medical Clinical, University of Milan,
Milan, Italy) Duodenal ulcer healing after
short term treatment with H₂-receptor antagonists is usually achieved in up to
80–85% of cases. Although in some patients prolonged treatment with the
same drug may ultimately result in healing, about 20% of duodenal ulcers seem to be
refractory to conventional medical therapy.

Aim of the present study was to investi-
gate the effectiveness of a different thera-
peutic approach in refractory duodenal ulcers. Twenty patients who had failed to
respond to an eight week treatment with either cimetidine 1 g daily (13 subjects) or
ranitidine 300 mg daily (seven subjects) were changed to therapy with sucralfate 3 g
daily for six weeks. Subjects showing a
reduction in the ulcer size after the initial
course with H₂-blockers were excluded from the study.

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At endoscopic control after sucralfate treatment complete ulcer healing was observed in 16 patients (80%). Sucralfate is an anti-ulcer agent which acts by protecting the gastroduodenal mucosa against acid,
pepsin, and bile salts without reducing gastric acid secretion. Our findings suggest that inhibition of gastric acidity is not always the proper management of
duodenal ulcer and that some patients may prove more sensitive to treatment with
drugs that increase mucosal defences.

F54
Do H₂ antagonists increase pepsin output (PO) in duodenal ulcer patients?
T Gledhill, M Buck, S P Gray, J A Billings, and R H Hunt
(Department of Gastroenterology, RN Hospital, Haslar, Gosport, Hants) Non-response to cimetidine may be because of increased vagal drive. Pepsin secretion is enhanced by cholinergic stimulation. We measured nocturnal PO in six cimetidine non-responders (NR). Patients were studied over two separate 24 hour periods receiving no treatment or cimetidine 1 g/day. After the first cimetidine nocturnal PO (IU/h) increased from 2-6±4-1 to 6-6±5-6 while acid (mmol/h) decreased from 6-7±6-5 to 3-9±5-2. A further six NR and six cimetidine responders were studied over three separate 24 hour periods receiving either placebo, cimetidine, or ranitidine. In the
NR, PO (IU/h) increased from 1-6±1-9 on
placebo to 2-9±5-2 on cimetidine and
3-1±2-1 on ranitidine while acid (mmol/h)
decreased from 5-2±4-1 on placebo to
3-8±3-0 on cimetidine and 1-7±1-3 on ranitidine. In the responders, PO (IU/h) increased from 0-4±0-2 on placebo to 2-8±1-6 on cimetidine and 2-6±2-1 on ranitidine while acid (mmol/h) decreased from 5-1±2-9 on placebo to 3-5±1-6 on cimetidine and 1-2±0-9 on ranitidine. When all duodenal ulcer patients were analysed together, cimetidine increased PO from 1-5±2-7 IU/h to 3-9±5-2 IU/h (p<0-05). Acid output decreased from
5-6±4-5 mmol/h to 3-7±3-3 mmol/h (p<0-01).

Cimetidine raises intragastric pH and pepsin is inactivated at high pH concentra-
tions. An increase in PO may not become apparent unless cimetidine has a reduced effect on acidity as occurs in non-responders. We conclude that H₂-
receptor antagonists may increase nocturnal PO and suggest this may be a reason for non-response to H₂ blockade.
Comparison of continuous maintenance with ranitidine or placebo after one year's successful maintenance treatment of duodenal ulcer with ranitidine

E J S Boyd, J A Wilson, and K G Wormsley (Department of Therapeutics, Ninewells Hospital, Dundee) Recurrence of duodenal ulcer during maintenance treatment with ranitidine 150 mg nocte has ranged from 16 to 59% during the first 12 months (49% in our centre). In order to determine whether this relapse rate was an 'annual' rate or whether the rate changed after the first year's treatment, we have continued maintenance treatment for a second year. Forty-seven patients endoscopically healed at the end of one year's maintenance treatment were randomised to either continued ranitidine or placebo in a double-blind trial. The cumulative annual recurrence rate in those receiving ranitidine was 18% and for those receiving placebo it was 87%. The recurrence rate during the second year of maintenance is significantly lower than that during the first year. We conclude that ulcers which remain healed after one year's maintenance treatment with ranitidine tend to remain healed if treatment is continued.

Sixteen of the 20 recurrences occurring in patients randomised to placebo were symptomatic and four were also associated with bleeding. Fifty-one patients developed ulcer recurrence during maintenance treatment with ranitidine (48 during the first year and three during the second year). Only 21 of these 51 recurrences were symptomatic and only one was associated with haemorrhage.

We conclude that recurrences during maintenance therapy with active treatment tend to be asymptomatic and clinically benign, while symptomatic and complicated recurrences are significantly more common in duodenal ulcer patients receiving no treatment (p<0.01). It appears that maintenance treatment is safer than no treatment in our patients.

Controlled trial of carbenoxolone (Duogastrone) and cimetidine in the management of duodenal ulcer

P I Reed, A Vincent-Brown, P J Cook, C B Colaco, S Perks, J H Baron, and D J Jewell (Gastrointestinal Unit, Wexham Park Hospital, Slough, Departments of Medicine, Royal Free Hospital, and St Charles Hospital, London, and Biorex Laboratories, London) In a double blind double dummy controlled trial in patients with endoscopically proven duodenal ulcer, of 33 taking carbenoxolone as Duogastrone capsules 50 mg qds, 20 (61%) healed at six weeks and 24 (73%) at 12 weeks, not significantly different from the 34 patients taking cimetidine 200 mg tds and 400 mg at night, in whom 23 (68%) healed at six weeks and 26 (76%) after 12 weeks' treatment.

Fifty patients whose ulcers had healed were subsequently followed clinically every six weeks and endoscoped after six and 12 months or earlier if symptoms recurred. The recurrence rate was lower in those whose ulcers had healed after carbenoxolone than in those healing after cimetidine. This difference was especially marked (p=0.06) during the 18- to 36-week period of follow up in those patients who had healed after six weeks' therapy.

At the end of the year of follow up only five ulcers healing on carbenoxolone (24%) and five of the post-cimetidine healed ulcers (19%) were still healed. Thus carbenoxolone and cimetidine heal similar proportions (two-thirds) of duodenal ulcers in six weeks, and the subsequent high relapse rate is similar (four-fifths) for both drugs after 12 months, even though there was an initially slower recurrence rate in the carbenoxolone healed ulcers. These findings are very similar to those previously reported for colloidal bismuth and sucralfate.

Some implications of the use of colonoscopy in IBD

G Holdstock and C L Smith (Southampton General Hospital, Southampton) Colonoscopic techniques have progressed considerably and it has become important to assess their exact role in the investigation and management of colonic disease. To this end we have compared the radiological and colonoscopic (macroscopic and microscopic) assessment of disease in 124 patients with IBD (70 ulcerative colitis, 54 Crohn's disease). Ten patients previously considered to have UC were reclassified as CD after the procedure. Ten (13%) were considered to have total colitis on barium enema, 40 (32%) on colonoscopy, and 71 (61%) on biopsy. Twenty-one patients with normal barium enemas were found to have histological evidence of total colitis. Twelve patients with CD were considered to have skip lesions radiologically, but none of these could be confirmed histologically. Indeed, histological evidence of skip lesions or rectal sparing were found only in patients with small bowel involvement and patients with CD confined to the colon had a similar distribution of disease to those with UC. Thus, this study confirms that colonoscopy is superior to radiology in unselected patients with ulcerative colitis and to 110 age- and sex-matched controls chosen randomly from the same general practices. The initial response rate has been 76% from cases and 64% from controls.

Seven per cent of 42 cases currently smoke compared with 37% of 70 controls, but 48% of cases said they had previously smoked at least five cigarettes a week for a year (controls 59%). At symptom onset only 14% of cases smoked (controls 49% at the same age), 15 cases stopping smoking before disease onset (mean nine years, range 0-5-70), and four after onset.

The estimated relative risk of non-smokers developing colitis was 14.7 (x²=12.6, p<0.001; Mantel Haenszel method for matched pairs) based on reported smoking habit at disease onset.

We confirm that patients with ulcerative colitis are much less likely to smoke than the general population. The estimated risk appears large, is unlikely to be explained by confounding by social class or alcohol intake, and as the association antedates symptom onset it may have aetiological implications.
assessing disease extent. This clear cut advantage indicates that colonoscopy with biopsies should replace barium studies as the investigation of choice in patients with proved or suspected IBD. Also, observations which depend on radiological assessment of disease, such as cancer risk, progression of proctitis to more extensive disease, and differentiation between CD and UC require revaluation. A method to record and standardise histological disease extent is proposed which would allow for comparison between follow up examinations and also between institutions.

F59
Segmental colitis: a new complication of diverticular disease
S J CAWTHORN, N M GIBBS, AND C G MARKS (The Royal Surrey County Hospital, Guildford, Surrey) Patients who complain of long standing rectal bleeding and who are found to have diverticular disease on barium enema frequently undergo colonoscopy to exclude polyps or carcinomas. We describe inflammatory bowel disease which was not similar in histological appearance to Crohn's disease localised to the segment of sigmoid colon involved by diverticular disease in three patients. There were no perianal lesions in these patients and sigmoidoscopy, rectal biopsy, and stool cultures were all normal. There were no other radiological signs of Crohn's disease in the sigmoid colon. At colonoscopy the sigmoid mucosa was oedematous and inflamed in the segment of diverticular disease with normal mucosa in the descending colon above and the rectum below. Biopsies of the sigmoid showed acute inflammation of the lamina propria with crypt abscesses without involvement of the submucosa or the presence of granulomas. Reddening of the mucosal folds has been described in diverticular disease. Microscopic examination of these areas showed chronic inflammation of the lamina propria with fibrosis similar to the changes seen in the solitary rectal ulcer. In two of the three patients the bleeding improved following treatment with salazopyrin.

F60
Collagenous colitis (CC)
W V BOGOMOLOTZ, F POTET, J P CAPRON, C TRIPLET, P DE LA LANDE, AND R SAVEGH Institut Jean Godinot, Reims, Hôpital Beaunon, Clichy, and Hôpital St Joseph, Paris, France) There is now accumulating evidence to suggest that CC is a distinctive clinicopathological entity. Collagenous colitis was first described in 1976 and so far 15 cases have been reported. Two hitherto unpublished cases of CC are presented and their morphological and clinical features compared with those previously recorded. Collagenous colitis is characterised clinically by chronic profuse watery diarrhoea and colicky abdominal pain. Radiological examination is negative. Endoscopic appearances may vary. Laboratory investigations are usually within normal limits with no evidence of intestinal malabsorption or identifiable pathogens. Biopsies of colorectal mucosa show a characteristic collagenous band like deposit (7 μm to 60 μm) under the surface epithelium. The collagen nature of this deposit is confirmed by histochmical, immunological, and ultrastructural studies. Most anti-diarrhoeal drugs are ineffective. Collagenous colitis is not associated with the other more common types of inflammatory bowel disease. The aetiology of CC is unknown but some disturbance of the pericryptal sheath of fibroblasts is probably involved.

F61
Inflammatory fibroid polyps in three generations of a Devon family: a new syndrome?
P P ANTHONY, D S MORRIS, AND K D J WOVLES Royal Devon and Exeter Hospitals and Postgraduate Medical School, University of Exeter, Exeter, and Green Lane Hospital, Auckland, New Zealand) Inflammatory fibroid polyp is a rare tumour-like lesion of stomach or ileum that is solitary and does not recur; its aetiology is unknown. We have followed, for some years, a Devon family in whom the lesion has repeatedly recurLed in three generations. The grandmother (59 years at first presentation) has had nine polyps resected over 11 years; the mother (35 years at first presentation) seven over 18 years; the daughter (22 years at first presentation and now living in New Zealand) two over six years. Age at first presentation is decreasing. None of the patients or their relatives has any allergies, dietary fads, or history of gastrointestinal disease. Light microscopy, immunohistology, and electron microscopy have shown the lesion to be similar to solitary cases previously reported; a significant histiocytic component has been identified. Multiple, recurrent, familial presentation of inflammatory fibroid polyp has not been recorded and is unlikely to be due to chance: it may represent a new syndrome.

F62
Role of the faecal stream in the maintenance of Crohn's colitis
P H HARPER, E C G LEE, M G W KETTLEWELL, AND D P JEWELL (The John Radcliffe Hospital, Headington, Oxford) Treatment of colonic Crohn's disease by surgical diversion of the faecal stream or the use of elemental diets may be beneficial, suggesting that the faecal stream contains factors causing or maintaining the disease. This hypothesis was tested by the reintroduction of small bowel effluent, and a sterile faecal ultrafiltrate, into the defunctioned colon of patients with colonic Crohn's disease. The ultrafiltrate was prepared by centrifugation and filtration through graded Millipore filters to 0-22 microns pore size. The effluent or ultrafiltrate were reintroduced daily for one week, and the effect was assessed clinically, by laboratory measurements and by colonoscopy and biopsy. Mucosal immunoglobulin containing cells were quantitated by a morphometric technique. The faecal challenge caused a relapse of disease in one patient and eight of 14 others had a clinically detectable response. The ESR rose (p<0.02) and the white count increased with a neutrophilia and relative lymphopenia (p<0.05). The ultrafiltrate challenge caused no clinical or laboratory changes. The mucosal plasma cell densities increased in response to the challenge with effluent. These results suggest that the faecal stream contains fraction(s) greater than 0-22 microns which may induce inflammation and be relevant in the pathogenesis of the disease.

F63
Endogenous intraperitoneal contamination without enterotomy in surgery for Crohn's disease
N S AMBROSE, MARGARET JOHNSON, D W BURDON, AND M R KEGHLEY (Departments of Surgery and Microbiology, General Hospital, Birmingham) Septic complications after elective surgery for Crohn's disease are still a major problem despite adequate surgery and antibiotic cover. Contamination after enterotomy is
thought to be the main cause of endogenous sepsis. Even in clean elective operations sepsis, however, is still a common problem. We have studied the bacteriology of intestinal serosa and lymph nodes in patients undergoing elective surgery for Crohn’s disease (n=29) and compared it with patients undergoing elective operations for other gastrointestinal disorders (n=18).

At laparotomy the following material was removed for microbiological culture. Crohn’s disease: serosa of involved bowel and draining lymph node and distant lymph node. Controls: serosa of bowel and mesenteric lymph node. In the controls only one serosal sample and one lymph node yielded a growth of bacteria. In the Crohn’s group, however, nine serosal samples (31%; p=0.078), 10 involved node samples (34%; p=0.045), and 10 uninvolved node samples (34%; p=0.045) showed bacterial growth. The bacteria isolated were typical of the pathogens responsible for postoperative sepsis in Crohn’s disease.

These data further support the need for therapeutic rather than prophylactic antibiotics in Crohn’s surgery as the gut serosa and its lymph nodes are commonly colonised by enteric pathogenic organisms.

F64

Clostridium difficile and its toxin in neonates

A H LISHMAN, T SHIBLEY, A J AL-JUMAILI, AND C O RECORD (Gastroenterology Unit, Royal Victoria Infirmary, Newcastle upon Tyne)

Clostridium difficile and its toxin have been found in the stools of apparently healthy neonates. In a search for a possible correlation between the presence of toxin and various neonatal conditions and for an explanation for the lack of symptoms in many infants, 45 neonates were studied. Stool samples were collected twice weekly on at least two occasions and examined for Clostridium difficile and its toxin. Blood samples from the infant and its mother were assessed for Clostridium difficile antigen in 28 cases.

The stools of 35 of the infants (78%) contained Clostridium difficile and in 30 infants (67%) toxin was present, although the concentration was never greater than 1:1000. There was no significant increase in the incidence or concentration of Clostridium difficile toxin in the stools of 14 infants receiving antibiotics (57%), six infants having exchange transfusions (67%), or eight with respiratory distress. The stools of four infants with bowel disorders were positive for toxin (56%) but in two infants with necrotising enterocolitis, including one who died, the stools were persistently negative for Clostridium difficile toxin. The blood of two infants showed antitoxin activity but the stools of these were organism and toxin negative.

We conclude that while Clostridium difficile and its toxin occurs commonly in infants, there is no apparent correlation with any specific disorder, particularly necrotising enterocolitis. Stool concentrations of toxin may be insufficient to cause symptoms in neonates.

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F65–F72

F65

Wirsungorrhagia: an uncommon cause of gastrointestinal blood loss

W VAN ROOYEN, M VAN BLANKENSTEIN, M EEFTINCK SCHATENKERK, H OBERTOP, H A BRUINING, AND H VAN HOUTEN (Departments of Surgery and Gastroenterology, Academic Hospital Dijkzigt, Rotterdam, The Netherlands)

Haemorrhage from the pancreatic duct is an uncommon cause of gastrointestinal blood loss. Aetiology is two-fold: (1) chronic pancreatitis (CP) can produce arterial erosion resulting in haemorrhage. (2) An aneurysm of the splenic artery (ASA) may rupture into the pancreatic duct.

From 1974–1982 five patients with a Wirsungorrhagia were operated on. Three had an ASA, rupturing into the pancreas and two patients had CP with a bloodfilled cavity in the pancreas. Four patients complained of acute intermittent sharp colicky pain in the left epigastric region with haematemesis and/or melaena. Endoscopy revealed haemorrhage through Vaters ampulla in three patients and in a fourth case blood was aspirated after injection of saline into the pancreatic duct. ERCP in three cases showed irregular cavities in two patients with ASA and duct-dilatation in one patient with CP. Arteriography revealed two ASAs and extravasation of contrast in the third ASA. Surgical treatment consisted of a subtotal pancreatectomy in one patient, distal pancreatectomy in three patients, and ligation of the splenic artery and pancreatic duct proximally and distally to the aneurysm in one patient. One patient died postoperatively from massive pulmonary embolism. Gastrointestinal blood loss did not recur in the other four patients, who were pain free. Excision pancreatic function is satisfactory in all four surviving patients, two became diabetic (one to nine years follow up).

In the literature only 13 patients with a Wirsungorrhagia due to a ruptured ASA and 33 patients with a Wirsungorrhagia caused by CP could be traced.

It is concluded that in patients with intermittent colicky pain in the left epigastric region with concomitant haematemesis and/or melaena for which no cause can be found at endoscopy, Wirsungorrhagia should be considered, and ERCP and arteriography of the coeliac axis performed.

F66

Progesterone receptors in pancreatic adenocarcinoma

T P CORBISHLEY, M J IQBAL, M L WILKINSON, P J JOHNSON, AND R WILLIAMS (The Liver Unit, King’s College Hospital and Medical School, Denmark Hill, London) Cytosolic and nuclear oestrogen receptors (ER) similar to those of the classically hormone responsive tissues such as breast and uterus have recently been reported in pancreatic tumours. As oestrogens induce progesterone receptor (PR) formation, the presence of PR in ER positive tissues is indicative of oestrogen responsiveness.

Patients with breast cancer who have both receptors respond to hormone treatment better than those with ER alone. In this study we have measured progesterone and oestrogen receptors in four samples of pancreatic cancer (two male) and two of normal pancreatic (one male) tissue. Premenopausal uterus, a tissue known to be rich in ER and PR, was used as a positive control. Three of four specimens of pancreatic cancer tissue were ER positive (mean cytosolic Ka 5.4×10⁹ L/M, 577 fM/mg soluble protein) and also expressed the progesterone receptor (mean cytosolic Ka 3.3×10⁸ L/M, 670 fM/mg). The single ER negative tumour (male) studied was PR negative. Normal pancreatic tissue was both ER and PR negative. Specimens of premenopausal uterus contained ER (mean cytosolic Ka 1.8×10⁹ L/M, 66 fM/mg) and PR (mean cytosolic Ka 6.0×10⁸ L/M, 305 fM/mg).
These data provide additional evidence that the oestrogen binding proteins previously reported in pancreatic cancer are functional oestrogen receptors and that this tissue may be responsive to oestrogens.

**F67**

Pancreatic exocrine and endocrine responses in chronic pancreatitis

A A Anagnostides, T M Cox, T E Adrian, N D Christofides, P N Maton, S R Bloom, and V S Chadwick (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Tests of pancreatic exocrine and endocrine function are useful in evaluation of patients with chronic pancreatitis and steatorrhoea but their value in patients with chronic pancreatitis without fat malabsorption is controversial. To test the discriminatory potential of certain indices of pancreatic function we measured trypsin, bicarbonate, and lactoferin outputs by duodenal perfusion and plasma concentrations of pancreatic polypeptide (PP) and motilin in the basal state and during continuous intravenous stimulation with Ceruleide 100 ng/kg/h and secretin 1 CU/kg/h. Three groups were studied, 12 normal volunteers (NV), six patients with chronic pancreatitis and no steatorrhoea (CP), and six with steatorrhoea (CPS).

Stimulated trypsin output was the best discriminant among the three groups NV vs CP (p=0.024); NV vs CPS (p=0.0001); CP vs CPS (p=0.003). Basal trypsin outputs showed similar patterns but failed to discriminate between NV and CP. Bicarbonate outputs were less discriminatory than trypsin outputs. Lactoferin outputs failed to discriminate but transient high peak outputs occurred in the initial stimulation period in the four patients with chronic calcific pancreatitis (washout effect). Stimulated PP concentrations (pmol/l) were 84.5±1.8 in NV, raised in CP (305±50, p=0.0001) and reduced in CPS (17.8±4.7, p=0.0254). These differences were also apparent in the basal state. Basal motilin concentrations were raised in CP (104±22) and CPS (63±7±14) compared with NV (28±4±6) pmol/l (p=0.0005 and 0.02 respectively) but differences in stimulated concentrations were not significant.

It is concluded that the best discrimination among the three groups (NV, CP, and CPS) was achieved using a combination of stimulated trypsin output and plasma PP responses.

**F68**

Transaminase and the recognition of gall stones in patients with acute pancreatitis: more sensitive than ultrasound?

A D Mayer and M J McMahon (University Department of Surgery, The General Infirmary, Leeds) In a pilot study it was found that, in patients with acute pancreatitis (AP), a plasma concentration of aspartate transaminase (AST) greater than 60 IU/l on the day of admission to hospital indicated a gall stone aetiology. The validity of this finding has been reassessed in a prospective series of 330 attacks of AP. Radiological investigations were adequate to confirm or refute the presence of gall stones in 215 attacks, of which 132 were associated with gall stones and 83 were without gall stones. An AST concentration of 60 IU/l continued to give the best discrimination between the two groups. One hundred and eleven of the attacks associated with gall stones had an AST >60 IU/l on admission to hospital compared with 12 of the attacks without gall stones. The test had a sensitivity of 84% and a specificity of 86%. In 91% of patients with stones, AST fell within the initial 48 h, but the rate of fall conferred no diagnostic advantage. Three of the 12 false positive results had an abnormality of the common bile duct and another five had a history strongly suggestive of stones. There was no correlation between the concentration of AST and the age or sex of the patient, the duration of symptoms, or the severity of AP.

From this data, measurement of AST on admission to hospital may have diagnostic advantages over ultrasound which has been reported to have a sensitivity of 50–60% in similar patients.

**F69**

Management of common bile duct calculi by endoscopic sphincterotomy in patients with gall bladders in situ

D L Carr-Locke, J P Neoptolemos, I Fraser, and D Fossard (Department of Medicine, University of Leicester, Leicester Royal Infirmary, Leicester) We report 82 consecutive patients with gall bladders in situ who underwent endoscopic sphincterotomy (ES) for common bile duct calculi: in 47 patients (mean age 78 years) considered unsuitable for surgery (group I) and in 35 relatively high risk patients (mean age 62 years) as a preliminary to simple cholecystectomy (group II). Endoscopic stone removal was successful in 73 patients (89%) without mortality. Surgery was undertaken in five patients in group I because of failed ES (n=3) or development of empyema of the gall bladder (n=2). Five patients died within six weeks after ES but in only one was this related to biliary sepsis. On follow up (mean 17 months; range 4–50 months) 28 patients had no symptoms, eight had minor dyspepsia, one had biliary colic, and there were five late deaths (unrelated to the biliary tract). Using ES as a preliminary to clear the bile duct before surgery, cholecystectomy was avoided in 27 patients in group II. Endoscopic sphincterotomy is an effective technique for treating patients with bile duct stones when the gall bladder is in situ either alone, in those who are high surgical risk, or as an adjunct to simple cholecystectomy in those who are only relatively high surgical risks.

**F70**

Cholecystotomy for biliary lithiases. T-tube drainage or primary closure? Effects on postoperative bacteraemia and T-tube bile infection

N J Lygidakis (Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London) To assess the difference in the incidence of postoperative bacteraemia in patients with cholelithiasis after either a primary closure of the cholecystotomy, or a T-tube drainage, 117 patients who underwent surgery in Athens, Greece, by the author between 1977 and 1981, were prospectively randomly studied.

All had intraoperative cholangiography and were comparable in terms of age, sex, length of history of symptoms, and incidence of intraoperative bile infection. Of those 117 patients, 60 underwent a primary closure of the cholecystotomy (group A) and 57 had a T-tube drainage (group B). Our results revealed that for patients of group A there was a 3.3% incidence of bacteraea compared with a 31.7% incidence seen to occur in patients in group B.

The above features were correlated with an increased incidence of bile infection from 75.4–92.3% which has been confirmed to occur postoperatively in patients of group B, and which was associated with a higher mortality and morbidity rate for patients of the above group. In conclusion it seems likely that T-tube drainage as a foreign body provokes exogenous acquisi-
tion of environmental micro-organisms and that simultaneously represents a means of potentiating infection from organisms which would not normally multiply in the presence of a free drainage.

Therefore, we may well accept that T-tube drainage should be possibly avoided and be replaced by either primary common bile duct closure after meticulous use of choledangiography and choledochoscopy, or by internal drainage.

F71
Value of choledochoscopy in exploration of the common bile duct
P J BROE, D J MAGEE, AND W O KIRWAN
(Department of Surgery, Regional Hospital and University College, Cork, Ireland) In recent years an extensive literature has been devoted to the postoperative management of retained calculi after exploration of the common bile duct (CBD). Much less attention has been directed to the prevention of the problem by improved methods of operative diagnosis. During a 33 month period from July 1979 to September 1982 operative rigid chole-
dochoscopy was performed in 107 patients undergoing exploration of the CBD. Completion T-tube choledangiography was also performed in all but six patients. Of the 107 patients who underwent choledochoscopy 88 (82%) had choledocholithiasis. In 22 of these patients the choledochoscope identified stones that had been overlooked by the usual methods of exploration. In four of these patients completion T-tube choledangiography after choledochoscopy identified residual calculi requiring re-exploration of the CBD. In these patients a transduodenal sphincteroplasty (three patients) or choledoco-duodenostomy (one patient) was performed. Overall, there was one instance of unsuspected residual calculus as documented by postoperative T-tube choledangiography. The choledochoscope was also of value in clarifying equivocal peroperative cho-
ledangiographic findings (16 patients) and in identifying other causes of biliary obstruction (benign stricture one patient, ampullary carcinoma two patients). One patient sustained significant trauma to the CBD with the choledochoscope. Thus, operative choledochoscopy combined with completion T-tube choledangiography is a safe and effective method of reducing the incidence of residual calculi and should be routinely performed during CBD exploration.

F72
Empyema of the gall bladder - neglected but often fatal
J R THORNTON, K W HEATON, H J ESPINER, AND W K ELTRINGHAM (University Department of Medicine and Department of Surgery, Bristol Royal Infirmary, Bristol) Empyema of the gall bladder receives scant, if any, mention in current textbooks and its very variable presentation appears to have been largely forgotten, though this was well described in surgical texts of earlier this century. To define its present day natural history, we studied 32 cases of empyema presenting to one hospital between 1976-1981 from 1327 patients with gall-bladder disease.

Remarkably, six patients had little or no abdominal pain. In those with pain, this had been present for a median of eight days and, in eight patients, for between one and four months. Apart from right hypochondral tenderness, physical signs were inconsistent. Only 56% had guarding, 41% an abdominal mass, and 44% a pyrexia >37.5°C. The presence of sepsis was rarely suspected and only 19% of patients had blood cultures taken. In four patients, empyema was found unexpectedly at necropsy or at operation for unrelated disease.

Eight patients (25%) died, usually from unsuspected septicaemia. Those who died were older than those who survived (83±1 vs 67±3 years, p<0.001). More of them had had little or no pain (5/8 vs 1/24, p<0.05), more had an abdominal mass (6/8 vs 7/17, p<0.05), and fewer had abdominal guarding (2/8 vs 16/24, p<0.05). This considerable mortality might be reduced by the wider use of blood culture in apparent 'cholecystitis' and by greater awareness that empyema of the gall bladder can be chronic, painless, and afebrile.

F73
Double blind trial of branched chain amino acid infusions in cases of hepatic encephalopathy
J G FREEMAN, M BASSENDINE, P HEATH, O F W JAMES, AND C O RECORD (Gastroenterology Unit, Royal Victoria Infirmary and University of Newcastle upon Tyne) The concentra-
tions of neutral amino acids in the brain may regulate the cerebral production of both normal and false neurotransmitters. Branch chain amino acid (BCAA) concentra-
tions in blood can influence the cerebral uptake of neutral amino acids and it has been suggested that infusions of amino acid solutions rich in BCAA improve hepatic coma. In the present study the effect of the addition of an infusion of BCAA or placebo to standard therapy for hepatic encephalopathy has been assessed in 17 patients with cirrhosis.

During a 48 hour period the patients were infused either a 4% branched chain amino acid solution (1 1/24 h) or an equivalent volume of placebo (5% dextrose). Before and after the infusion patients were assessed for coma grading and had plasma amino acid profiles and ammonia measured. An EEG, the Conn modified number connection test and serial seven subtractions were also carried out. During the infusion period they also received a normal liver support regime (neomycin and lactulose). If they remained encephalopathic at 48 hours they were crossed over to the alternative therapy for a further 48 hour period.

After infusion of BCAA solution there was no significant improvement in clinical, biochemical, or psychometric status compared with the placebo solutions despite normalisation of plasma amino acid profiles. We conclude that infusions of BCAA do not improve encephalopathy in patients with decompensated liver disease.

F74
Serum procollagen-III-peptide concentration in primary biliary cirrhosis (PBC)
A SMITH, N Y HABOURI, AND T W WARNES (University Department of Gastroenterology, Manchester Royal Infirmary, and Department of Clinical Pathology, Withington Hospital, Manchester) The aim of this study was to determine serum procollagen-III-peptide concentrations in a large group of PBC patients and to correlate this marker of collagen biosynthesis with histological and biochemical parameters of disease.

Procollagen-III-peptide concentrations were determined in 57 serum samples from 46 PBC patients using the radioimmuno-
assay produced by Hoechst UK Ltd. The mean serum procollagen-III-peptide concentration in PBC patients (18.8±6.9 ng/ml) was significantly higher than in control sera (7.6±3.1 ng/ml) (p<0.001).
Serum procollagen-III-peptide concentrations were significantly less (p<0.006) in early (Ludwig stages I and II) PBC (mean 12.5±4.3 ng/ml) than in late stage (III and IV) disease (mean 19.4±6.8 ng/ml). Procollagen-III-peptide concentrations were significantly higher (p<0.01) in those patients with pericellular fibrosis (Rappaport zone I) (mean 19.6±5.8 ng/ml) than in those with no fibrosis (mean 11.8±4.8 ng/ml). There was a highly significant correlation (p<0.0014) between procollagen-III-peptide concentrations and serum bilirubin.

In PBC, serum procollagen-III-peptide concentrations correlate with the stage of the disease as assessed biochemically, as assessed histologically by the Ludwig staging and also with the degree of fibrosis as assessed histologically. It therefore appears to be a useful means for monitoring the course of this disease and especially the effects of antimicrobial drugs such as penicillamine and colchicine.

F75 Bacteriuria and primary biliary cirrhosis (PBC)

A K BURROUGHS, J ROSENSTEIN, O EPSTEIN, J HAMILTON-MILLER, W BRUMFIT, AND SHEILA SHERLOCK (Departments of Medicine and Medical Microbiology, Royal Free Hospital School of Medicine, London) Women with PBC are not known to be more susceptible to infection. Significant bacteriuria, however, surveyed prospectively using mid-stream urine (MSU) specimens cultured quantitatively, was more common in women with PBC than those with other types of liver disease. In consecutive inpatients 19 of 89 (21%) PBC had bacteriuria, and seven of 90 (8%) non-PBC (p<0.05); in outpatients 17 of 87 (19%) PBC and six of 89 (7%) non-PBC (p<0.05). Subsequent prospective study of 131 consecutive PBC women surveyed whenever attending hospital, documented 117 bacteriuric episodes (59% asymptomatic) in 45 (34%) patients during one to 18 months follow up, with 22 having more than one episode and two acute pyelonephritis. Escherichia coli was isolated most frequently (69% episodes) with similar biotypes, antibiotic sensitivities, and cure rates to those causing bacteriuria in the community. No abnormal adhesiveness was shown for normal or PBC uroepithelial cells. Bacteriuria was unrelated to age, jaundice, or medication, but was associated with histological fibrosis in 40 of 96 patients, as against five of 35 with none (p<0.05). The immunological phenomena of PBC are consistent pathogenetically with a microbial agent, the specific M2 antibody is directed against a mitochondrial complex with structural similarity to plasma membranes of microorganisms. Bacteriuria thus may be a unique infection in PBC, and may be involved in its pathogenesis.

F76 Multiorgan granulomata and mitochondrial antibodies

E A FAGAN, J C MOORE-GILLON, J G HAY, AND M TURNER-WARWICK (Institute of Cardiothoracic Medicine, Brompton Hospital, London) The finding of serum mitochondrial antibodies and a negative Kveim-Siltzbach test in a patient with hepatic granulomata has previously been considered important in differentiating primary biliary cirrhosis (PBC) from hepatic sarcoidosis. Conversely, prominent pulmonary features together with multiorgan granulomata has been held to favour a diagnosis of sarcoidosis rather than PBC. We present five patients with prominent pulmonary signs and symptoms, all with mitochondrial antibodies; in four hepatic and pulmonary granulomata were found. The pulmonary features chest radiographs, positive Kveim-Siltzbach tests (two patients), non-caseating granulomata in lung and liver and initial clinical responses to corticosteroid therapy would be consistent with sarcoidosis. The mitochondrial antibodies (serum titres 1:512–1:2560), negative Kveim-Siltzbach tests (three patients), and serial liver histology showing progressive fibrosis with portal tract and bile duct destruction (four patients) and later cirrhosis and portal hypertension (two patients) would favour the alternative diagnosis of PBC. In addition they show clinical, serological, and histological features that overlap with Sjogren's syndrome, coeliac disease, and mixed connective tissue disease. These patients do not appear to conform to any single conventional disease category and any attempt to classify them as 'sarcoidosis' or 'PBC' may be misplaced. We prefer to consider them as forming an intermediate group that serves to link rather than divide the above and similar conditions.

F77 Abnormal monocytes receptors in primary biliary cirrhosis

M AL-AGHBAR, J NEUBERGER, AND A L W F EDDLESTON (Liver Unit, King's College Hospital and Medical School, Denmark Hill, London) Previous studies have shown reduced clearance of complement coated cells from the circulation of patients with primary biliary cirrhosis (PBC). In this study, we have directly examined the C3b and Fc receptors on peripheral blood monocytes (PBM) isolated from patients with PBC and other chronic liver diseases. Peripheral blood monocytes were isolated from patients with PBC (13), HBsAg negative chronic active hepatitis (nine), alcoholic liver disease (nine), and from normal controls (10). The number of complement and IgM coat sheep red blood cells (SRBC) binding to 100 PBM from patients with PBC (23±12) was significantly less when compared with normal controls (57±17, p<0.01) and other liver diseases (57±14, p<0.01) indicating impaired C3b receptor function. There was no significant difference in the number of IgG coated SRBCs attached to PBM in any of the groups indicating normal Fc receptor function. To determine whether the abnormal C3b receptor in PBC was because of inherent monocyte defect or to blocking of the receptor site by serum factors, PBM from normal individuals were preincubated with normal or PBC serum before assessing C3b receptor function. After exposure to PBC serum, there was a significant reduction in the number of complement coated SRBCs binding to the normal monocytes (72±18 and 28±11, p<0.05). The blocking effect of PBC seen on the C3b receptor was still present after removal of circulating immune complexes by pretreating the serum with 2% polyethylene glycol. These results show a specific C3b receptor defect on monocytes from patients with PBC which appears to be due to serum factors other than immune complexes.

F78 Spontaneous bacterial peritonitis (SBP) in children with chronic liver disease (CLD). A predictable and preventable condition?

Y V LARCHER, N MANOLAKI, D VERGANI, AND A P MOWAT (Departments of Child Health and Immunology, King's College Hospital and Medical School, London) Spontaneous bacterial peritonitis (SBP), a well-established complication of adult CLD, is rarely diagnosed in children. We therefore
analysed clinical and bacteriological features in 12 episodes of SBP in 11 children (four boys, seven girls, median age 5-5 years) with CLD. As complement deficiency is associated with serious bacterial infection in children with acute liver disease we assessed its possible role in pathogenesis of SBP.

All patients had cirrhosis and ascites; eight had gross splenomegaly, one was asplenic. Symptoms (mean duration 48 hours) included increased abdominal distension (12), pyrexia (10), abdominal pain (eight), GI disturbance (seven), and encephalopathy (four). All had evidence of peritonism and reduced bowel sounds. Ascitic culture grew S pneumoniae (nine), Klebsiella (two), H influenzae (one); blood cultures grew identical organisms in nine.

Despite appropriate antibiotic therapy seven died.

All had appropriate leucocyte response to infection; 9/9 had normal serum immunoglobulins; six were receiving immunosuppressants. Deficiency of C3, C4, and yeast opsonisation (with functional deficiency of factors B, D, C4, C5 in four) were detected in 9/9 before onset of SBP; though four tested at diagnosis of CLD had been normal. These observations suggest that CLD induced complement deficiency may be an important pathogenic factor in SBP.

Spontaneous bacterial peritonitis must be excluded as a cause of pyrexia and abdominal symptoms in children with CLD. Pneumococcal vaccination or antibiotic prophylaxis may be beneficial in immunodeficient CLD patients.

F79

Hepatitis B virus infection in children with beta thalassaemia major treated in UK

G MEILL-VERGANI, D VERGANI, Y WHITE, A P MOWAT, AND E WONKE (The Thalassaemia Unit, Whittington Hospital, London, and Departments of Child Health, Immunology, and Liver Unit, Kings College Hospital, London) Chronic liver disease has emerged as a frequent complication in B-thalassaemia, as survival has improved with high transfusion regimes. Although liver damage has been attributed to iron overload chelation therapy does not prevent it. In endemic areas hepatitis B virus (HBV) infection has also been implicated. To investigate whether HBV is associated with liver damage in B-thalassaemia in non-endemic areas we have studied by radioimmunoassay serum HBV markers in 32 patients attending a London hospital. Fourteen (43-7%) had one or more HBV markers. One had HBsAg, evidence of circulating viral particles, while three had anti-HBs alone, reflecting a previous infection. Anti-HBc, compatible with either previous infection or ongoing viral replication, was found alone in three patients and in association with anti-HBs in seven. HBV markers were present in nine of 14 children with raised serum transaminases, but in only three of 15 with normal transaminases (χ² = 5.85, p<0.025). Eight of the 14 children with HBV markers had lived and been transfused exclusively in the United Kingdom suggesting that present HBV screening of blood donors did not prevent HBV infection. The high incidence of HBV markers, possibly associated with chronic liver damage in our series suggests that B-thalassaemic patients should receive active HBV immunisation even in non-endemic areas.

F80

Gamma-glutamyl-transpeptidase (GGTP) isoenzyme studies in primary hepatocellular carcinoma (HCC)

A SMITH, P KAY, P JOHNSON, R WILLIAMS, AND T W WARES (University Department of Gastroenterology, Manchester Royal Infirmary, Manchester, and the Liver Unit, King's College Hospital, London) The aim of this study is to examine GGTP isoenzyme patterns in serum from patients with known HCC. Two groups were studied: 40 patients with HCC confirmed histologically by biopsy or at necropsy and a control group of 40 patients with various forms of liver disease but not known to have HCC. Gamma-glutamyl-transpeptidase isoenzymes were separated by polyacrylamide gradient gel electrophoresis. Staining patterns were examined for increased GGTP activity in the hepatoma (H-GGTP) region designated by Kojima et al as 1. Hepatoma specific alkaline phosphate (H-ALP) and α-fetoprotein (AFP) were measured in the HCC group.

An increased concentration of staining in the one region was detected in 30 of the HCC patients (75%) but in only two controls (5%), both alcoholic cirrhosis. A raised AFP was found in 27 of the HCC group (68%) and nine (23%) showed a hepatoma-specific band of ALP. In two (5%) only H-ALP was positive, in four (10%) only AFP was raised, and in seven (18%) both markers were raised. In only four patients (10%) were all three markers negative. In 28 cases (70%) two or more of the markers were in agreement.

We can confirm that a specific isoenzyme of GGTP is detectable in HCC; the sensitivity is similar to that of AFP. In 32-5% of HCC cases AFP concentrations were normal; 75% of these patients could be diagnosed by the presence of H-ALP or H-GGTP. This comparative study shows that the three markers studied are complementary and that a multiple marker approach to the detection of hepatocellular carcinoma is required.
which may cause ulcers in humans or experimental animals.

In volume 1 the gastroenterologist will find conventional reviews by the usual experts on physiology, H2 blockers, old and new anticholinergics, antacids, carbenoxolone, prostaglandins, zinc, and bismuth.

It is always difficult enough to choose the contributors to a multi-author book, and even more difficult to ensure they cover the necessary topics without overlap. Unfortunately in volume 1 the same drug and therapy may be described in detail in different chapters, yet other anti-ulcer treatments are largely (amylopectin, pepstatin, sulphamate, sulpiride, trimipramine) or completely (acetazolamide anisotroprine, benzimidazoles, beta2 adrenergic agents, deglycyrrhizinated liquorice, gefarnate, metoclopamide, oestrogens, pifarnine, proglumide, secretin, trithiozine) ignored.

Volume 2 has similar problems of selectivity so that the chapter on experimental duodenal ulcer is almost entirely devoted to one particular model favoured by its authors, the cysteamine type.

Within these limitations the ulcerologist with $180 to spend will find in these slim volumes useful reviews of topical problems on the production and healing of ulcers by drugs.

J H BARON

Books received


Controversies in acute pancreatitis Edited by L F Hollender. (Pp. 344; illustrated; $43.60.) Heidelberg: Springer-Verlag, 1982.


News

The British Digestive Foundation (Scottish Appeal)
The Foundation invites applications from workers in Scottish institutions who wish support for research work related to any aspect of normal or disordered structure and function of the alimentary tract. A wide variety of forms of support will be considered ranging from that required for apparatus or reagents, to Fellowships. There is no requirement that applicants be medically qualified.

Applications should be submitted before 15 September, 1983; application forms can be obtained from: The Secretary, The British Digestive Foundation (Scottish Appeal), 9 Queen Street, Edinburgh EH2 1JQ.

Increase in size of Gut
We are pleased to announce that starting with this issue the size of the journal will be increased by eight pages.

Opioid Peptides in Periphery

The physiological role of the opioid peptides in periphery will be the main topic of this symposium to be held in Rome, 23–25 May 1984. Further details from the Organising Secretary, APE, via Giorgio Vasari 4, 00196, Rome, Italy.

Correction

The following papers:
T1: Assessment of gastro-oesophageal collateral veins in portal hypertension by means of endoscopic ultrasonography. G Caletti, L Bolondi, V Arienti, E Brocchi, S Testa, M Ferrentino, L Zani, A Passaniti, and G Lobo and
F36: Staging of gastric cancer by means of endoscopic ultrasonography. G Caletti, L Bolondi, E Brocchi, P Casanova, L Zani, S Gaian, S Testa, G Guzzardi, and G Lobo although selected for the BSG Programme were not presented or discussed at the meeting.