The British Society of Gastroenterology

The 46th Annual Meeting of the British Society of Gastroenterology was held at the University of Newcastle upon Tyne from 18–20 September 1985, under the presidency of Professor E L Blair. Out of the papers submitted, the Programme Committee of the Society selected 136 for presentation as posters, and 52 for oral presentation; the abstracts* are printed below. Further details of the meeting appear in the News column on p. 1098.

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**BSG/BASL LIVER**

W1–13

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**W1**

Erythrocyte aldehyde dehydrogenase activity in health and disease and its value as a marker for hepatic aldehyde dehydrogenase activity

K MATTHEWSON and C O RECORD (Gastroenterology Unit, Royal Victoria Infirmary and University of Newcastle upon Tyne) Considerable controversy surrounds the role of hepatic aldehyde dehydrogenase in alcoholic liver disease. Its activity is reduced and this could be a pre-existing abnormality or simply a non-specific consequence of alcohol consumption. Erythrocytes contain an enzyme identical to the hepatic cytosolic enzyme which could prove to be an accurate marker of the hepatic enzyme with the added advantage of ready availability. Using a spectrophotometric technique, erythrocyte aldehyde dehydrogenase was assayed in 15 healthy controls, seven actively drinking alcoholics (ADA), five subjects with alcoholic liver disease currently abstaining (AALD) and seven with non-alcoholic liver disorders (NALD). In addition the hepatic cytosolic enzyme was also assayed in 18 of the subjects. The ADA group had significantly reduced erythrocyte enzyme activity (p<0.01) but the AALD and NALD groups did not. The correlations between erythrocyte and hepatic cytosolic activity for all subjects considered together, for the NALD group alone, and for the ADA and AALD groups considered together were all insignificant. In the control group alone, however, there was a significant positive correlation (r=0.943, p<0.05). We conclude that erythrocyte aldehyde dehydrogenase activity is reduced in actively drinking alcoholics but that red cell activity gives a poor indication of hepatic cytosolic activity in subjects with liver disease. In contrast, it appears a good marker of hepatic activity in normal subjects, and might therefore be used to study enzyme activity in 'pre-alcoholic' subjects.

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**W2**

Decreased red cell aldehyde dehydrogenase activity in patients with alcoholism

N R TURNER, S THOMAS, M J P ARTHUR, AND R WRIGHT (Professorial Medical Unit, Southampton General Hospital, Southampton) Acetaldehyde has been implicated as a mediator of hepatic injury in alcoholic liver disease. Alcoholics develop higher blood acetaldehyde concentrations than normal subjects after drinking alcohol. Reduced activities of aldehyde dehydrogenase (AldDH) have been reported in liver samples from alcoholic subjects. An enzyme similar to the cytoplasmic AldDH of liver cells is present in red blood cells and shows a similar reduction of activity in alcoholic patients. If this reduction is specific for excess alcohol consumption, it may be useful in the detection and follow up of patients with early alcoholism.

The red cell AldDH activities of patients with a history of alcoholism (ALC, n=35) were compared with those activities found in patients with non-alcoholic liver disease (NALD, n=21) and a group of normal controls (NC, n=32). AldDH activities in the ALC group were significantly lower than those in both the NALD (p<0.05) and NC (p<0.01) groups. Moreover, patients with clinical evidence of continued drinking had the lowest activities. Activities in the NALD group, however, were themselves lower than those in the NC group (p<0.05). These results suggest that decreased red cell AldDH activity is of some value in the detection of alcoholism but its major clinical potential is as a marker of continued drinking in alcoholics.

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**W3**

Immunoregulatory defects and aberrant cellular reactivity to liver cell antigens in families of patients with autoimmune chronic active hepatitis

C J O'BRIEN, S VENTO, A L W F EDDLESTON, AND R WILLIAMS (Liver Unit, King's College Hospital and School of Medicine & Dentistry, Denmark Hill, London) The finding of a T suppressor cell defect specific for liver membrane antigens in autoimmune but not HBsAg positive chronic active hepatitis (CAH) raises the possibility that a discrete defect in immunoregulation may be fundamental to the pathogenesis of this condition. As non-specific disturbances in immune function have been observed in relatives of patients with autoimmune CAH, we have assessed T lymphocyte responses to liver derived antigens and their suppressor T cell (Ts) control in healthy relatives and spouses of patients with autoimmune CAH. Using an indirect T lymphocyte migration inhibitory factor assay it was found that 18/18 patients, 8/41 relatives, 3/11 spouses and 0/23 unrelated controls exhibited sensitisation to a liver membrane lipoprotein (LSP) complex. In contrast to all nine patients studied, none of the LSP sensitised relatives exhibited sensitisation to the asialoglycoprotein receptor – a purified constituent of LSP. In T cell co-culture experiments, using patient and non-patient cells in a 9:1 ratio, T lymphocytes from 20/41 relatives and 1/11 spouses (p<0.05) were
unable to suppress T cells from patients sensitised to LSP. These studies suggest that a T cell defect for liver membrane antigen(s) is a genetically determined marker of susceptibility for autoimmune CAH. Clinical disease only arises when in addition to the defect, T cell sensitisation to the asialoglycoprotein receptor appears.

W4

Natural killer (NK) cell activity in acute viral hepatitis

L. CHEMELLO, M. MONDELLI, F. BORTOLOTTI, E. SCHIAVON, A. ALBERTI, E. G. BONDANELLI, AND G. BRADDA (Istituto di Medicina Clinica, Cattedra di Clinica Medica II, University of Padua, and Department of Infectious Diseases, IRCCS Policlinico S Matteo, University of Pavia, Italy) Recent experiments in animal models suggest that natural killer (NK) cells play an important role in resistance to viral infections. In this study, we have investigated natural cytotoxicity for the NK-susceptible K562 target cells in 24 patients with acute hepatitis B (AHB) and in 11 with acute non-A, non-B hepatitis (NANBH), using a standard 51Cr-release assay. Simultaneously, serum levels of α-interferon (α-IFN) were determined by radioimmunoassay. Peripheral blood mononuclear cells showed significantly increased cytotoxicity in patients with AHB at all effector to target cell ratios ranging from 10:1 to 80:1 (p<0.01). Percent specific lysis was significantly higher in patients tested within 20 days of clinical onset compared with those tested during convalescence, in whom cytotoxicity was not statistically different from healthy controls (mean % cytotoxicity±SEM: 20.7±2.5, 34.3±3.5, 50.5±3.7, 65±3.2, and 12±1, 21.3±2.2, 32.3±3.4, 46.2±4.6, respectively, p<0.01). In contrast, patients with NANBH, all studied in the early phase, showed normal cytotoxicity. Serum concentrations of α-IFN were normal in both groups of patients. These functional studies support recent data showing increased proportions of lymphoid cells with NK phenotype in the liver infiltrate of patients with AHB. The finding of enhanced cytotoxicity in the early phase of AHB suggests that NK cells may be important in controlling HBV infection before virus-specific cytolytic T cells become fully operative. Non-A and non-B agents do not generate significant NK activity and this may be one of the factors contributing to frequent progression to chronicity. Serum concentration of α-IFN was unrelated to NK cytotoxicity, at least in this setting.

W5

Clinical and experimental studies of the influence of ethanol on paracetamol hepatotoxicity

J. M. TREDGER, HEATHER M. SMITH, R. B. READ, B. PORTMANN, R. WILLIAMS (Liver Unit, King’s College Hospital and School of Medicine & Dentistry, Denmark Hill, London) Repeated ethanol ingestion is thought to potentiate paracetamol hepatotoxicity while ethanol taken concomitantly with paracetamol may reduce liver damage. Of 247 patients seen at King’s College Hospital after paracetamol overdose, alcohol was used in 60 (24%). There was no significant difference in clinical course or outcome between patients consuming alcohol either chronically (>80 g/week), and concomitantly with paracetamol or both chronically and concomitantly. In mice, however, ethanol had pronounced effects on paracetamol metabolism and hepatotoxicity evaluated using semi-quantitative histology (scale 0–5). Concomitant ethanol administration prevented liver damage (score: 0±0 vs 3±2±0.5 after paracetamol alone) and decreased the production of toxic paracetamol metabolites. Ethanol had no effect on paracetamol covalent binding in vitro. Chronic ethanol consumption potentiated paracetamol hepatotoxicity (score: 3±0±0; mortality 27% (0% in control); p<0.05) but did not induce the enzymes catalysing paracetamol intoxication. In mice given ethanol both chronically and concomitantly, paracetamol was mildly hepatotoxic (score: 1±1±0.7; 0% mortality) and the acute metabolic effects of ethanol were reduced. Interindividual variations in dosages of ethanol and paracetamol, in the use of antidotes and in metabolising activity, may explain the differences between our human and animal data.

W6

Partial hepatectomy enhances proliferation of ectopically sited liver cells in experimental animals

S. GUPTA, R. JOHNSTONE, Y. PRICE, H. DARBY, A. C. SELDEN, AND H. J. HODGSON (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Experimentally, isolated hepatocytes transplanted into the spleen in syngeneic animals eventually proliferate, forming confluent hepatic cord structures. This procedure offers a model for exploring control of hepatocyte growth in a vascular bed not receiving portal blood, and also offers a potential therapy for metabolic disorders. We have explored the effect of partial hepatectomy, the strongest known stimulus to hepatic regeneration, on established ectopic grafts of liver cells in August rats. Ten months after implantation, two groups of animals (n=6) underwent 70% partial hepatectomy or sham laparotomy. Cell proliferation was assessed 24 hours later by autoradiography, after administration of colchicine and 3H-thymidine. In normal liver, <2 cells/1000 were labelled, compared with 300 cells/1000 in regenerating liver. Ectopic hepatocytes in spleens without the stimulus of partial hepatectomy, were in a state of proliferation shown by a greater labelling index in comparison with normal liver (9 cells/1000), which moderately increased after partial hepatectomy (20 cells/1000). These results show that the regenerative stimulus of partial hepatectomy reaches the systemic circulation, and ectopic hepatocytes respond to this stimulus albeit not to the same degree as the liver itself. Either local factors, or the presence of nutrients in portal blood, may account for this difference.
the degree of fibrosis ‘blind’. All patients had normal serum liver function tests and normal static isotope scans. In 54 cases where the biopsy showed no fibrosis or only periportal or pericentral fibrosis the dynamic scan was normal in 44. In six cases where the biopsy showed bridging fibrosis or cirrhosis the dynamic liver scan was normal in one. Although the predictive value of an abnormal dynamic scan is low at 5/15 (33%), the predictive value of a normal dynamic scan is high at 44/45 (97-8%).

It may thus be possible to reduce liver biopsies by 75% in psoriasis patients by biopsying only those with an abnormal dynamic liver scan.

W8  
Effects of portasystemic shunting on hepatic haemodynamics in the cirrhotic rat

S A Jenkins, J N Baxter, P Devitt, and R Shields  
(Department of Surgery, University of Liverpool, Liverpool)

The aim of selective portasystemic shunts is to reduce portal pressure while maintaining a satisfactory liver blood flow. As there is little evidence to support the theoretical advantages of selective shunts we compared the effects of different types of portasystemic shunts on hepatic haemodynamics in the cirrhotic rat. Rats with dimethyltinamine-induced cirrhosis underwent one of the following shunts: end-to-end portacaval (n=10); side-to-side mesocaval (n=10); mesocaval H-graft (n=10); or splenopancreaticocaval (n=10). Liver blood flow (LBF) and wedged hepatic venous pressure (WHVP) were measured before, immediately after and four weeks following shunting. Immediately following end-to-end portacaval shunting there were significant reductions (p<0.05 Student’s t test) in WHVP (13±4±0.4 to 6±5±0.5 mmHg) and LBF (18±6±1.3 to 10±1±1.7 ml/min/100 g). After side-to-side mesocaval shunting LBF and WHVP fell by approximately the same magnitude. Mesocaval H-grafting preserved liver blood flow to a greater extent (19±3±1.2 to 14±7±0.9 ml/min/100 g) and reduced WHVP from 12±8±0.7 to 8±9±1.1 mmHg. However, 60% of the grafts became thrombosed. Most marked preservation of LBF followed splenopancreaticocaval shunting, but the reduction in WHVP was the least, falling from 13±8±0.6 to 10±3±0.9 mmHg. No further significant changes occurred one month after operation. These results suggest that shunt operations for cirrhosis with portal hypertension which maintain liver blood flow may not decompress the splanchnic circulation as effectively as portacaval shunts.

W9  
Effects of a long acting analogue of somatostatin (SMS 201-995) on hepatic haemodynamics in the pig and on intravariceal pressure in cirrhotic patients

S A Jenkins, J N Baxter, W A Corbett, and R Shields  
(Department of Surgery, University of Liverpool, Liverpool)

SMS 201-995 is a new analogue of somatostatin with a longer biological half life. Furthermore, preliminary studies have shown that SMS 201-995 is more potent than somatostatin in inhibiting glucagon and insulin release and gastric secretion. In view of the greater potency of SMS 201-995 we studied the effects of the analogue on hepatic haemodynamics in the pig and on intravariceal pressure in patients with cirrhosis.

Pigs (n=6), received iv infusions of 250 µg/h of SMS 201-995. Portal venous flow, hepatic artery flow, portal pressure (PP), systemic blood pressure and cardiac output were measured before and after the infusion of the SMS 201-995. In six patients with cirrhosis, intravariceal pressure was measured before and after iv administration of 50 µg SMS 201-995.

In pigs, systemic administration of 250 µg SMS 201-995 significantly reduced PP (15±6±2±4 to 12±3±2±5 mmHg), portal venous flow and hepatic artery flow. In nine patients with cirrhosis, a bolus injection of 50 µg SMS 201-995 significantly (p<0.05, Student’s paired t test) reduced the intravariceal pressure (27±4±2±5 to 15±8±2±1 mmHg). Furthermore, in one patient undergoing an elective portacaval shunt, the PP was reduced from 29 to 22 mmHg following iv administration of 50 µg SMS 201-995.

These results suggest that SMS 201-995 is effective in lowering PP and may be of value in the control of acute variceal haemorrhage.

W10  
Effect of acute and chronic propranolol administration on antipyrine and paracetamol clearance in chronic liver disease

P C Hayes and I A D Bouchar  
(University Department of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland)

The effect of propranolol on hepatic drug metabolism was examined in 12 patients with chronic liver disease in a placebo controlled double blind study. Clearance of antipyrine and paracetamol which are oxidised and conjugated respectively by the liver was determined before, after 120 mg of propranolol over 24 hours and after six and 12 months of a long acting propranolol preparation (Inderal LA 160 mg).

Propranolol therapy caused an acute reduction in antipyrine clearance (1586±1177 to 1349±1198 ml/h) compared with the placebo treated patients (1202±534 to 1444±229 ml/h; p<0.01). This reduced clearance, however, did not persist with chronic administration.

The clearance of free paracetamol remained unchanged throughout the treatment period but clearance of total (free and conjugated) paracetamol fell on propranolol from 5824±2249 to 4101±1898 ml/h compared with the placebo group (4551±1202 to 4421±1148 ml/h; p<0.05). The reduced clearance of total paracetamol was probably because of impaired renal excretion of the conjugated metabolite and was accompanied by a rise in serum urea in the propranolol group which became significant after 12 months therapy.

Propranolol therapy therefore has an acute effect on hepatic drug metabolism which is not maintained with chronic administration although renal excretion of drug metabolites may be modified.

W11  
Prophylactic sclerotherapy of oesophageal varices: a preliminary report

D R Triger and A G Johnson  
(University Departments of Medicine & Surgery, Royal Hallamshire Hospital, Sheffield)

Fifty three patients (age 21-70) with cirrhosis and oesophageal varices which had not bled were subjected to wedged hepatic vein pressure (WHVP) measurement. Those with WHVP ≥12 mmHg were randomised to either sclerotherapy (n=19) or observation (n=18). Groups were comparable with regard to age, aetiology, presence of ascites and Child’s grading. Cirrhosis was due to alcohol (21), PBC (16), CAH (10) and others (6). Patients with WHVP <12 mmHg were not randomised (n=16). Patients in any group who subsequently presented with variceal bleeding were treated by sclerotherapy. During a mean follow up of 28 months survival in those receiving prophylactic sclerotherapy was slightly better than in the control group (one year 81% vs 62%; two years 67% vs
45%). This was entirely due to improved survival in the alcoholics receiving sclerotherapy. Survival in the non-randomised group was 89% at one year and 77% at two years. Variceal haemorrhage occurred in 6/19 undergoing sclerotherapy, 7/18 in the control group and 3/16 in the non-randomised group. Size of varices correlated poorly with WHVP and was a poor predictor of haemorrhage. Only 6/16 deaths to date have been due to variceal bleeding. No patient in the non-randomised group has died of bleeding varices. Preliminary results do not suggest that prophylactic sclerotherapy in non-alcoholic cirrhosis prolongs survival; the beneficial effect in alcoholic cirrhosis might be related to alteration in alcohol consumption. Longer follow up with larger numbers of patients is required.

W12 Prophylactic propranolol therapy in chronic liver disease
P C HAYES AND I A D BOUCHIER (University Department of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland)
The effect of long term propranolol (Indepal LA-160 mg) therapy in patients with chronic liver disease was examined in a double blind placebo controlled study. Ninety five patients (41 alcoholic cirrhosis; 18 primary biliary cirrhosis; nine chronic active hepatitis; six cryptogenic cirrhosis and 21 ‘other’), predominantly Child’s group A & B, took part in the study, 47 in the propranolol and 48 in the placebo group. The groups were well matched for age, sex and severity of liver disease. Twenty five patients were withdrawn because of adverse reactions (13 placebo; 12 propranolol) and 64 patients completed 12 months in the study. Fifteen patients were changed to half strength trial medication. Eleven patients died during the 12 month study period, eight in the placebo group (17%) and three in the propranolol group (6-5%).

Four of the deaths in the placebo group were related to upper gastrointestinal haemorrhage and/or hepatocellular failure compared with none in the propranolol group. Hepatoma and cardiovascular deaths appeared with similar frequency. There was no consistent change in Child’s category in either group and the only significant change between the two groups was a fall in serum testosterone on propranolol (p=0.02).

Long term propranolol therapy in patients with chronic liver disease is free from serious side effects, does not impair liver function and may improve survival.

W13 Enhanced respiratory burst activity of C parvum elicited hepatic macrophages compared with normal Kupffer cells in the rat
M J P ARTHUR, P KOWALSKI-SAUNDERS, AND R WRIGHT (Department of Medicine, Southampton University Medical School, Southampton) We have previously shown that oxygen derived free radicals promote hepatocellular necrosis in the C parvum/endothxin rat model of liver injury. The aim of this study was to compare the respiratory burst activity of normal Kupffer cells (KC) with C parvum (28 mg/kg, given iv, six days previously) elicited hepatic macrophages (CHPM). These were isolated by collagenase perfusion of the portal vein and purified by centrifugal elutriation. Respiratory burst activity was studied in the ‘resting’ state and after stimulation with phorbol myristate acetate (PMA) by 1-14C-glucose oxidation via the hexose monophosphate shunt (HMPS). This reflects the production of oxygen derived free radicals.

There was a significantly increased yield of CHPM (mean×10^5±SD, 376±145) compared with normal KC (47±24, p<0.001). CHPM (n=8) demonstrated enhanced HMPS activity compared with normal KC (n=8) both in the resting state and after PMA stimulation (mean±SD, CHPM vs KC: (a) resting, 3.41±1.65 × 10^5 vs 1.12±0.33, p<0.01; (b) PMA stimulated 5.35±2.99 × 10^5 vs 1.18±0.31 CPM×10^5/mg protein/60 min, p<0.001).

The increased number of CHPM and their enhanced respiratory burst activity demonstrate a substantially increased potential for release of cytotoxic oxygen derived free radicals in this model of liver injury.

OESOPHAGUS
P1-17

P1 Abnormal response to distension in oesophageal clearance disorders
G P N KENDALL AND D G THOMPSON (St Mark’s and The London Hospital, London) Motor responses to oesophageal distension were studied in 13 normal subjects and five patients with poor oesophageal clearance without structural abnormality. Oesophageal manometry was performed, both proximal and distal to a balloon sited 10–15 cm from the gastro-oesophageal junction, during five minute periods of balloon inflation (I) and deflation (D). During distension, primary peristalsis was unaltered proximally, but was reduced distally ((D) 7.5±1.8 (mean contractions/5 min±SEM) vs (I), 3.7±1.4, p<0.05). Secondary peristalsis increased proximal to the distension ((I) 22.8±3.6 vs (D) 2.9±1.1, p<0.001) with a small distal reduction ((D) 5.2±1.5 vs (I) 3.5±1.3). Powerful aboral propulsion of the balloon was induced.

Supine radionuclide transit was prolonged in all patients. One patient with corkscREW oesophagostomosis, exhibited no distal inhibition. In two patients with hypertrophy and two with normal manometry, distension induced neither a proximal increase in contractions nor aboral propulsion of the balloon.

These results show a propulsive response to balloon distension in the normal oesophagus, resembling the in vitro ‘peristaltic reflex’. Abnormalities of this response may be a cause of impaired oesophageal clearance. Addition of balloon distension to standard manometry thus appears useful for identifying specific propulsive abnormalities in such patients, particularly when other manometric parameters are normal.

P2 Barium radiology in gastro-oesophageal reflux disease – a reappraisal
R J SELLSAR, J S DE CAELESTEECK, AND R C HEADING (Department of Radiology and Department of Medicine, Royal Infirmary, Edinburgh) Forty six patients (24 with heartburn, 22 with non-cardiac chest pain) were studied using radiology, endoscopy and 24 hour ambulatory intraoesophageal pH monitoring. Barium radiology was carried out using a ‘physiological’ method (rolling the patient into the right decubitus position) and a ‘compression’ method (abdominal binder inflated to 100 mmHg) to induce reflux. Double contrast oesophagrams were also obtained.

Thirty one patients had significant acid reflux by pH probe. Using this as a standard, the ‘physiological’ method detected 17, the ‘compression’ method 23 and
endoscopy 14 refluxers, with three, five and one false positives respectively. 'Compression' barium was the most sensitive (74%) and accurate (71%), while endoscopy was the most specific (93%) but least accurate (58%) in detecting acid refluxers. Using double contrast barium technique, measurement of the internal diameter of the cardiac oesophagus ([IDCO); ≥25 mm abnormal] had a sensitivity of 67%, specificity 91% and accuracy 74% in detecting acid refluxers. When the results of 'compression' method and measurement of the IDCO were combined, sensitivity was 87%, specificity 69% and accuracy 81%. These results suggest that, by combining a test to provoke reflux with a double contrast technique to measure IDCO, barium radiology becomes a sensitive screening test for reflux disease.

P3
Endoscopic ultrasonography in the investigation of oesophageal strictures

P J SHORVON, R A FROST, W R LEES, AND P B COTTON (Departments of Radiology and Gastroenterology, The Middlesex Hospital, London) Diagnosis of oesophageal strictures is made by barium swallow and endoscopy, but neither method supplies information beyond the mucosa. Endoscopic ultrasonography (EUS) enables assessment of the depth of mucosal lesions and the detection of associated enlarged lymph nodes.

We have carried out EUS on five patients with oesophageal strictures, using the prototype Olympus ultrasonic endoscope which has a 7.5 MHz transducer. Three patients had known oesophageal carcinoma. In one EUS demonstrated a small resectable tumour with no enlarged lymph nodes, confirmed at operation. CT had suggested more advanced disease. In the other two patients the ultrasonic endoscope could not be passed beyond the tumour despite prior endoscopic dilatation in one. Inoperability was demonstrated by visualisation of an extensive tumour extending into the mediastinum and an enlarged subaortic node in one, however. In the other no associated lymph nodes were seen above the tumour, and this was confirmed at operation.

One patient had an oesophageal stricture proximal to the anastomosis of an oesophageogastronomy two years before. No mucosal abnormality was visible and EUS clearly showed that the stricture was be-
cause of compression by surrounding enlarged lymph nodes.

The last patient had a recurring benign stricture despite dilatation. It was decided to diathermy the stricture endoscopically and this was adjudged safe after demonstration of the depth of fibrosis by EUS. Endoscopic ultrasonography gives unique information about oesophageal strictures and a study is in progress to assess its accuracy in staging of oesophageal cancer.

P4
Gastro-oesophageal reflux in the irritable bowel syndrome

H L SMART, D NICHOLSON, AND M ATKINSON (University Hospital, Queen's Medical Centre, Nottingham) The irritable bowel syndrome (IBS) and symptomatic gastro-oesophageal reflux (GOR) are common gastrointestinal disorders which may be related. To investigate this possibility we examined oesophageal symptoms, endoscopic appearances and undertook oesophageal manometry and pH recording in 25 consecutive patients with IBS. Weekly symptoms of GOR were significantly more common (p=0.0003) in IBS patients (52%) than in age and sex matched controls (17%). Similar significant differences were observed for globus and dysphagia. Endoscopy revealed macroscopic evidence of oesophagitis in eight cases and microscopic oesophagitis in a further 11 subjects. Patients with IBS had a significantly lower (p<0.001) lower oesophageal sphincter pressure (14.0±5.3 cmH2O (mean±standard deviation)) than 25 age and sex matched controls (19.4±5.1 cmH2O) without symptoms of GOR. No other significant manometric abnormalities were found. Ambulatory radiotelemetric oesophageal pH monitoring revealed abnormal reflux in 16 of 21 IBS patients. Two of 13 patients with frequent GOR symptoms had a normal pH study, whereas five of eight with infrequent symptoms had an abnormal study.

We conclude that GOR is significantly commoner in IBS and that the lower oesophageal sphincter pressure is significantly lower in IBS. These two findings may be causally related.

P5
Comparison between three methods of oesophageal pH recording in the diagnosis of gastro-oesophageal acid reflux

G BIANCHI PORRO, F PACE, S BARONI, F PARENTE, AND M LAZZARONI (Gastrointestinal Unit, L Sacco Hospital, Milano, Italy) Oesophageal pH-monitoring is the most sensitive method of detecting and quantitating gastro-oesophageal reflux (GOR). Prolonged pH testing is usually done as a 24 hour investigation, in order to take into account postural or other circadian changes in oesophageal pH. The superiority of a 24 hour period of study over shorter tests, however, such as overnight or postprandial test, has not been extensively evaluated in terms of specificity and sensitivity. The purpose of this study is to assess if these two shorter tests retain the diagnostic validity of a 24 hour test. Oesophageal pH testing was undertaken for 24 hours (with subjects in upright position during the day and supine when retiring) in 20 patients (14 men, six women, mean age 46 years, range 18-64 years) with endoscopic and/or histologic diagnosis of oesophagitis, and in 20 healthy volunteers (nine men, 11 women, mean age 25 years, range 19-42 years) free of any symptoms of GOR. The 24 hour test, as well as the 12 hour and the postprandial ones, yielded no false positive results, with a 100% diagnostic specificity and a 100% positive predictive value. Twelve hour and postprandial tests showed a lower diagnostic sensitivity than the 24 hour test (50% and 70% vs 81%), respectively.

We conclude that a 24 hour oesophageal pH monitoring is the most accurate and desirable clinical test of GOR.

P6
Oesophageal dysmotility after myocardial infarction

J K RAMAGE, M DEAKIN, R EDGE, L JENKINS, AND J G WILLIAMS (Departments of Gastroenterology and Nuclear Medicine, RH Hospital, Haslar, Gosport, Hants) The relationship between oesophageal chest pain and the pain of cardiac ischaemia has not yet been fully established.

We have measured the time to clear 90% of a liquid bolus of 99m Technetium sulphur colloid from the oesophagus in 13 patients with ischaemic heart disease (proven on exercise testing or angiography) and 37 patients within 10 days of myocardial infarction (MI). Mean ages were 60-3 years (infarcts) and 54-3 years (IHD).
Of the patients with recent MI, 70% had abnormal transit times (greater than 17 seconds) and 40% had transit times greater than 120 seconds. In the ischaemic heart disease group, only one was abnormal at 47 seconds, the rest being less than 17 seconds. There was no correlation of transit time with age, sex, drug therapy with the beta blockers, maximum enzyme rise or site of infarct. Six of the infarct patients were studied again more than two months later. Five of these improved (four returned to normal) and one remained the same at 20 seconds. Four patients had died before they could be restudied – all had acute transit times greater than 120 seconds.

Oesophageal transit time is abnormal after myocardial infarction, indicating dysmotility which may be a cause of episodes of chest pain in the postinfarct patient.

P7
Does dilatation of benign oesophageal strictures (BOS) affect gastro-oesophageal reflux?

R PENAGINI, M AL DABBAGH, P F EVANS, I F TROTMAN, AND J J MISIEWICZ (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) The role of oesophageal dilatation in the management of peptic oesophageal strictures is well established. Dilatation improves dysphagia but it is not known if it has any effect on gastro-oesophageal reflux.

We studied nine consecutive patients (median 61 years; range 29–77 years, five men), with a BOS, admitted to hospital for oesophageal dilatation. Before and four days after the procedure each patient had a standard meal composed of foods with different consistency to assess dysphagia (score 0–20), a standard swallow with a high density barium suspension to measure the diameter of stricture and 22 hour intraoesophageal pH monitoring (Synectics system). All dilations were undertaken using the Celestin dilator to 18 mm. Analysis of results was done with the paired Wilcoxon test.

After dilatation the dysphagia score improved from (mean±SEM) 10.2±2.0 to 18.9±2.0 (p<0.01), the diameter (mm) of the stricture increased from 7.7±0.7 to 9.4±0.6 (p<0.05), while % of time intraeosophageal pH was <4 in the upright, supine and upright+supine position did not change significantly, being respectively 13.7±2.7 vs 20.1±6.2, 18.2±6.2 vs 19.7±2.7 and 15.6±3.2 vs 19.3±4.7.

We conclude that oesophageal dilatation has a minor effect on radiologically determined bore of BOS, does not make gastro-oesophageal reflux worse and has a striking effect on dysphagia.

P8
Computed tomography evaluation of oesophageal carcinoma – intubate or operate?

G P MCENTEE, J P DUIGNAN, D A O’CONNELL, E O’MALLEY, AND D BOUCHER-HAYES (Mater Misericordiae Hospital, Dublin, Eire) Recent studies have recommended placing peroral endoprostheses in patients with extensive oesophageal carcinoma, thus avoiding unnecessary surgery. This study analysed the role of computed tomography (CT) in evaluating oesophageal cancer with respect to other organ involvement and tumour resectability. Fifty patients with histologically proven disease (17 middle third, 33 lower third) were assessed using CT and subsequently re-assessed at surgery. The findings were correlated by an independent observer and the accuracy of CT determined separately for middle third and lower third lesions.

The accuracy of CT in evaluating organ involvement in middle third tumours was 84% (false positives five, false negatives four, total observations 51) compared with 94% for lower third tumours (false positives four, false negatives six, total observations 165). Regarding tumour resectability, the accuracy of CT for middle third tumours was 64–7% (false positives zero, false negatives six) compared with 90% for lower third lesions (false positives zero, false negatives three). Tumours deemed resectable on CT were always resectable at surgery, but nine tumours deemed unresectable on CT were in fact resectable at operation.

In conclusion CT provided useful information pre-operatively regarding extra-luminal tumour spread but was not sufficiently accurate to replace surgery as the final arbiter of tumour resectability.

P9
Oesophageal ulceration after extravesication of sodium tetradecyl sulphate and ethanolamine olate during endoscopic sclerotherapy

J D R ROSE AND P M SMITH (Department of Gastroenterology, Llandough Hospital, Penarth, S Glam) It is said that 3% sodi:m tetradecyl sulphate (STD) produces more ulceration during oesophageal sclerotherapy than 5% ethanolamine olate (EO). Twenty cirrhotic patients with oesophageal varices were randomly treated with either EO or STD, and at weekly injection sessions the volume of sclerosant used, the number of radiologically demonstrable extravasations of a contrast-sclerosant mixture and the number of ulcers were recorded. The 10 patients in each group were similar, except for their initial variceal score, being higher for those receiving EO (mean 19.9, range 9–32) than those receiving STD (mean 14.2, range 7–20; p<0.05). Two patients from each group did not complete the trial; two requiring oesophageal transaction and two dying of hepatic failure.

Four oesophageal ulcers developed after 56 EO extravasations and four after 44 STD extravasations (NS). The mean number of treatments required to obliterate the varices was 6–4 (range 4–10) for EO and 4–5 (range 2–6) for STD but allowing for initial size of the varices, the two agents were equally effective.

We conclude that EO and STD and equally effective for oesophageal sclerotherapy, and, in small quantities, are equally safe.

P10
Endoscopic sclerotherapy for bleeding gastric varices

YASSIN M YASSIN, MOHAMED S EITA, AND ABDEL MONEIM HUSSEIN (Gastroenterology Unit, Medical Academy General Hospital, Kobri-El-Kobba, Cairo, Egypt) Gastric varices are often associated with oesophageal varices in portal hypertension, but bleed less frequently and seem to be more difficult to control. The results of endoscopic sclerotherapy to control their bleeding are reported. Total obliteration of all gastric variceal channels was possible in only six of the 35 cases reported (17.1%), otherwise it was limited to bleeding and distended columns. The main complication was large deep sclerotherapy ulcers in eight cases (25.7%) with four deaths; two of uncontrollable haemorrhage and two of rupture. Three more patients died in hospital of intra-procedural cardiac arrest, failure to stop bleeding, and hepatic failure. Bleeding renewed early in five more cases, two only from their gastric varices, and one died eventually of a bleeding antral ulcer. Hospital deaths totalled eight (22.9%). During a one year follow up, bleeding recurred in five patients (only one...
from gastric varices); two died. Two more patients died of hepatic failure. The one year survival rate was 65.7%. These results indicate that the serious complications of endoscopic sclerotherapy for bleeding gastric varices including recurrent bleeding are numerous and frequently fatal. We suggest it should be limited to selected cases. Necrotic complications are greater with old age and poor hepatic function.

P11
Flow cytometric analysis of the DNA content of gastric cancer
K C BALLANTYNE, P D JAMES, R A ROBINS, R W BALDWIN, AND J D HARDCASTLE (Departments of Surgery & Histopathology, University Hospital, Nottingham, and Cancer Research Campaign Laboratories, Nottingham) Abnormal tumour cell DNA content (aneuploidy) is associated with worse prognosis in a variety of cancers and in a recent Japanese study only 17/54 (32%) gastric cancers were aneuploid.

Seventy two consecutive patients, median age 67 years (43-88 years) who underwent gastrectomy between 1979-1982 were studied. DNA content was measured by flow cytometry after disaggregating representative paraffin embedded sections (2×20μ) with diaminophenylindole hydrochloride.

Forty four (61%) had a significant population of cells (<10%) with an abnormal DNA content (aneuploid). Two separate tumour blocks were examined in 22 cases and concordance found in 17 (77%). No correlation was found between DNA content of primary tumours and histological type, histological grade or pathological stage. Curative resection was carried out in 40 cases. Twelve patients survived over two years and nine remain disease free. The median survival was 17 months (n=13) for diploid tumours and 18 months (n=27) for aneuploid tumours.

We conclude that factors other than tumour cell DNA are responsible for the aggressive nature of gastric cancer. Only 39% of cancers studied were diploid compared with 68% of tumours in Japan; this may reflect a difference in the geographical pattern of this disease.

P13
Local gastric antibodies to Campylobacter pyloridis
B J RATHBONE, J I WYATT, B WORSLEY, S SHIERES, L K TREJDOSEWICZ, R V HEATLEY, AND M S LOSOWSKY (Departments of Medicine and Pathology, St James University Hospital, Leeds, and Department of Microbiology, University of Leeds, Leeds) The association between Campylobacter pyloridis (CP) and active chronic gastritis is now well established. The colonisation of normal gastric mucosa and the subsequent development of gastritis has also been demonstrated. We have previously identified raised circulating IgG and IgA antibodies in CP +ve patients, but this systemic immune response probably has little relevance to events at the mucosal level.

Using immunohistochemical techniques and an enzyme linked immunosorbent assay (ELISA), local antibodies to CP were studied both in gastric biopsies and gastric juice. Twenty two dyspeptic patients were studied: seven out of 13 CP +ve patients had demonstrable IgA to CP in their gastric juice, IgM was shown in three +ve patients. No IgG antibody was detected in any patient.

IgG, IgA and IgM antibodies were consistently shown coating the surface of organisms on inflamed mucosae. No antibody labelling could be detected on organisms deep in the gastric pits, however.

The local antibody response to CP does not appear to inhibit bacterial colonisation. One possible reason is that the organisms situated deep in the gastric pits are, by their position, protected from the secreted antibody.

P12
Therapy in symptomatic advanced gastric carcinoma
G RUSTIN, E S NEWLANDS, R H J BEGENT, K D BAGSHAWE, J L MATTHEWS, AND T COOKE (INTRODUCED BY A PARKINS) (Charing Cross Hospital, Fulham Palace Road, London) Effective therapy is required for symptomatic unresectable or recurrent gastric carcinoma. Following the response of a gastric cancer producing HCG to a drug regimen used in choriocarcinoma, we have assessed its efficiency in further patients.

Twelve patients with advanced gastric carcinoma received a weekly schedule of etosopide, metotrexate and actinomycin D (EMA) alternating with cyclophosphamide and vincristine (CO). Treatment continued for 12 weeks unless there was evidence of progression. In 10 tumours DNA ploidy values were determined by microdensitometry after Feulgen staining and DNA histograms plotted and classified as aneuploid or diploid. Response to chemotherapy was determined symptomatically and by WHO criteria.

Five of the seven patients (71%) with objectively assessable disease responded. Only two patients in the total group had progressive disease during the three months of chemotherapy. Of the five patients without assessable disease, symptoms improved with complete pain relief, loss of ascites or relief of obstruction and in two, marked improvement at repeat gastroscopy. By manipulating dosage appropriately, chemotherapy was well tolerated.

Six patients had both measurable disease and DNA ploidy estimations. Four had aneuploid tumours and responded, two patients with diploid profiles had progressive disease.

The initial results using this novel chemotherapy regime suggests it may be of value to patients with gastric carcinoma.

P14
Ranitidine for stress ulceration: effect of bolus or infusion administration
D L MORRIS, S MARKHAM, A BEACHEY, FIONA HICKS, K SUMMERS, P LEWIS, AND A BYRNE (Department of Surgery, University Hospital Nottingham) Stress ulcers are a common problem in critically ill patients and may largely be prevented by antacid or H2 antagonist administration. The optimal mode of ranitidine administration is unknown. Forty patients who all required respiratory support on our intensive care unit underwent an untreated control period of 12 hours and were then randomly allocated to (1) ranitidine 50 mg six hourly by iv bolus, (2) ranitidine infusions 0.125 mg/kg/hr, or (3) ranitidine infusion 0.24 mg/kg/hr. Gastric juice was aspirated hourly for pH measurement. Serum concentrations of ranitidine were assayed by HPLC.

pH Data is currently available in 20 patients and good pH control was achieved (>pH 4) in all but three patients. Sixteen of 140 samples were <4 in group 1 compared with two of 100 in group 2, and 19 of 101 in group 3.

High peak serum concentrations (mean 2359 μg/l ±1593 SD) were seen immediately after bolus administration with a mean trough concentration of 243±49 at six hours. In the infusion groups a much steadier serum level was achieved. Mean serum concentrations at four and 12 hours were 280 and 461 μg/l for group 2 and 429
and 740 µg/l for group 3.

Ranitidine infusion produces adequate pH control and has possible pharmacokinetic advantages over bolus administration.

P15
SK&F 93574 – Preliminary evaluation of a potent and long-acting parenteral H₂-receptor antagonist in man

W L Burland, Jane G Mills, Linda Richardson, and Kathie Wareham (Smith Kline & French Research Ltd, The Frythe, Welwyn, Hertfordshire) SK&F 93574 is a potent and specific histamine H₂-receptor antagonist in animals with a long duration of action. The parenteral administration of an antisecretory compound with such a profile of activity could offer therapeutic advantage in several indications, including (1) the management of patients at risk from developing stress-related lesions of the upper gastrointestinal tract; (2) the reduction of gastric acidity and volume, which are associated with morbidity and mortality in the event of pulmonary aspiration.

Two studies have been conducted in healthy male subjects. Inhibition of the heart rate response to the intravenous injection of imipramine 300 mcg was used to establish an effective dose-range for SK&F 93574 in man and to examine the time course of the response. Eleven subjects aged 24–41 years were studied on three or four separate occasions when they received doses of 10 to 60 mcg/kg by 15 minute intravenous infusion: SK&F 93574 is at least 25 mcg/kg inhibited the response to imipramine, the effect was dose related and appeared to be maximal after two to three hours. At doses ≥50 mcg/kg the increase in heart rate was reduced by at least 50% 30 minutes after the start of the infusion; 20–24 hours after SK&F 93574 50 or 60 mcg/kg the heart rate response to imipramine was reduced by 48% (n=4).

SK&F 93574 2.5–15 mcg/kg had no significant effect on imipramine stimulated gastric acid secretion; three hours after the start of the infusion of SK&F 93574 25 mcg/kg stimulated gastric acid output was reduced by 69–78% (n=3); within the first hour of the infusion of SK&F 93574 50 mcg/kg acid output was reduced by 36 to 52% (n=4) increasing to 96 to 100% in the second hour with 59 to 80% inhibition still present during the sixth hour. The iv administration of SK&F 93574 was well tolerated.

P16
A new role for polycrylates in gastric mucosal protection

P W Detmar, A G Lynn, E C Leach, and J G Lloyd-Jones (introduced by A Allen) (Departments of Pharmacology and Clinical Sciences, Reckitt & Colman, Hull) The role of polycrylates in preventing ethanol-induced gastric necrosis and their ability to bind to gastric mucus adherent to the gastro mucosal surface of the rat has been investigated. These studies showed that there was a synergistic effect on the sodium polycrylate/carbomer 934P, which is a high molecular weight non-absorbed polymer, was administered together with the anti-ulcer agent carbenoxolone sodium with a resultant increase in gastric mucosal protection.

The minimum dose of carbenoxolone to significantly protect against the ethanol-induced gastric necrosis was 60 mg/kg (69.1% protection, p<0.01), carbomer possessed only weak mucosal protection activity maximal at 50 mg/kg (39.1%, p<0.02). When 50 mg/kg carbomer was combined with an inactive dose of carbenoxolone (5 mg/kg) significant protection (92.5%, p<0.001) was produced – that is, synergism was exhibited.

Alcian blue was used to detect the presence of carbonbomer binding to mucus adherent on the surface on the rat gastric mucosa. At the above dose carbonbomer binding increased by 118.9% (p<0.001) compared with control treatment and persisted for up to five hours.

The gastric mucosal protection afforded by a combination of carbenoxolone and carbonbomer is currently being clinically evaluated for the treatment of gastrointestinal

P17
Early and median term results of vertical banded gastroplasty in the management of morbid obesity

E R T C Owen, F D Beggs, and A E Kark (introduced by A G Cox) (Department of Surgery, Northwick Park Hospital, and Clinical Research Centre, Harrow, Middlesex) We report the results of 21 cases of vertical banded gastroplasty undertaken with modification of the Mason technique. Essential technical features are exposure, pouch size construction and accurate outlet banding which will be illustrated. At presentation patients were between 30% and 154% above their ideal weight (mean 96-3%).

One death occurred six weeks after leaving hospital from pulmonary embolism, seven patients had minor wound infections, but nine had a cholecystectomy carried out at the same operation. One patient had a wound dehiscence. The average hospital stay was nine days.

The mean follow up period was 12 months. Mean weight loss for all patients during this period was 27 kg (range 8-5-47 kg). At 26 weeks patients were a mean of 57% above their ideal weight. These figures compare favourably with other forms of gastroplasty.

After weight loss many patients have had cosmetic procedures – a total of 12 operations have been carried out.

We conclude that vertical banded gastroplasty is a relatively safe, simple and reliable procedure. Surgeons performing bariatric surgery should appreciate the inevitable further multiple cosmetic procedures which are necessary following weight loss.

P18
Gastric mucosal protection by a thromboxane synthesis inhibitor (T×SI)

C J Hawkey, R P Walt, R T Kemp, B Filipo-wicz, J Davies, and N K Baskar (Department of Therapeutics, University Hospital, Nottingham) Prostaglandins (PDs) are protective to gastric mucosa but thromboxane synthesis enhances damage. We have investigated whether the T×SI dazmegrel affords protection. Male Wistar rats (200–220 g) were dosed orally with vehicle or dazmegrel 1.5 or 25 mg/rat (n=8 all experiments). After two hours they were challenged with sodium taurocholate 100 mM in HCl 0.2 N and mucosal damage subsequently graded 'blind'. Other rats were killed two hours after dosing and in vivo release of T×B₂ and PGE₂ from gastric mucosal fragments measured by radioimmunoassay.

Dazmegrel 1 mg/rat inhibited T×B₂ synthesis by 23±8% (mean±SEM, p<0.05), did not significantly affect PGE₂ synthesis (12±24% control) and reduced mucosal damage (median grade 2.5 to 1.5, p<0.05). Dazmegrel 5 mg/rat inhibited T×B₂ synthesis (by 34±5%, p<0.001), did not affect PGE₂ synthesis (102±16% control) and reduced mucosal damage.
(grade 2-5 to 1, p<0.01). Dazmegrel 25 mg/rat inhibited synthesis of both T×B2 (by 46±7%, p<0.001) and PGE2 (by 27±9%, p<0.05), without significant effect on mucosal damage (grade 2-5 to 2).

Thus, lower doses of dazmegrel selectively inhibit thromboxane synthesis and protect gastric mucosa. At higher doses both selectivity and protection may be lost. Assessment of T×S1’s in man is worthwhile.

P19
Antigenic determinants of wheat protein in coeliac disease
C O’MAHONEY, C O’FARRELLY, M MANSFIELD, D G WEIR, A WHELAN, AND C F FEGHERY (Departments of Immunology and Clinical Medicine, St James’s Hospital, Dublin, Eire) Wheat protein antibodies are found in patients with untreated coeliac disease (CD). The major antigenic determinants of this antibody response are found in crude gliadin – a complex mixture of alpha, beta, gamma, and omega gliadins. Interest has recently focused on alpha-gliadin, due to its remarkable amino acid sequence similarity to adenovirus 12 – a virus which may be implicated in the aetiology of coeliac disease

Using two assay systems we tested fractions of crude gliadin (obtained by ion exchange chromatography) with sera from patients with coeliac disease (CD) and normal controls (N). (1) In the enzyme linked immunosorbent assay sera from patients with untreated CD reacted with most of the gliadin fractions. The highest antibody levels were, however, found using the alpha-gliadin fraction.

(2) Crude gliadin and its fractions were further separated on agarose isoelectric focusing and then immunoblotted onto nitrocellulose paper strips. The strips were then incubated with sera from patients and controls. The areas of reactivity were stained by immunoperoxidase. Again, all major antigens were contained in the alpha-gliadin fraction. Finally, a monoclonal antibody to alpha-gliadin reacted to several bands of fractionated alpha-gliadin suggesting the presence of a recurring identical antigenic moiety.

This work confirms that alpha-gliadin is the major antigen of crude gliadin. This may be due to a repeating antigenic site on the molecule. Thus it is a susceptible individual, a damaging immune response, first elicited by a viral infection, could be perpetuated by immune activity against cross-reactive alpha-gliadin and cause the enteropathy of coeliac disease.

P20
Does gastric fundic pH or distension effect ileal absorption?
A Bilge AND J B Elder (University Department of Surgery, Manchester Royal Infirmary and University of Keele, Keele) No data are available on the influence of gastric fundic pH or gastric distension on ileal absorption. Male Sprague-Dawley rats were prepared under general anesthesia with a 4 cm ileal loop and the gastric fundus isolated by ligation of the oesophago-gastric junction and cross clamping of the antrafundic junction. Five minutes after the introduction of tracer (100 mCi 99mTc) to the ileal loop, 0.1 ml portal blood samples from an indwelling cannula were obtained at five minute intervals for 50 minutes. The IVC was cannulated and infused with 0.154 M NaCl containing 0.1% albumin at 3 ml/h. Thirty four control rats (fasting gastric fundic pH (GF pH) 1.5–5, no gastric distension), and four groups each of six rats with GF pH buffered at pH 1.2–2, 4, 7, 9 and a group with GF pH in the fasting resting range but with the gastric fundus distended by injection of 3 ml air were studied. When GF pH was held at four ileal tracer absorption increased by 27% at 10 minutes and 32% at 15 minutes (p<0.001); when the gastric fundus was distended by air ileal absorption after 15 minutes was 38% above control (p>0.01). Alkaline GF pH reduced ileal absorption (p<0.01). Four weeks after trunical vagotomy and pyloroplasty the increased ileal tracer absorption noted after gastric fundic distension was abolished (n=5), but the effect of intraluminal acid (GF pH, n=5) enhancing ileal absorption remained. These data suggest a humoral effect from the gastric fundus on ileal absorption in the rat.

P21
Correlations between the acute effects of thioacetamide on hepatic morphology and on hexokinase activity and isoenzymic composition in the rat
M A Jepson, G M Lawrence, AND D G Walker (INTRODUCED BY R Coleman) (Department of Biochemistry, University of Birmingham, Birmingham) In normal adult rat liver, four hexokinase isoenzymes contribute to total glucose-phosphorylating activity. The major, high-Km form, glucokinase, constitutes 88% of the total activity, is entirely cytoplasmic and occurs only in hepatocytes where it has a predominantly perivenous zonal distribution. The remaining, low-Km, activity is largely confined to non-parenchymal cells. Ten per cent are tightly associated with the outer mitochondrial membrane and up to 70% are due to type I hexokinase.

During the two to three day period after a single 200 mg/kg body weight injection of thioacetamide, there is a 300–500% increase in low-Km hexokinase activity whereas high-Km activity decreases to 10–20% of control values. Up to 20% of the raised low-Km activity is mitochondrial bound and the type II and type III isoenzymes predominate in both the soluble and the particulate fractions.

Recovery begins three to four days after treatment and low- and high-Km activities return to control levels six to seven days later.

The early changes in hexokinase activity correlate with rapidly developing perivenous hepatocytic necrosis and with the proliferation of non-parenchymal, oval cells. The return to normality coincides with the disappearance of the proliferating zones, the reappearance of the original parenchymal cell morphology and the re-emergence of normal metabolic zonation patterns.

P22
Permissive role for the vagus nerves in the genesis of antro-antral reflexes in the anaesthetised ferret
D Grundy, D Hutson, and T Scratcherd (Department of Physiology, The University of Sheffield, Western Bank, Sheffield) An increase in antral motility after distension of the stomach depends, in part, on a vago-vagal reflex activated by mechanoreceptors in the corpus. In the present study we have considered the possible reflex effects of antral distension.

The experiments were carried out on urethane (1·5 g/kg) anaesthetised, splanchnecotomised ferrets. Antral motility was recorded manometrically from a catheter inserted through the pylorus. Antral distension was achieved by passing saline through a second catheter inserted through the mouth and secured in the antrum by a ligature across the incisura. Antral distension with 5–10 ml of saline increased the amplitude of antral contractions. Vagal blockade, achieved by cooling the cervical
vagi to <4°C, caused a fall in antral tone and attenuated the contractions evoked by antral distension. This might implicate a vagal reflex in the genesis of the evoked contractions. In vagotomised animals, however, close arterial infusions of acetylcholine sufficient to return antral motility to basal levels allowed the reflex to again become manifest. We conclude, therefore, that the increase in antral motility following antral distension is mediated by local reflexes which require a tonic vagal input.

P23
Secretin stimulates gastric mucus barrier thickness without increasing luminal mucus

N J H CARROLL, A ALLEN, AND B H HIRST (Department of Physiological Sciences, Medical School, University of Newcastle upon Tyne) The anaesthetised rat provides a suitable model for studying simultaneous changes in the protective adherent mucus barrier and the output of luminal mucus. Ligated stomachs were perfused via a double lumen orogastric tube, and gastric contents recovered and analysed for mucus glycoprotein. The thickness of the adherent mucus barrier was measured on unfixed gastric mucosal sections.

Secretin, 4 U/kg/h iv, caused a significant progressive rise in adherent mucus thickness reaching a maximum median value of 175 μm (quartile values 165–230) (n=6), compared with controls 100 μm (60–130) (n=6). Significant increases in adherent mucus thickness were also observed with topical 16,16-dimethyl prostaglandin E2 (dm-PGE2 5 μg/ml) (44% increase) and carbachol (100 μg/kg ip 55% increase). Luminal mucus glycoprotein output was unchanged following secretin infusion; 0.17±0.02 (n=6) mg/30 min (mean±1 SEM) compared with control values of 0.14±0.02 (n=6) mg/30 min. In contrast dm-PGE2 resulted in a seven-fold rise in luminal mucus glycoprotein output.

These experiments show a novel stimulatory effect of secretin on gastric mucus barrier thickness. Further, increases in adherent mucus thickness are not necessarily associated with increased luminal mucus output.

P24
Mechanism for the mucosal protective action of polyacrylate on the gastric mucus barrier

S N E FOSTER, A ALLEN, AND J P PEARSON (Department of Physiological Sciences, University Medical School, Framlington Place, Newcastle upon Tyne) Carbomer 934P, a polyacrylate (3×10⁶) acts synergistically with carbonoxolone, protecting against ulceration.

Carbomer (1–10 mg/ml), when added to gastric mucus glycoprotein (range 5–10 mg/ml) in isotonic pH 2 buffer, produced a large synergistic increase in mucus viscosity rising with mucus and carbomer concentration to over 1000% of the theoretical additive viscosity (mucus/carbomer both at 10 mg/ml). Carbomer also caused a smaller synergistic increase in the viscosity of the pepsin degraded glycoprotein (95% increase).

Pepsin activity at pH 2.2 was inhibited by carbomer (45% inhibition of albumin hydrolysis at carbomer 4 mg/ml, pepsin 1–0 μg/ml). Two methods (centrifugation and ultrafiltration) which measured bound pepsin compared with free showed this inhibition can be explained primarily by reversible binding of pepsin to carbomer. At low pepsin concentrations (0.01–0.4 mg/ml) the percentage bound to carbomer (4 mg/ml) rose linearly plateauing at higher pepsin concentrations (1–5 mg/ml). Pepsin binding was also dependent on carbomer concentration – for example, for pepsin 2 mg/ml, carbomer 4 or 0.4 mg/ml, percentage bound = 73% and 31% respectively.

The above results show that carbomer may act in mucosal protection by physically strengthening the mucus barrier and by inhibiting degradation by pepsin.

P25
Mechanism of acetate absorption in normal rat jejunum

A J M WATSON, M J KELLY, M WILKS, M J G FARTHING, AND P D FAIRCLough (Department of Gastroenterology and Department of Bacteriology, St Bartholomew’s Hospital, London) Acetate has been proposed as an alternative to bicarbonate in oral rehydration solutions for correction of acidosis due to diarrhoeal disease. Our previous experiments show that in the normal rat jejunum acetate, like glucose, stimulates sodium and water absorption. Although acetate is absorbed at a similar rate to glucose, its transport mechanism is still unclear. Studies of the absorption kinetics, competition with propionate, and ion dependency have therefore been performed using steady state perfusion of the normal rat jejunum in situ. Acetate absorption from isotonic solutions containing 5–150 mmol/l of acetate apparently followed saturation kinetics (Vmax = 13 μmol/min/g, Km = 47 mmol/l). Competition experiments showed that acetate absorption from a 30 mmol/l solution was inhibited by 70 mmol/l propionate (5±2±0.3 μmol/min/g vs 2.9±0.3 μmol/min/g; p<0.01). Absorption of propionate from a 70 mmol/l solution was also inhibited by 80 mmol/l acetate (9.9±1.5 μmol/min/g vs 5.6±0.4 μmol/min/g; p<0.01). Ion substitution experiments (sulphate replacing chloride, and choline and lithium replacing sodium) failed to show chloride or sodium dependence in this model.

Demonstration of saturation kinetics and inhibition by propionate are compatible with carrier-mediated transport of acetate by the rat small intestine.

P26
Secretion of adherent mucus gel by amphibian gastric mucosa in vitro

J P KEOGH, S MCQUEEN, A ALLEN, AND A GARNER (Department of Physiological Sciences, Medical School, Newcastle, and ICI Pharmaceuticals Division, Alderley Park, Macclesfield) The secretion of adherent mucus gel has been studied in vitro using gastric mucosal sheets (mounted in Ussing chambers) and stomach sacs (oesophageal intubated, pylorus ligated) from Rana temporaria.

In control mucosal sheet preparations mucus thickness increased after one hour by 2.7 fold (from mean 72±11 μm to 92±16 μm), while in the stomach sacs no increase was observed (from 83±7 μm to 71±8 μm). This may be related to mucosal stretching when mounted in the Ussing chambers since distension of stomach sacs by applying a luminal hydrostatic pressure (3 cm) caused a 2.2 fold increase in mucus thickness after one hour.

16,16-dimethyl prostaglandin E₂ (10⁻⁵ M) significantly stimulated mucus thickness after one hour on mucosal sheets and stomach sacs (dose dependent) by 1.4 fold and 2.7 fold respectively over the corresponding one hour control values. Carbachol (10⁻³ M, nutrient side) also significantly increased adherent mucus thickness by 1.4 fold in mucosal sheet preparations, a response inhibited by atropine. Addition of cimetidine (10⁻⁴ M, nutrient side) did not affect mucus thickness on mucosal sheets after one hour although acid secretion was inhibited.

These results are the first demonstration in vitro of stimulated secretion of adherent
mucus by prostaglandins, cholinergic mechanisms and mucosal distension.

**P27**

Eicosanoids on amphibian duodenal luminal alkaline secretion in vitro

J P KEOGH, A M STANIER, J R HEYLINGS, A ALLEN, and A GARNER (Department of Physiological Sciences, Medical School, Newcastle, and ICI Pharmaceuticals Division, Alderley Park, Macclesfield) Epithelial bicarbonate secretion is believed to be an important mechanism in duodenal mucosal protection against luminal acid. We have compared the stimulatory effects of various eicosanoids on bicarbonate secretion in the duodenum in vitro.

Segments of Rana catesbeiana proximal duodenum were mounted as cylinders in glass chambers and rates of luminal alkalinisation measured by continuous back titration to pH 7.4. Cumulative dose responses were determined to serosal administration of eicosanoids. Prostaglandin E2 (1 μm) was administered at the end of each experiment to elicit a maximal response in order to standardise responsiveness between individual mucosas. The following agents (10 μm) produced significant increases in alkaline secretion, expressed as percentage of PGE2 maximal response: PGE1 (100%), PG12 (68%), PG2(64%), PGD2 (62%), arachidonic acid (60%) 6 keto-PGF1α (55%), leukotrieneD4 (48%), PGA2 (48%), thromboxaneB2 (42%). Linoleic acid and leukotrieneD4 (lum) were inactive. Indomethacin (lum) attenuated arachidonic acid response and enhanced that to PGE2.

While prostaglandins of the E series are the most potent stimulants of HCO3- secretion a variety of other eicosanoids are also active.

**P28**

Effects of protein kinase C activation on intestinal fluid transport and blood flow

J D FONDACARO, J S STEFANKIEWICZ, L S HENDERSON, and A SJÖQVIST (Smith Kline and French Laboratories, Philadelphia, PA, USA) Studies were designed to examine the effects of protein kinase C (PKC) stimulation on fluid transport and blood flow in the small intestine of the anaesthetised cat. The phorbol ester 4β-phorbol 12,13-dibutyrate (PDB) was used to activate PKC. Intraluminal administration of PDB into a segment of isolated small bowel produced a copious intestinal secretion and a concomitant mesenteric hyperaemia. Net fluid movement in the intestine was converted from absorption in the control state to secretion following PDB. Intravenous atropine reduced PDB-induced secretion by 56%; clonidine abolished the remaining secretory response. Intraluminal administration of PDB produced intense vasoconstriction. Furthermore, intraluminal PDB caused increased segmental contractions in the bowel segment, which were totally inhibited by atropine. In Ussing chamber studies of the rat ileum, PDB increased short-circuit current, inhibited net Na+ and Cl− absorption and increased serosal-to-mucosal Cl− flux. These studies demonstrate that stimulation of PKC produces a full secretory response in the small intestine. Secretion is likely to be a result of inhibition of Na+ and Cl− absorption and stimulation of electrogenic Cl− secretion. Evidence suggests that this secretion is accompanied by a metabolic hyperaemia. We propose that PKC plays an important role in the regulation of intestinal fluid transport.

**P29**

Duodenal brush border membrane HCO3-ATPase, implicated in HCO3- secretion is an expression of alkaline phosphatase

J M WILKES, A GARNER, and T J PETERS (Clinical Research Centre, Watford Road, Harrow, Middx, and ICI Pharmaceuticals plc, Mereside, Alderley Park, Macclesfield) HCO3-activated ATPase has been implicated in duodenal HCO3- secretion, an important process in mucosal protection against acid. Rat duodenal brush border membrane (BBM) was isolated by Ca2+-precipitation, forming tightly sealed right-side-out vesicles capable of Na+-dependent glucose transport. The BBM was enriched 16-fold in α-glucosidase, with a 30% recovery. HCO3-ATPase was enriched seven-fold, confirming an association with the BBM. The activity was strongly inhibited by 10 mM L-phenylalanine, an inhibitor of alkaline phosphatase.

BBM HCO3-ATPase, solubilised in Triton X-100, was subjected to anion exchange, gel exclusion and phenyl boronate column chromatography. In all cases HCO3-ATPase co-eluted with alkaline phosphatase. A number of detergents used over a range of concentrations failed to show significant latent HCO3-ATPase in intact BBM vesicles. Brush border membrane alkaline phosphatase shows similar activation by HCO3 as Mg2+-dependent ATPase activity. Detergent solubilised duodenal BBM HCO3-ATPase therefore appears to be an expression of alkaline phosphatase activity.

**P30**

Site of kinin action in the intestine

G W ARWHURST, M LEES, N HIGGS, and L A TURNBEG (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) Kinins as mediators of the inflammatory response are potent secretagogues and may, therefore, be important in secretory diarrhoea associated with inflammatory diseases. Their mechanism of action involves an increase in the production of prostaglandins. We have examined the cellular site of these actions by studying the influence of kallidin on isolated rat enterocytes and subepithelial tissues. Kallidin increased cyclic AMP concentrations in a dose-dependent manner in whole mucosa (epithelium + subepithelial tissue) (4±1 0±0.52 in control tissues to 9.85±0.81 at 10−5 M and 12±1±0.56 at 10−4 M pm/g protein, n=5). Kallidin did not, however, influence cyclic AMP concentrations in isolated epithelial cells alone. Prostaglandin E2 and forskolin, however, did stimulate cyclic AMP concentrations in whole mucosa and epithelial cells. Kallidin stimulated a 30-fold increase in prostaglandin E2 production in whole mucosa within one minute (0±036±0±02 in control tissues and 1±18±0±12 mg/min after 1×10−6 M kallidin). Prostaglandin release was partially inhibited by the removal of Ca2+ from the bathing medium. Kallidin failed to stimulate prostaglandin E2 production in suspensions of epithelial cells alone. We conclude that kinins raise prostaglandin production by subepithelial tissues and that the prostaglandins then activate epithelial cell adenylate cyclase and cyclic AMP production so leading to ion secretion.

**P31**

Effect of electrical field stimulation on bicarbonate secretion by isolated amphibian duodenum

J R CRAMPTON, L C GIBBONS, and W D W REES (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) Electrical field stimulation (EFS) is a technique used to provoke release of neurotransmitters from endogenous neurones in both gut and exocrine
glands. Using an in vitro chamber preparation, the effect of EFS on bicarbonate secretion by a 2 cm segment of bullfrog (Rana catesbeiana) proximal duodenum has been examined. Repetitive trains of impulses were passed longitudinally through the mucosa by a pair of platinum electrodes in contact with the epithelium. Preliminary experiments established thresholds of pulse wavelength (0.5 ms), voltage (50 V) and frequency (5 Hz) below which no change in secretion occurred. A stimulus of one train per second with train length of 0.5 s containing square waves of 2 ms duration and 100 V amplitude at a frequency of 10 Hz was found to give an increase in the rate of alkali secretion of 50±28% (mean±SE, n=5, p<0.05). With cessation of stimulation secretion returned to basal levels. Repeat stimulation produced a similar response for as long as the tissue remained viable. Addition of the specific neurotrotokin tetrodotoxin (10^{-6} M) reduced the secretory response to EFS by 68±18% (mean±SE, n=5, p<0.05) indicating that the mode of action is primarily related to excitation of endogenous neurones and may be due to release of neurotransmitter. This study shows that EFS is likely to prove a useful method of determining the role of enteric neurones in the control of bicarbonate secretion.

P32

Cisapride inhibits the secretory action of serotonin (5-HT) in mammalian small intestine

K J Moriarty, N B Higgs, M Woodford, G Warhurst, and L A Turnberg (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) Cisapride is a synthetic drug which stimulates gastrointestinal motor activity in animals and man. This effect may be mediated in part by inhibition of serotonin (5-HT). Furthermore, cisapride has been shown to bind in vitro to type 2 serotonin receptors. We examined the influence of cisapride on ion transport across intestinal mucosa in vitro and studied its effect on the action of 5-HT. Segments of ileum of male Sprague-Dawley rats were stripped of muscle layers and mounted in flux chambers. The addition of cisapride (5×10^{-5} M) to the mucosal and serosal aspects of the mucosa had no effect on the short-circuit current, transmural potential difference, resistance or sodium and chloride fluxes across the mucosa. The application of serotonin (10^{-5} M) to the serosal aspect of the mucosa caused a rapid increase in short-circuit current and potential difference. Cisapride, however, inhibited this response in a dose-dependent manner and blocked it completely at a concentration of 5×10^{-5} M. Serotonin (5×10^{-5} M) serosally increased serosal to mucosal fluxes of chloride from 12.6±2.8 to 15.2±2.0 μmol/cm^2/h (p<0.05). This effect was completely blocked by cisapride (5×10^{-5} M). In summary, cisapride inhibits the secretory action of 5-HT in the rat small intestine, possibly by blocking type 2 serotonin receptors.

P33

Is cholera toxin-induced intestinal secretion mediated via a neurogenic mechanism?

K J Moriarty, N B Higgs, M Woodford, and L A Turnberg (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) Cholera toxin is thought to stimulate intestinal secretion by direct activation of mucosal adenylate cyclase. Lundgren and coworkers, however, provide evidence that cholera toxin stimulates secretion in vivo indirectly via enteric nervous reflexes. We examined this hypothesis further by studying the influence of neuronal blockade on cholera toxin-induced changes in fluid transport across rabbit ileum in vitro. Mucosa, stripped of muscle layers, was mounted in flux chambers and crude cholera toxin (1 μg/ml mucosally) caused a delayed but sustained rise in the short-circuit current and electrical potential difference (PD). The nerve blocking drug, tetrodotoxin (10^{-7} M and 5×10^{-6} M serosally), failed to influence the subsequent response to cholera toxin and addition of tetrodotoxin at the peak response to cholera toxin also had no effect. That tetrodotoxin could block neurally-mediated secretagogues was confirmed by the demonstration that the short-circuit current and PD responses to neureotensin (10^{-7} M) were blocked by tetrodotoxin (5×10^{-6} M). Furthermore, the response to cholera toxin of segments of ileum, which included circular and longitudinal muscle layers as well as enteric neurones, was not influenced by tetrodotoxin. An analysis of sodium and chloride flux responses to cholera toxin in the presence and absence of tetrodotoxin suggested that the effects of cholera toxin on ion secretion were not inhibited by neuronal blockade.

We conclude that cholera toxin-induced intestinal secretion in vitro is not mediated via a neurogenic reflex arc.

P34

Electrophysiological recording along the crypt-villus axis of rat ileum in vitro

C P Stewart and L A Turnberg (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) In this study, surface epithelial cells at different sites on the crypt-villus axis were impaled with micro-electrodes under visual control. Using an in vitro preparation of stripped rat ileum at 31°C, the middle and basal third of the villus were punctured, as well as cells at the crypt openings and at a short distance within the crypt. In glucose-free medium, transmural potential difference (V_m) declined with time to<1 mV. The brush-border membrane potential (V_b) was 45.9±4.4 mV (n=7) in mid- and 52.8±2.7 mV (n=25) in base-villus cells, whereas at the crypt opening and within the crypt itself, V_b was 58.2±2.0 mV (n=23) and 59.2±2.8 mV (n=5) respectively. Resistance (R) was 100±11·2 Ω cm^2 (n=10), and fractional resistance (ΔV/ΔV_m) was 0·61±0·05 (n=15), indicating that more than half of R resides in the brush-border membrane. The response to 10 mmol/l D-glucose was assessed during some impalements. Serosal glucose had no effect on the above parameters, but mucosal addition caused a partial depolarisation of V_b in some villus cells but not in crypt openings. ΔV/ΔV_m and R did not change significantly. The results show that it is possible to characterise transporting epithelial cells along the crypt-villus axis in rat small intestine by means of electrophysiological recordings.

P35

Osteoporosis in patients with inflammatory bowel disease

D Judd, W Evans, E O Crawley, C Evans, J Rhodes, and J E Compston (Departments of Gastroenterology, Radiology and Medical Physics, University Hospital of Wales, Heath Park, Cardiff) The prevalence of osteoporosis in patients with inflamma-
tory bowel disease (IBD) has not been accurately established. Using single photon absorptiometry of the radius and vertebral quantitative computerised tomography to measure bone mineral content (BMC) we have determined the prevalence of cortical and trabecular osteoporosis in 58 patients (25 men) with large bowel (n=17) or small bowel (n=14) IBD.

Osteoporosis defined as >2 SD below mean BMC was shown in 13 patients (eight women) with mean age 43 years (range 21–77 years). Four had both cortical and trabecular osteoporosis, six cortical only, and three trabecular only. Of these, two women aged 33 years and 38 years had severe clinical osteoporosis with loss of height and multiple vertebral fractures: three other patients had one or more vertebral fractures. All 13 patients with low BMC had small bowel IBD with previous resections and 10 had received large doses of steroids (>10 g total). Three of the seven premenopausal females with low BMC were amenorrhoeic.

In this group of patients with IBD, cortical and/or trabecular osteoporosis was present in 22%, with severe clinical disease in two young women. Patients with small bowel IBD and previous resections who have received large doses of steroids appear to be mainly at risk. Within this category, premenopausal women with amenorrhoea may develop severe clinical osteoporosis and oestrogen replacement therapy should be considered in such patients.

P36
Effect of codeine and loperamide on carbohydrate malabsorption in postvagotomy diarrhea (PVD)
J D O'Brien, D G Thompson, H Ibbotson, W R Burnham, and E Walker (Departments of Gastroenterology, The London and Oldchurch Hospitals, London) Codeine phosphate (60 mg) is more effective than loperamide (4 mg) in reducing the speed of upper gut transit in normal subjects (Br J Clin Pharmacol 1985; 19: in press). Our aim was to examine the effects of these drugs in patients with diarrhea after truncal vagotomy, a disorder in which symptoms are associated with rapid upper gut transit and nutrient malabsorption.

Orocaecal transit was studied in seven patients and in seven matched controls by exhaled breath hydrogen (H₂) sampling after a 20 g lactulose containing meal. Control transit was 63±3±2.9 min (mean±SEM) vs PVD, 28·1±1·5 min, p<0·01.

The functional absorptive capacity for carbohydrate was then studied using a meal comprising 50 g glucose in 250 ml water. No control showed a breath H₂ rise, indicating complete absorption. In contrast, all patients showed a breath H₂ rise (>20 ppm) with subsequent diarrhoea, indicating incomplete absorption. Repeat studies with barium added to the meal and caecal screening, confirmed that this H₂ rise was due to rapid transit, not bacterial overgrowth. Prior administration of codeine (60 mg) abolished the H₂ rise and diarrhoea in all patients, indicating improved glucose absorption. Loperamide (4 mg) had no effect. After one month codeine therapy, all patients reported symptomatic relief. Codeine thus seems to be a more rational therapy than loperamide for reducing carbohydrate malabsorption in PVD.

P37
Galanin in gut peptide secreting tumours and its diagnostic value in phaeochromocytomas
F E Bauer, G W Hacker, T E Adrian, J M Polak, and S R Bloom (Departments of Medicine and Histochmistry, RPMs, Hammersmith, London) The new intestinal peptide galanin, originally isolated from porcine gut with potent biological actions on smooth muscle contractility and inhibition of insulin secretion, was found in significant quantities in the gastrointestinal tract of different species including man. Therefore, we investigated galanin-IR in gut peptide secreting tumours and phaeochromocytomas with a newly developed radioimmunoassay with both N- and C-terminal directed antibodies and by immunocytochemistry. In none of the pancreatic endocrine tumours was galanin significantly raised compared with normal pancreatic tissue. In phaeochromocytomas, however, the galanin content was significantly higher (tissue: 21±2·3 pmol/g, n=11, ±SEM, plasma: 161±21·5 pmol/l, n=6) than those of normal adrenals (2·6±0·9 pmol/g, n=4) and plasma of volunteers (<50 pmol/l, n=6). Gel chromatography and HPLC of adrenal and phaeochromocytoma extracts revealed two molecular forms compared with one form in the porcine standard. The C-terminal antibody did not detect human galanin suggesting C-terminal molecular differences. Immunocytochemistry localised galanin-IR to cells in phaeochromocytomas. There is no evidence that galanin-IR is produced by peptide secreting gastrointestinal tumours. The raised galanin levels in phaeochromocytomas, however, may be responsible for some symptoms - that is, abdominal pain, constipation and hyperglycaemia. Plasma galanin could be a marker in the diagnosis of these tumours.

P38
Comparison of modular elemental and polymeric liquid diets on growth, nitrogen (N) balance, N wastage, faecal residue and hepatic lipid in rats
R H R Park, D Duncan, G Mitchell, W East, and R I Russell (Gastroenterology Unit, Royal Infirmary, Glasgow) New modular enteral liquid diets offer greater flexibility of nutritional therapy. A controlled metabolic study was carried out to investigate their metabolic and nutritional effects. Vivonex (VHN), enteral 400 (E), elemental 028 (Elepe), pepdite (P), MCT pepdite (MCT), and control rat chow (Oxoid 41B) (O), differing in composition, were fed to six rats (six rats in each group) for 28 days in isocaloric amounts (62 kcal (260 kJ) per rat per day). Mean weight gain (mean±SEM % of initial weight) was less for P (41±3·5) and MCT (40±3·3) than O (59±4·3) (p<0·01), VHN (52±3·3) (p<0·05 and E (68±3·4) (p<0·001). N balance (mmol/24 h) was significantly increased with VHN (26·7±1·37) compared with E (17·4±1·5) (p<0·001), ELE (14·7±0·56) (p<0·001), P (15·5±0·81) (p<0·001) and MCT (16·9±0·99) (p<0·001). No significant differences were observed for mean N wastage (N excretion as % intake). Faecal residue (mg/24 h dry faecal weight) for VHN (203±5) was reduced significantly compared with ELE (304±8) (p<0·001), P (386±22) (p<0·001) and MCT (267±5) (p<0·001). Hepatic lipid (mg/g liver) was increased significantly with the elemental diets VHN and ELE (57±2·4 6 and 56±5·1 respectively) compared with the polymeric diets E (41±4·1·8) (p<0·01) and P (42±7±4·5) (p<0·05). New modular enteral liquid diets do not offer extra nutritional advantages and VHN remains the diet of choice for very low faecal output.

P39
α-1-antitrypsin (AT) and 51-CR-albumin (CRA) in the assessment of faecal protein loss
E M M Quigley, I N Ross, R Haaney, I B Holbrook, and M N Marsh (University Departments of Medicine and Chemical Pathology and Department of Immunology, Hope Hospital, Salford) Although faecal AT has been proposed as a reliable measure of enteric protein loss the accuracy and reproducibility of this method remains uncertain. Our aim was to compare AT excretion with the standard 31Cr-labelled albumin and CrA excretion were compared in: (i) single 24 hour stools from 20 normal subjects, (ii) five day stool collections pooled from each of 35 patients with various GI diseases, and (iii) eight serial 24 hour collections from each of seven patients with small intestinal disease. Faecal CrA was expressed as % injected dose excreted during the collection period. α-1-antitrypsin was measured by single radial immunodiffusion and expressed as: (i) faecal excretion (mg/g dry weight or mg/ml faeces), and (ii) intestinal clearance (ml AT/24 h). Mean values for excretion and 24 hour intestinal clearance of AT in normal subjects were 0.7 mg/g dry weight (range 0.1–6), 0.3 mg/ml faeces (0.03–2.3) and 5.2 ml/24 h (0.4–73.4) respectively. In the GI patients sensitivity and specificity of AT excretion in defining excess protein loss were 44% and 88% respectively, compared with CrA. Measuring AT excretion in serial 24 hour collections did not improve its accuracy indicating that sampling error alone cannot explain the poor sensitivity. We conclude that while excretion of AT is significantly increased in patients with various gastrointestinal diseases, there is considerable overlap with the control range so that correlation with CrA loss is extremely weak ($r^2$: 0.02–0.34). In individual patients AT excretion underestimates true protein loss and is therefore an unreliable test.

P40 How does dietary lipid lower blood alcohol levels?

J M Lj Welch, A M cfarlane, L Pooley, and N W Read (Clinical Research Unit, Royal Hallamshire Hospital, Glossop Road, Sheffield) To determine the mechanism, whereby food lowers blood alcohol levels, gastric emptying and blood alcohol profiles were measured in six healthy male volunteers after ingestion of a 200 ml solution of vodka and orange juice containing 0.5 g/kg alcohol. Subjects were studied on two separate occasions during infusion of isosmotic solutions of either intralipid or saline into the ileum. Gastric emptying was significantly delayed by ileal infusion of intralipid ($t_1/2$: 149±17 vs 46±6 min, p<0.005) and the peak blood alcohol levels were significantly depressed (24±4 vs 37±3 mg/100 ml, p<0.01). Similar effects were observed in three subjects when the solutions were infused into the duodenum ($t_1/2$: 126±28 vs 34±6 min) (peak alcohol 19±4 vs 36±3 mg/100 ml). The results suggest that the reduction in alcohol absorption by lipid in food does not depend on the physical relationship between the alcohol and lipid or between the lipid and absorbing epithelium, but is probably caused by a delay in the delivery of alcohol to the upper small intestine where it is rapidly absorbed.

P41 IgG subclass antibodies to wheat gliadin in patients with coeliac disease

P J Ciclitira, H J Ellis, and M J Kemeny (Gastrointestinal Unit, Department of Medicine, The Rayne Institute, St Thomas’ Hospital, and Department of Medicine, Guy’s Hospital, London) Circulating antibodies to dietary antigens including wheat gliadin are present in coeliac patients. Untreated coeliac jejunal mucosa secretes more IgG, M and A antibodies to gliadin than casein. IgG can be divided into four subclasses of which IgG1 and 3 can bind and therefore activate complement while IgG2 can to a lesser extent and IgG4 cannot.

Titres of circulating IgG1, 2, 3 and 4 subclass antibodies to gliadin and casein, a dietary control protein, were measured by ELISA in normal subjects (n=12), treated (n=12) and untreated coeliac patients (n=12). Untreated coeliac patients had greater IgG1 titres to gliadin and casein (p<0.01) than controls with results from the treated patients falling in between. IgG2, 3 and 4 antibodies to gliadin and casein could only be detected in a minority of subjects; the results for these subclasses were not significantly different for the three subject groups.

The majority of circulating IgG1 gliadin and casein antibody in untreated coeliac patients is IgG1. This suggests that circulating complement fixing gliadin antibodies are not involved in the disease mechanism but does not exclude a pathogenetic role for locally produced specific antibody. The presence of raised circulating IgG1 antibodies to both gliadin and casein in untreated coeliac patients implies that these antibodies are because of dietary antigen absorption.

P42 Postprandial gut hormone profile after intestinal glycosidase inhibition

R H Taylor, H M Barker, E A Bowey, J E Canfield, and K D Buchanan (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London, and Department of Metabolic Medicine, Queen’s University, Belfast) Postprandial gut hormone profile is determined by meal composition, volume and other factors. The purpose of this study was to measure changes in this response to a standard meal given with intestinal glycosidase inhibitors.

Six healthy subjects took a standard test breakfast three times with either placebo, BAY m1099 50 mg or BAY 01248 20 mg in random order. These are potent, reversible glycosidase inhibitors of different substrate specificity. Blood samples were taken for 3 hours for measurement of glucose, insulin, GIP, N-terminal glucagon-like immunoreactivity (N-GLI), C-GLI and gastrin. Breath hydrogen was measured as an indirect index of carbohydrate malabsorption compared with lactulose 25 g alone.

Both inhibitors reduced the postprandial glucose peak (placebo 7.2±0.5 mmol/l; m1099 5.3±1.0 mmol/l, p<0.01; o1248 5.9±0.2 mmol/l, p<0.05) and the serum insulin peak (placebo 89±13 mU/l; m1099 39±3 mU/l, p<0.01; o1248 37±3 mU/l, p<0.01). Insulin release was reduced significantly from 30–120 min (p<0.05). GIP release was reduced significantly between 30 and 150 min and peaks fell from 995±395 ng/l to 260±50 (m1099) and 305±60 (o1248). N-GLI rose from 60 min (m1099) and 90 min (o1248) to 134±7 ng/l (placebo, 222±31 (m1099, p<0.05) and 190±19 (o1248, p<0.05) at 180 min. Gastrin levels rose in all groups and C-GLI did not change.

Breath hydrogen indicated carbohydrate malabsorption of 10±4 g (m1099) and 21±9 g (o1248).

We conclude that glycosidase inhibition slows digestion, reducing insulin and GIP release, but unabsorbed nutrients stimulate N-GLI distally. Slow absorption does not affect gastrin or C-GLI release. These experimental changes simulate those found in digestive impairment due to enzymic or mucosal abnormality.

P43 Regulation of ileal Na⁺-dependent bile acid transport in man
Tilburg, regulation of ileal transport (INBAT) in colono- 
sopy, from which brush border membrane vesicles (BBMV) were prepared. INBAT was measured in vitro as the uptake of H- 
taurocholate (4 μM) into BBMV in the presence of a 100 mM NaCl gradient. Uptake was followed during one minute. INBAT was quantified in pmoles taurocholate/20 sec/mg membrane protein.

Patients were placed in 10 diagnostic categories. Mean INBAT values in six categories did not differ significantly, three categories had a significantly decreased INBAT, ileal disease (n=11, 19±4-7±4), ileal resection (n=5, 17±4-9±4), and constipation (n=8, 37±2±6±0). Inincreased INBAT was found in patients (n=8) with bile acid losing diarrhoea with an endoscopically and histologically normal ileum (12±5±17±3).

Our results show that in patients with increased faecal bile acid loss (FBAL) INBAT is high, while in constipated patients, presumed to have a low FBAL, INBAT is low. This suggests that INBAT is regulated by the availability of bile acids to the ileal enterocytes.

P44 Improvement of abnormal lactulose/ram- 
noise permeability in active Crohn’s disease of the small bowel by an elemental diet

I R Sanderson, P Boulton, J Menzies, and J A Walker-Smith (Department of Child Health, St Bartholomew’s Hospital, Institute of Child Health, St Thomas’ Hospital, London) Elemental diet is as effective as steroids in the induction of remission of small bowel Crohn’s disease in children, as judged by disease activity, ESR, CRP and albumin. Intestinal sugar permeability is an objective marker of small bowel function which can assess the efficacy of elemental diet during treatment. Fourteen children aged 11–17 years with active small bowel disease (proven by radiology and ileal histology) were given an elemental diet for six weeks. All had the following sugar permeability study undertaken before and after treatment. An 80 ml solution containing 5-25 g lactulose (L) and 0-75 g rham- 
noise (R) was ingested after an overnight fast. L/R ratio was calculated from the percentage recovery of each of the sugars in a 5 hour urine collection. Seven children with no disease of the small intestine acted as controls. They had L/R ratios below 0.08, the upper limits of normal found by Beach et al. All 14 children with Crohn’s disease had an abnormally raised permeability ratio (0.25±0.037) before treatment which fell significantly (p<0.001, paired Student’s t test) after elemental diet (0.93±0.012). This coincided with marked clinical improvement assessment by disease activity index. An elemental diet produces marked reduction in the severity of small bowel Crohn’s disease as measured objectively by sugar permeability.

P45 Does glycine content affect the efficacy of amino acid solutions in TPN?

R G Rees, G K Grindle, P Frost, F Al-Ubaidi, and D B A Silk (Departments of Gastroenterology and Nutrition and Chemical Pathology, Royal Middlesex Hospital, London) Despite the fact that the value of glycine as a source of nitrogen for protein synthesis is disputed, it often represents a significant proportion of non-essential amino acid solutions for TPN. If glycine N is not retained, but channeled to urea, lower levels of N balance and plasma proteins might be expected when glycine-rich solutions are used.

We have prospectively compared two solutions of differing glycine content in a heterogeneous group of seven patients (24–63 years) who required TPN. All were metabolically stable without significant organ failure and received two consecutive five-day feeding regimens in random order. Amino acids were supplied as Vamin N or ‘old’ formula Synthamin providing 14-1 g and 14-3 g N with 2-7% and 25% respectively, contributed by glycine. The regimes were isocaloric and provided 2200 Kcal/day from a 45%/55% energy lipid/glucose mixture.

Twenty four hour total urinary N and urea and serum urea were measured daily. Plasma albumin, prealbumin and transferrin were measured on day five of each regime.

There were no differences between matched pairs for any parameter. Values for Vamin and Synthamin (mean±SEM) were N balance (cumulative) −4±0.9 vs −14±8±13 g; urinary urea N total N 80±2% vs 82±2%; alb 26±2 vs 26±2 g/l; prealbumin 122±17 vs 107±19 mg/l; transferrin 2.2±0.1 vs 2.1±0.2 g/l; BUN 12±2±1.6 vs 14±6±2.8 mmol/l.

We conclude, from these data, that there is no nutritional disadvantage for parenterally fed patients when significant amounts (up to 23%) of total amino acid N is provided as glycine.

P46 Intestinal absorption and laxative threshold of lactitol – a new hydrogenated derivative of lactose

D H Patil, G K Grindle, and D B A Silk (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Lactitol is a high soluble disaccharide with excellent taste properties. As animal studies suggest that it is poorly absorbed, it has potential as a bulk sweetener of a low caloric value in the food industry. This potential has been investigated by characterising its assimilation by the human small intestine and by determining its laxative threshold.

In vivo jejunal perfusion experiments were carried out in normal human subjects (n=6). Intestinal uptake from isotonic solutions containing 10, 30, 60 and 100 mmol lactitol/l was not significantly different from zero.

To determine laxative thresholds, 21 healthy volunteers entered a single blind randomised cross over trial. Taking, in divided doses, increasing amounts (10 g/day) of lactitol, sorbitol or placebo. The laxative thresholds of lactitol (74±7±SEM 6-3 g/day) and sorbitol (71±9±4-9) were similar and the incidence of gastrointestinal side effects were not significantly different on similar doses of sorbitol and lactitol. We conclude that as lactitol is not absorbed in the small intestine and has a laxative threshold of >40 g/day, its potential as a low calorie bulk sweetener in the food industry is confirmed. At high doses (>70 g/day) Lactitol could find an important place as an osmotic cathartic agent.

P47 Low phytate wheat bran inhibits zinc absorption less than standard bran

M J Hall, D Ene, D Farah, and I Downs (University Department of Medicine, Bristol Royal Infirmary, Bristol) Binding of zinc in the intestine by the phytate and/or fibre content of cereal products can lead to zinc deficiency which has been increasingly
reported in gastrointestinal disorders. We have compared the effect of a new wheat bran, Testa Triticum Tricium, containing 80% fibre but low in phytate, with phytate-rich bran on zinc absorption in healthy fasting volunteers.

Twenty subjects in two equal groups each took zinc sulphate 220 mg. Plasma zinc was measured beforehand and up to six hours afterwards by atomic absorption spectrophotometry. The experiment was repeated with group 1 taking, in addition, 17 g standard wheat bran and group 2 a similar quantity of low phytate bran. A control group of six subjects took Rice Krispies instead of bran.

Zinc absorption expressed as area under the plasma zinc time curve (AUC) fell from (mean±SEM) 99·6±8·8 to -4·6±2·1 (p<0·001) after standard bran, from 74·6±7·4 to 18·5±4·2 (p<0·001) after low-phytate bran and from 105·9±10·7 to 47·3±10·1 (p<0·05) after Rice Krispies. Mean percentage reduction in AUC after standard wheat bran was significantly higher than after low-phytate bran (104·9±1·9 vs 75·9±4·8, p<0·001).

We conclude that wheat bran is a potent inhibitor of zinc absorption which can be improved by reduction of the phytate content.

P48
Effect of somatostatin analogue SMS 201–995 on fluid and electrolyte transport in a patient with secretory diarrhoea

C A EDWARDS, P A CANN, N W READ, AND C D HOLDSWORTH (Gastrointestinal Unit, Royal Hallamshire Hospital, Sheffield) SMS 201–995, a long acting analogue of somatostatin can be administered subcutaneously and has been shown to be of benefit in the treatment of diarrhoea secondary to tumours secreting vasoactive intestinal polypeptide (VIP). We used steady state perfusion techniques to investigate its effect on fluid and electrolyte transport in the jejunum and ileum of a patient with a VIPoma. Fifty micrograms of the analogue was given subcutaneously following a 60 minute control period and measurements repeated after a 40 minutes equilibration. In the jejunum, endogenous flow was abolished (110±4–0 ml/h), net fluid absorption increased (4·2±7·3 g/l/25 cm/h), sodium secretion reversed (1·2–1·0±11.0 mmol/25 cm/h), potassium absorption increased (0·14–0·49 mmol/25 cm/h) and chloride absorption increased (0·5–6·56 mmol/25 cm/h). Ileum: endogenous flow (488·4–283·8 g/l/25 cm/h), net fluid absorption (24–5–86·3 g/l/25 cm/h), sodium (1·6–12·2 mmol/l), potassium (0·1–0·3) and chloride (3·3–19·3 g/l/25 cm/h). Plasma VIP fell from 168 pmol/l (control) to 99 pmol/l (end of test period). Clinically the patient was able to return to a normal diet and leave hospital on a regime of 50 µg tds. He maintained a stool output of less than 1 litre daily during treatment, enabling him to live normally until the eventual resection of the tumour four months later.

P49
Intestinal transit times and stool output during intake of a hypocholesterolaemic dose of guar in man

PENAGINI, P VELIO, AND P A BIANCHI (INTRODUCED BY J M MISIEWICZ) (Cattedra di Patologia Medica III, Istituto di Clinica Medica I, University of Milan, Italy) Guar gum is generally believed to prolong mouth-to-caecum transit time (MTT) and this has been suggested to play a role in its metabolic effects. Previous studies of MTT used liquid meals and large doses of guar. Whole gut transit time (WGTT) and stool output were reported to be unaffected by guar, but data are scanty.

Six healthy male volunteers, aged 21–28 years, ate a controlled diet (2721 Kcal and 22 g dietary fibre daily) for two periods of two weeks (CD1 and 2) with a two-week interval on an unrestricted diet; during CD2 guar gum 5·7 g bd was given daily in a solution of guar gum. Daily stool weight and WGTT (measured with radio-opaque markers given on three consecutive days) were determined in the second week of CD1 and CD2 and total serum cholesterol at the beginning and the end of each CD period. After both CD periods, MCTT of a solid test meal (554 Kcal) was measured using the hydrogen breath test; guar gum 5·7 g in a solution of guar gum was added to the second test meal. Results were analysed using the paired Wilcoxon’s test and expressed as mean±SD. Serum cholesterol changes were -5·5 mg/dl and -30±17·6 (p=0·05) in CD1 and CD2 respectively. MCTT (276·7 min±112·7 vs 266·7±128), WGTT (46·2 h±8·5 vs 53·8±17·6) and daily stool output (67·9±15·4 vs 76·2±35·2) showed no significant variations.

We conclude that guar exerts its hypocholesterolaemic effect without any significant change in MCTT and does not affect WGTT and stool output in healthy humans.

P50
Bile salt uptake by Giardia lamblia: possible role in fat malabsorption

C E W HALLIDAY, P M G INGE, J WEBB, AND M J G FARTHING (Department of Gastroenterology, St Bartholomew’s Hospital, London) Our preliminary observations indicate that Giardia lamblia (GL) trophozoites can take up bile salts (BS) in vitro. Although the biological implications for the parasite are as yet unknown, we have attempted to characterise this uptake process and estimate its potential impact on intraluminal BS concentration and on BS flow. Giardia lamblia trophozoites were cultivated axenically and BS uptake was investigated with respect to time (0–4 h), temperature (4 and 37°C), trophozoite fixation (1% glutaraldehyde), parasite growth phase (active or stationary) and BS concentration (glycocholic (GC) acid, 0–10 mmol/l). Glycocholic uptake was determined using [14C]-GC and expressed per unit number of organisms. Glycocholic uptake plateaued at one hour, was inhibited ~50% at 4°C and almost completely abolished by glutaraldehyde fixation. Uptake was greater during stationary growth phase (50·6 mmol/mg/108 trophs/h) than during active multiplication (2 mmol/mg/108 trophs/h). Uptake was concentration dependent and appeared to follow saturation kinetics (Km = 0·45 mmol/l; Vmax = 0·55 mmol/min/108 trophs) compatible with an active transport process. This Km for GC is similar to published data for intact human and rat ileum. Infection with 1012 organisms would result in the consumption of 1 mmol GC per day which represents ~20% of the normal adult BS pool. Chronic infection may lead to reduction of intraluminal BS concentration which might contribute to fat malabsorption in giardiasis.

P51
Trypsin-sensitive surface ligand mediates attachment of Giardia lamblia (GL) to rat enterocytes

P M G INGE, A D PHILLIPS, AND M J G FARTHING (Department of Gastroenterology, St Bartholomew’s Hospital, London) We have shown previously with an erythrocyte model of attachment that GL has surface lectin-like activity which may be important in mediating parasite-enterocyte interaction. We have now further characterised this ligand and its intestinal receptor using
isolated rat enterocytes. Cultivated GL trophozoites and citrate-EDTA eluted rat enterocytes (>10⁵ cells of each) were incubated 1:1 in microplates and parasite attachment was quantified by phase microscopy. Attachment was maximal after one hour at 37°C, was markedly inhibited at 4°C but remained unaltered in the absence of divalent cations. Relatively high concentrations of D-mannose (0.1 M) and the mannose-rich glycoprotein mannan (10 mg/ml) inhibited attachment by 49±10% and 48±10% respectively, whereas other sugars were without effect. Subagglutinating concentration (1:256) of heat inactivated, non-cytotoxic rabbit polyclonal anti-giardia antiserum with surface specificity also inhibited GL attachment (42±9% inhibition), confirming the importance of surface determinants for attachment. Trypsin pretreatment (1 mg/ml, 30 min) of GL significantly reduced attachment (10-6±1.8%) trophozoites attached vs 19-4±1.8% control, p<0.001, although viability was unchanged. However, short term (4 h) recultivation of trypsin-treated GL normalised their ability to attach to enterocytes. We conclude that attachment of GL to rat enterocytes is mediated by a trypsin sensitive, lectin-like surface ligand whose intestinal receptor may include D-mannosyl residues.

Mean [H+] was 36-1±7-9 mmol/l on Pla, 16-7±8-6 on Pir 100 mg (<54%, p<0.01) and 16-6±6-0 on Pir 150 mg nocte (<53%, p<0.01). Acid output was reduced by 10% by both doses (p<0.001), Volume was reduced by 47% and 52% by Pir 100 and 150 mg respectively. Pepsin output was not altered. AUC was 251-9±5-7 mmol H⁺ h/l on Pla, 115-8±5-9 on Pir 100 mg (<54%, p<0.05) and 110-7±3-8 on Pir 150 mg (<56%, p<0.05). Side effects of dry mouth occurred only with Pir 150 mg.

Pirenzepine given as a single night time dose significantly reduced nocturnal acid secretion. There was no significant difference between the doses studied. As side effects were frequent with Pir 150 mg, the optimal night time dose is 100 mg. This dose should be evaluated in a controlled clinical trial.

**P52 Effects of single nocturnal doses of pirenzepine on overnight gastric secretion**

C W HOWDEN, D W BURG, C CILLETI, M DICKER, AND R R HUNT (Department of Gastroenterology, McMaster University, Hamilton, Ontario, Canada) Treatment of DU has focused on single nocturnal dosing with H₂ antagonists but pirenzepine (Pir) has not previously been evaluated in this manner.

In a double-blind randomised study, six healthy men were given a three day course of placebo (Pla), Pir 100 mg nocte and Pir 150 mg nocte. On day three, nocturnal hydrogen ion activity [H⁺], and acid output (AO) were measured. Inhibition by Pir was assessed by percentage reduction of mean [H⁺], and the area under the H⁺ activity/time curve (AUC) (linear trapezoidal rule).

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**P54 Are there immunological forms of duodenal ulcer (DU) as a consequence of gastric parietal cell stimulating antibodies (PCSA-Ab)?**

F DE LAZZARI, R MIRKIAN, C VANTURI, M BORTOLAMI, R NACARRATO, D DONIAJ, AND G F BOTTAZZO (Gastroenterology Department, Padova University, Italy, Immunology Department, Middlesex Hospital Medical School, London) Previous reports indicated that IgG obtained from some patients with DU stimulate acid secretion when injected into rats by an action on the histamine receptors (H₂-R) on gastric parietal cells (PC). We investigated this stimulatory activity directly by measuring cAMP responses in PC enriched cultures from guinea pig gastric mucosa. Ammonium sulphate precipitated Ig's from 30 DU patients and 20 healthy controls have been studied. The DU cases were selected on the basis of pentagastrin-stimulated (MAO) hyperacidity or high serum pepsinogen-I levels, and response to treatment (cimetidine or ranitidine). The PC suspensions were obtained by step collagenase digestion (0.5 mg/ml, Worthington type IV) of selective body mucosa to avoid contamination with antral endocline cells. After several washes and centrifugations, the enriched PCR preparations (45-55%) were cultured overnight to allow their full recovery and incubated for four hours with 2 and 4 mg/ml of Ig with added 2 mM 3-isobuthyl-1-methyl-xantine (IBMX). cAMP was measured by RIA (Amersham kits). Control cultures contained IBMX only, positive, negative and controls Ig were included in every batch of tests and all samples were tested in duplicate. 10⁻³ M histamine produced maximum cAMP stimulation at 30 min. Pentagastin and G1-17 had no effect. Igs from 15 of the 30 DU cases produced a significant dose related increase in total cAMP indicating the presence of PC stimulating antibodies (PCSA-Ab) similar to the well known thyroid stimulating antibodies of Graves' disease (TS-Ab). 8/13 stimulating-antibody-positive DU patients were non responders to anti-H₂-R drugs as compared with 3/17 of the negative cases. Pepsinogen-I serum levels were over 100 nmol/ml in 10/13 positive cases and in 6/17 of negative cases. These results suggest that some patients, particularly those resistant to cimetidine.
hypersecretors, duodenal ulcer disease may result from an autoimmune stimulatory receptor antibody, acting selectively on the histamine-2-receptor.

P55 Peptic ulcer in Bangladesh – an endoscopic survey

M HASSAN, SHAH MD K ALI AND A K AZAD KHAN (Department of Gastroenterology, Institute of Postgraduate Medicine and Research, and Department of Epidemiology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders, Dhaka) A survey on peptic ulcer was carried out in a rural community in Bangladesh. All subjects of 15 years or above (n=2675) were surveyed by a questionnaire and those with ulcer dyspepsia (n=1106) were selected on the basis of predetermined criteria. A random sample (n=313) of these subjects were chosen for endoscopy and 283 of them (89.5%) have been endoscoped.

Duodenal ulcer was found in 48, duodenal erosions in nine, deformed bulb in 23 and gastroenterostomy in two subjects. The prevalence of duodenal ulcer disease was 11.9%. Gastric ulcer was found in 24 (prepyloric 14, antral eight, body two) subjects, the prevalence rate being 3.5%. Both duodenal ulcer and gastric ulcer subjects were predominantly males. No case of carcinoma of the upper GI tract was detected.

Duodenal ulcer is common but gastric ulcer is uncommon in this population. Reasons for the high prevalence of duodenal ulcer remain unknown. Those with and without ulcer have been identified in a defined population and further studies on genetic and environmental factors can now be undertaken.

P56 Pathogenic role of campylobacter-like organisms in duodenal ulcer

W M HUI, S K LAM, P Y CHAU, J HO, M T NG, C L LAI, AND A LOK (Departments of Medicine, Pathology and Microbiology, University of Hong Kong, Queen Mary Hospital, Hong Kong) Campylobacter-like organisms have been associated with antral gastritis and duodenal ulcer. To study the pathogenic role of these organisms in duodenal ulcer, endoscopic biopsies, two from the first part of duodenum, four from antrum, and four from body and fundus were taken in random order before and after four weeks of cimetidine treatment (1.2 g/day) from 49 patients with active duodenal ulcer that healed at the end of the treatment period. The biopsies were examined for the presence and severity of any inflammation histologically, and for campylobacter-like organisms by smear and culture. Before treatment, inflammation was present in 71%, 98%, and 25%, while the organisms were present in 37%, 89%, and 82% of the duodenal, antral and fundal biopsies respectively. With complete healing of duodenal ulcer, inflammation was present in 64%, 100%, and 27%, while the organisms were positive in 39%, 83%, and 81% of the respective mucosae. With ulcer healing, duodenitis and antral gastritis became milder and significantly so for antral gastritis. These findings indicate that healing of duodenal ulcer is not influenced by the presence of campylobacter-like organisms, which are frequently found in the gastroduodenal mucosa of patients with duodenal ulcer, but do not appear to be associated with mucosal inflammation except in the antrum.

P57 Neutral micro-climate lines human gastro-duodenal mucosa in vivo

E M M QUIGLEY AND I A TURBERG (Department of Medicine, Hope Hospital (University of Manchester School of Medicine, Eccles Old Road, Salford) Gastro-duodenal mucosa may protect itself by maintaining a neutral zone in the mucous layer. The demonstration of a neutral pH on the mucosa in vitro and in vivo in animals lends credence to this hypothesis and we now present evidence for a similar phenomenon in vivo in man. In 21 normal subjects (aged 22–86 years) pH was measured using a flexible pH electrode (OD 1.35 mm) passed through the biopsy channel of an endoscope. At six sites (lower oesophagus, fundus, body, antrum, duodenal cap and loop) pH was recorded with the electrode (a) in the lumen and (b) touching the mucosa. In nine subjects duodenal recordings were repeated during luminal acidification. In five subjects electrical potential difference (PD) readings were taken at the same sites. Lumen (L) to mucosal (M) pH gradients were identified in oesophagus (L 3.29±0.32 vs M 4.18±0.25; p<0.006), gastric fundus (L 2.01±0.17 vs M 4.84±0.7; p<0.003), body (L 1.82±0.12 vs M 5.0±0.15; p<0.001) and antrum (L 3.5±0.34 vs M 5.42±0.29; p<0.004). In duodenum, luminal and mucosal pH were near neutral but on luminal acidification a gradient was detected in both cap (L 2.57±0.15 vs M 6.7±0.13; p<0.005) and loop (L 2.44±0.14 vs M 6.39±0.20; p<0.001). Potential difference (mV) in the lumen and at the mucosa were similar in oesophagus (L −15.3± M −15.4), body (L −23.3± M −24.4), antrum (L −19.5± M −22.6) and duodenum (L −5.2± M −5.2). We conclude that lumen-to-mucosal pH gradient is present in the human upper gut and supports the importance of surface factors in mucosal protection.

P58 Luminal and mucosal pH in patients with duodenal ulcer, reflux oesophagitis and antral gastritis

E M M QUIGLEY AND L A TURBERG (Department of Medicine, Hope Hospital (University of Manchester School of Medicine, Salford) We sought evidence for a defect in the ‘mucus-bicarbonate’ barrier in upper GI diseases by recording juxtamucosal pH with a flexible pH electrode (ED 1.35 mm) passed through the biopsy channel of a standard endoscope. Luminal and mucosal pH were measured in lower oesophagus, fundus, body, antrum, duodenal cap and loop and repeated in duodenum and oesophagus during intra-ulceration to maintain a neutral zone in the mucous layer. The demonstration of a neutral pH on the mucosa in vitro and in vivo in animals lends credence to this hypothesis and we now present evidence for a similar phenomenon in vivo in man. In 21 normal subjects (aged 22–86 years) pH was measured using a flexible pH electrode (OD 1.35 mm) passed through the biopsy channel of an endoscope. At six sites (lower oesophagus, fundus, body, antrum, duodenal cap and loop) pH was recorded with the electrode (a) in the lumen and (b) touching the mucosa. In nine subjects duodenal recordings were repeated during luminal acidification. In five subjects electrical potential difference (PD) readings were taken at the same sites. Lumen (L) to mucosal (M) pH gradients were identified in oesophagus (L 3.29±0.32 vs M 4.18±0.25; p<0.006), gastric fundus (L 2.01±0.17 vs M 4.84±0.7; p<0.003), body (L 1.82±0.12 vs M 5.0±0.15; p<0.001) and antrum (L 3.5±0.34 vs M 5.42±0.29; p<0.004). In duodenum, luminal and mucosal pH were near neutral but on luminal acidification a gradient was detected in both cap (L 2.57±0.15 vs M 6.7±0.13; p<0.005) and loop (L 2.44±0.14 vs M 6.39±0.20; p<0.001). Potential difference (mV) in the lumen and at the mucosa were similar in oesophagus (L −15.3± M −15.4), body (L −23.3± M −24.4), antrum (L −19.5± M −22.6) and duodenum (L −5.2± M −5.2). We conclude that lumen-to-mucosal pH gradient is present in the human upper gut and supports the importance of surface factors in mucosal protection.
rality could be identified in patients with reflux oesophagitis or antral gastritis.

P59 Isolated pyloric contractions (IPCs) in fasted and fed human subjects

N W Read, L A Houghton, R Heddle, G J Maddern, J Dent, J Downton, J B Wyman, and T Touli (Departments of Medicine and Surgery, Flinders Medical Centre, and Royal Adelaide Hospital, Adelaide, Australia) It is controversial whether phasic pyloric contractions occur in humans independently from antral and duodenal contractions. We have recorded pyloric pressures in nine healthy subjects with a 4.5-cm-long small sensor, positioned by measurements of transmucosal potential difference. Pressures were also measured with perfused side holes at four sites in the duodenum and three sites in the antrum.

Under fasting conditions five subjects exhibited sequences of between 18 and 89 regular pyloric contractions (frequency, 2.9 to 3.3 min) which were not associated with contraction in the antrum or duodenum 1 cm from either end of the sleeve. IPCs occurred immediately before the onset of phase III of the MMC in four subjects and within 15 minutes of the end of phase III in four subjects.

Ingestion of 300 ml chocolate milk elicited IPCs in all subjects (19 to 153 contractions occurring between 2.5 and 2.9 min) postprandial in subjects 25±8% (SEM) of recording time compared with 7±4% during fasting. Postprandial IPCs were also more likely to be interspersed with episodic peristaltic waves which swept from the antrum into and along the duodenum. Isolated pyloric contractions may play a role in the control of transpyloric flow, especially in the fed state.

P60 New evidence for the pathophysiology of postvagotomy diarrhea

S A Raimes, V Smirniotis, E J Wheldon, C W Venables, and I D A Johnston (University Department of Surgery, Newcastle upon Tyne) Diarrhea is more common after truncal vagotomy than after other gastric operations, but there is no satisfactory explanation for this. The hypertonic glucose ‘dumping provocation test’ reproduces diarrhea in those patients for whom this is an important complaint. We have investigated the malabsorption of glucose during this test by measuring changes in breath hydrogen. Four groups of unselected male subjects were studied – 42 after truncal vagotomy and pyloroplasty (TV+P), 14 after proximal gastric vagotomy (PGV), 12 after Bilroth I gastrectomy (BG) and 10 healthy controls. Glucose malabsorption was significantly more common in the TV+P group (39/42 vs PGV: 5/14; p<0.001, vs BG: 4/12; p<0.001 and vs controls: 0.10; p<0.001; Fisher exact test). Small bowel colonisation by hydrogen producing bacteria was excluded by repeating tests with lactulose. Twenty patients experienced diarrhea during the test, all but one in the TV+P group. In the TV+P group those patients with diarrhea had a greater fall in plasma volume (median 13% vs 8%; p=0.001; Mann-Whitney Test) and a shorter mouth-caecum transit time (median 15 minutes vs 20 minutes; p<0.048; Mann-Whitney Test).

We conclude that patients after TV+P do not fully absorb a hypertonic glucose load. This is abnormal and helps to explain the pathophysiology of postvagotomy diarrhea.

P61 Emergency peptic ulcer surgery – an association with NSAIDs

A J Walker and E P Dewar (Professorial Surgical Unit, RN Hospital, Haslar, Gosport, Hants) The elderly have a disproportionately high mortality from complications of peptic ulceration. They may have more concomitant diseases, be treated less aggressively or be prescribed more ulcerogenic drugs, particularly NSAIDs.

For three years all patients admitted with an episode of upper GI tract haemorrhage or perforation of a PU who required emergency surgery were studied.

Sixty patients were admitted with 64 ulcers. Thirty two (25 DU, seven GU) operations for haemorrhage and 32 (17 DU, 15 GU) for perforation were performed.

Fifty per cent of the patients were taking NSAIDs, the incidence in women double than in men. Sixty seven per cent were over 60 years old, women significantly older than men.

Perforation in association with NSAIDs in the over 60s was double that in the under 60s.

In an aggressive surgical policy the mortality from haemorrhage was 3-4% and from perforation 9-7%. Contrary to surgical tradition only four partial gastrectomies were performed. Of three deaths from perforation, all were over 60 and all taking NSAIDs.

P62 Does cimetidine alter the prognosis after perforated duodenal ulcer?

C J Simpson, G Lamont, J McDonald, and I S Smith (Victoria Infirmary, Glasgow) Sixty consecutive patients with perforation of a duodenal ulcer undergoing emergency simple closure were randomised to receive full dose cimetidine for eight weeks, followed by maintenance of 400 mg nocte for a further 18 weeks, or, not to receive any anti-ulcer therapy. Follow up on all patients took place at one month, two months, six months and 12 months and endoscopy was undertaken on symptomatic patients. Both groups were comparable in age, pre and postoperative smoking habits, prior treatment with ulcer healing agents, dyspeptic history and duration of perforation before surgery. Although cimetidine did not affect immediate recovery, there being three (10%) deaths in the cimetidine group and five (16%) in the control group, the cimetidine group did enjoy a significant benefit (p<0.001) in the long term. Eleven (45%) patients in the control group developed recurrent ulcer symptoms, three requiring emergency surgery for bleeding or reperforation and eight requiring medical treatment. The cimetidine group remained symptom free for 12 months.

P63 Effect of glucomannan on postprandial reactive hypoglycaemia after gastric surgery

W P M Hopman, G M P Houben, P A J Speth, and C B H W Lamers (Departments of Gastroenterology-Hepatology, Universities of Nijmegen and Leiden, The Netherlands) Presently no satisfactory treatment is available to patients who suffer from postprandial reactive hypoglycaemia after gastric surgery. A-glucoside hydrolysing inhibitors (acarbose) are poorly tolerated because of side effects due to carbohydrate malabsorption, while pectin is unpalatable.
and effective only when ingested in very large doses. Glucomannan, a polysaccharide consisting of glucose and mannose, is tasteless and has strong gel-forming properties. In a double-blind study of eight patients (21–61 years) with reactive hyperglycaemia after gastric surgery we have compared the effect of 5-2 g glucomannan, 2-6 g glucomannan and 2-6 g placebo, and 5-2 g placebo added to a normal carbohydrate-rich breakfast on plasma glucose, plasma insulin and breath hydrogen excretion. Glucomannan had no significant effect on the peak glucose increment (4-4±0-6 mmol/l with placebo, 4-2±0-5 mmol/l with 2-6 g and 3-9±0-5 mmol/l with 5-2 g of the fibre). On the other hand, glucomannan induced a dose dependent significant (p<0-05) inhibition of the postprandial decrease in plasma glucose (2-2±0-3 mmol/l during placebo, 1-5±0-2 mmol/l during 2-6 g and 0-7±0-9 mmol/l during 5-2 g of the substance) and of the peak insulin increments (154±19 mmU/l during placebo, 80±16 μU/l during 2-6 g and 75±21 μU/l during 5-2 g of glucomannan). Six of the patients had a breath hydrogen excretion of more than 15 ppm during placebo, three after 2-6 g and one after 5-2 glucomannan.

We conclude that glucomannan is highly effective in preventing postprandial reactive hyperglycaemia in patients with previous gastric surgery.

P64
RP 40749 in the treatment of duodenal ulcer and its influence on serum gastrin, serum pepsinogen I and gastrin content of the antral mucosa

G F NELIS, C B H W LAMERS, AND G PALS (INTRODUCED BY J J MISIEWICZ) Sophia Ziekenhuis, Zwolle, Radboud Ziekenhuis, Nijmegen, and Institute of Human Genetics, Free University (Amsterdam). We evaluated the effectiveness of two doses of a new H+-K+ ATPase antagonist (RP 40749, pyridyl-2-tetrahydrothiophene) in the treatment of 20 patients with duodenal ulcer. Treatment was prescribed double-blind either as 100 mg or 200 mg as a single daily dose for four weeks. Blood samples and gastric biopsies were taken immediately before treatment and at the last day of treatment. There was a rapid clinical improvement and after four weeks all ulcers were healed endoscopically, except for one in the 100 mg group. Side effects did not occur, there were no changes in the routine laboratory parameters and gastric histology.

We evaluated the influence of RP 40749 on basal and meal-stimulated serum gastrin and serum pepsinogen I and the gastrin content of the antral mucosa. After treatment there was a significant rise in basal serum gastrin (55-6 vs 83-8) and pepsinogen I (59-0 vs 136-7), meal-stimulated serum gastrin (96-0 vs 144-4) and antral gastrin (17-2 vs 27-1). There were no major differences between the 100 and 200 mg group.

P65
Effect of H2 receptor antagonists on prostaglandin E2 and leukotriene B4 production in duodenal ulcer disease

J P WALSH, F J BLOOMFIELD, W J MAXWELL, F P HOGAN, D KELLEHER, AND P W N KEELING (Department of Clinical Medicine, TCD Medical School, St James’ Hospital, Dublin, Eire) Prostaglandins (Pg) may play a role in the prevention and treatment of duodenal ulcer (DU) disease by antiserocyte and cytoprotective mechanisms. The effects of pro-inflammatory leukotrienes (LT) have not yet been quantified. This study examines PgE2 and LT B4 production by peripheral blood monocytes (PBM) of DU patients, stimulated with opsonised zymosan, before and after four weeks treatment with H2 antagonists.

Twenty patients with active DU were studied. Reduced PgE2 production was seen in untreated DU compared with normal control subjects (CS) (n=20, 18-2±1-8 vs n=20, 40±8-0 ng/106 PB, x±SE p=0-001, DU vs CS), with a rise after DU treatment to 19-7±2-45 ng/106 PB. Leukotriene B4 production was markedly raised in untreated DU compared to CS (n=20, 6-1±1 vs n=10, 1-3±0-2 ng/106 PB, p<0-001, DU vs CS) with a significant reduction to 3-94±0-60 ng/106 PB after DU treatment.

Reduced PgE2 production in the untreated DU may result form diversion of arachidonic acid substrate to an activated lipoxgenase pathway with consequent enhanced LT B4 production. LT B4 may be of pathogenic importance in the persistence of chronic inflammation. Reversal of these abnormalities by H2 antagonists suggests an additional mode of action for these agents.

P66
Effect of sucralfate on isolated amphibian gastroduodenal bicarbonate secretion

J R CRAMPTON, L C GIBBONS, AND W D W REES (Department of Medicine, Hope Hospital (University of Manchester School of Medicine, Salford) Sucralfate is a basic aluminium salt of sucrose sulphate which exhibits ulcer healing and cytoprotective properties in man and experimental animals. There is evidence that its cytoprotective activity may be, in part, prostaglandin mediated and gastric luminal prostaglandin E2 release has been shown to be stimulated by the drug. As prostaglandins of the E series have been shown to stimulate gastroduodenal alkali secretion the effect of sucralfate on the rate of bicarbonate secretion by stripped bullfrog (Rana catesbeiana) antral, fundic and duodenal mucosa has been examined. An isolated chamber preparation has been used enabling pH stat titration of the luminal solution and recording of transmucosal potential difference. Addition of sucralfate 0-5 g/l at pH 7-4 to the mucosal side solution induced, within 15 minutes, an increase in the rate of bicarbonate secretion by fundus (mean±SE: 183±87%, n=4, p<0-05) and antrum (mean±SE: 156±58%, n=5, p<0-005). At this concentration there was no effect on duodenum (mean±SE: 4±15%, n=6, NS) but in a higher dosage of 1 g/l there was an increase in alkalinisation (mean±SE: 42±15%, n=6, p<0-05). Transmucosal potential difference was not altered in these studies. These results suggest that the cytoprotective and anti-ulcer activity of sucralfate may, in part, be mediated by an increase in mucosal bicarbonate secretion and enhancement of the mucous-bicarbonate barrier.
is incubated with juice. (3) Quantitation of the different pepsin types in gastric juice by electrophoretic separation on agar gels, elution and assay of pepsin activity.

At pH 2-0 pepsin 1 had twice the mucolytic activity of pepsin 3. At pH 4-0 pepsin 1 had six times more mucolytic activity than pepsin 3 and caused substantial mucolysis up to pH 5-1. Gastric juice from duodenal ulcer patients exhibited substantial mucolytic activity between pH 2 to 5, similar to pepsin 1. Gastric juice from non-symptomatic volunteers exhibited little mucolytic activity above pH 4.

These studies suggest increased peptic degradation of the mucus barrier, associated with higher pepsin 1 activity, could be important in the pathology of peptic ulcer patients.

**P68**
*Treatment of duodenal ulcer by H2 blocker, large single daily dose, how much and when?*

M DEAKIN, H GLENNY, J K RAMAGE, JANE MILLS, W BURLAND, S P GRAY, J BILLINGS, AND J G WILLIAMS (Department of Gastroenterology, Royal Naval Hospital, Haslar, Smith Kline and French Research, Welwyn, Herts.) The therapeutic efficacy of a single night time dose of H2 antagonist is proven but treatment is usually given on retiring. During a 24-hour period the longest period of unbuffered intragastric acidity covers the evening and night. It is possible that more effective inhibition of peptic ulceration could be achieved by higher or earlier dosing.

We have undertaken identical studies of 24-hour intragastric acidity, nocturnal acid and pepsin output in two groups of volunteers with duodenal ulcers in remission, dosing at either 1800 (n=8) or 2300 hours (n=10).

Compared with placebo mean hourly hydrogen ion activity during the evening and overnight period (1800–0730) was decreased by 51-4% (cimetidine 800 mg, 2300 hours), 54% (C800 mg, 1800 hours), 54% (cimetidine 1600 mg, 2300 hours), 78% (C1600, 1800 hours) and 80% (ranitidine 300 mg 1800 hours). Despite considerable reduction in overnight acid output by dosing at 1800 hours, decrease in pepsin output was less marked than following a 2300 hours dose. After dosing at 1800 hours pH readings ranged from 3-6, (making significant denaturation unlikely), whereas after 2300 hours dosing with cimetidine 1600 mg all specimens were anacidic, and denaturation of pepsin probably occurred.

While more effective overall control of intragastric acidity is achieved by 1800 hours dosing, we would not recommend dosing at this time because overnight acidity is sufficient to allow peptic activity to remain.

**INFLAMMATORY BOWEL DISEASE**

**P69**
*Sero logical studies in Crohn’s disease*

J P IBBOTSON, R N ALLAN, AND P PEASE (The Gastroenterology Unit, General Hospital, Steelhouse Lane, Birmingham) It has been suggested that cell-wall deficient forms of *Pseudomonas maltophilia* might be involved in the aetiology of inflammatory bowel disease. In addition, certain serotypes of *Yersinia enterocolitica* cause a self-limiting ileitis which resembles Crohn’s disease. The aim of this study was to measure antibody levels to these organisms and to *Klebsiella aerogenes*, a common inhabitant of the gut, in sera from inflammatory bowel disease patients.

Serum samples were obtained from 20 patients during exacerbation of Crohn’s disease and from 20 age- and sex-matched patients with active ulcerative colitis and 20 healthy controls. Antibody levels were measured using an enzyme linked immuno-sorbent assay.

In comparison with control groups, there was a significant number of patients with Crohn’s disease that had raised antibody levels to *Y. enterocolitica* and *K. aerogenes*. Levels to *P. maltophilia* were not significantly raised. Patients with ileal Crohn’s disease had significantly higher levels than those in other groups. There was no correlation between antibody levels and disease activity.

Although the raised antibody levels may be due to leakage of normal gut flora across a damaged mucosa, it could be that a range of organisms are primarily involved in the aetiology of the disease.

**P70**
*Patient education in Crohn’s disease*

H L SMART AND J F MAYBERRY (University Hospital, Nottingham) Three hundred and fifty patients with Crohn’s disease were offered an information booklet about their condition. This provided information on symptoms, investigations and treatment together with addresses of self-help organisations. A copy was requested by 232 patients and 175 of these completed a questionnaire assessing its value. The majority of patients (85%) who completed the booklet found it helpful, but required more information about complications of the disease. Long term prognosis, cancer risk and inheritance of the condition. Seventy eight per cent of the patients felt that such a leaflet should be given to all patients shortly after diagnosis.

One year later a further survey was conducted to assess the effect this booklet had on anxiety and consultation levels. One hundred and sixty of the original group of 175 patients who completed the questionnaire were contacted and 78% responded. There was a significant reduction in anxiety; 30% of patients felt less anxious compared with 13% who were more anxious (χ²=10-2 p<0-005) and this was associated with a reduction in consultation rates by 17% of the patients compared with an increase by 5% (χ²=8-5 p<0-005). Improved patient education may alter the clinical management of this disease in the future.
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(six with schistosomal polyposis) and five normal Egyptian controls.

Normal colonic epithelium was negative for HLA-DR, but become HLA-DR+ in schistosomiasis patients, expression being strongest by glandular epithelium. HLA-DR+ epithelium was observed in colonic mucosae of schistosomal colitis and schistosomal polyposis patients, as well as in the polyps themselves. By contrast, expression of HLA-A,B,C was high in the surface epithelium of controls, and only slightly weaker in the glandular epithelium. Essentially, no differences in HLA-A,B,C expression was observed in the patients, irrespective of whether polyposis was present.

These data suggest that colonic epithelium expresses Class II MHC antigens as a consequence of parasitic egg deposition, which in turn may allow the HLA-DR+ epithelial cells to act as antigen-presenting cells in the development and maintenance of local anti-parasite immunity.

P72

T-lymphocyte subsets in the colonic mucosa of patients with intestinal schistosomiasis

S BADR EL-DIN, L K TREJOSIEWICZ, J OAKES, R V HEATLEY, G JANOSZSY, AND A ABOU-KHADR (Departments of Medicine, St James's University Hospital, Leeds, and Alexandria University, Egypt, and Academic Department of Immunology, Royal Free Hospital, London) The mechanisms of immune resistance to schistosomiasis are not fully understood, and it is not known why, in chronic intestinal schistosomiasis, about 10% of patients develop multiple colonic polyps. Little is known of the role of T cell subpopulations in the local immune responses to parasite eggs.

T cell subsets were studied by double-label immunofluorescence in cryostat sections of colonoscopic mucosal biopsies using a panel of monoclonal antibodies. Thirteen patients with schistosomal colitis (seven with schistosomal colitis and six with schistosomal polyposis) and five normal Egyptian controls were studied, as were the actual polyps from two patients. In schistosomiasis, there were marked changes in the intra-epithelial T cells: there was a significant increase (p<0.05) in all patients in the percentage of T4+ (helper/inducer) cells, the majority of which co-expressed the T2 marker of T lymphocyte stimulation. There was also an increased tendency for the T8+ (cytotoxic/suppressor) cells to co-express the T1 'pan-T' marker (p<0.01 in schistosomal polyposis). In the lamina propria, there were no major differences between controls and schistosomal colitis patients, however, although in polyposis, the T4:T8 ratio was significantly decreased (p<0.05), whereas paradoxically in the actual polyps, the T4:T8 ratio was greatly increased (7.1 versus 2.1).

These results show that there are considerable alterations in immunoregulatory T lymphocyte subpopulations in the colonic mucosa in chronic intestinal schistosomiasis. Polyp formation may be a function of infiltrating T4+ cells, which migrate from the lamina propria of the colonic mucosa.

P73

Enhanced prostaglandin E3 production by colonic epithelial cells and resident macrophages in inflammatory bowel disease

W J MAXWELL, F J BLOOMFIELD, F P HOGAN, J P WALSH, D KELLEHER, AND P W N KELLEHER (Department of Clinical Medicine, TCD Medical School, St James's Hospital, Dublin, Eire) Prostaglandin (PgE2) produced in the colon may have important modulatory functions in inflammatory bowel disease. PgE2 is produced by both colonic epithelial cells and resident macrophages and has important cytoprotective and secretory effects. As recent evidence suggests that PGs also act as immunomodulators in inflammatory bowel disease (IBD), the aims of this study were to assess the relative production of prostaglandin E2 (PGF2) by colonic epithelial cells and tissue fixed macrophages, isolated from inflamed (In) and non-inflamed (NIn) tissue from patients with IBD and challenged with opsonised zymosan. As controls, cells isolated from tumour free resection margins of colonic cancer (CC) were used.

PgE2 production by In colonic epithelial cells was enhanced relative to NIn cells (n=5, 7.8±1.8 vs n=5, 3.3±1.0 ng/106 cells, \( \times \) SE, In vs NIn p<0.02). Similar enhancement was seen by macrophages from In mucosa in response to Zyg (n=5, 21±5±2 vs n=5, 8.9±1.9 ng/106 cells In vs NIn, p<0.02). Control (CC) PgE2 production by epithelial cells was 9.1 ng/106 cells and macrophages 14±1 ng/106 cells. PgE2 production by stimulated macrophages in this study were higher than those previously reported for spontaneous secretion indicating an enhanced response to immune challenge.

In conclusion, these data support the concept that increased local production of prostaglandins in areas of disease activity may be of pathogenic significance in the chronic inflammatory response.

P74

Inhibition of PgE2 secretion by Salazopyrin and prednisolone in normal and Crohn's disease monocytes

W J MAXWELL, F J BLOOMFIELD, F P HOGAN, J P WALSH, D KELLEHER, AND P W N KELLEHER (Department of Clinical Medicine, TCD Medical School, St James's Hospital, Dublin, Eire) Salazopyrin (SP) reduces intestinal prostaglandin (Pg) secretion in Crohn's disease (CD). Salazopyrin and its active moiety, 5 amino salicylic acid are, however, both weak cyclooxygenase inhibitors. We studied the in vitro effects of direct addition and 24 hour preincubation with SP and prednisolone (Pred), a phospholipase A2 (PLA2) inhibitor on PgE2 secretion by peripheral blood mononuclear cells (PMBC) stimulated by opsonised zymosan (Zy) or Zy+10 mMol arachidonic acid (AA) for 30 min at 37°C. Secretion was corrected for the number of esterase positive PBMC.

Crohn's disease monocytes had significantly enhanced PgE2 secretion compared with normal subjects (NS) when stimulated with Zy (n=7, 70±15 vs n=7, 21±5 ng/106 monocytes, ±SE, p<0.001, CD vs NS), and Zy+AA (n=7, 2343±577 vs n=7, 322±123 ng/106 monocytes, p<0.001). Direct addition of SP resulted in a non significant increase in PgE2 secretion by both CD and NS monocytes using Zy stimulation only. Pred added directly had no effect on PgE2 secretion. Twenty four hour preincubation with Pred, however, resulted in marked reduction of PgE2 secretion in both CD and NS monocytes using Zy stimulation (78% and 69% reduction, CD and NS respectively, partially reversible on addition of AA (16% and 31%, CD and NS). A less marked inhibition of PgE2 secretion was seen following preincubation with SP on Zy stimulation (39% and 26%, CD and NS) which was reversible on addition of AA (2% and 3%, CD and NS).

Both Pred and SP reduced PG production by 24 hour cultured monocytes. This is not because of cyclooxygenase inhibition as it is reversible by addition of exogenous AA. Reduced PgE2 production by SP may be because of PLA2 inhibition. Alternatively because mixed mononuclear cells are used, it may be due to an indirect effect on intercellular signalling.
Factors affecting suppression of cell mediated immunity in inflammatory bowel disease

C AINLEY, J CASON, R A WOLSTENCROFT, B M SLAVIN, AND R P H THOMPSON (The Gastrointestinal Laboratory, Department of Immunology, and Department of Chemical Pathology, St Thomas's Hospital, London)

There is abnormal suppression of cell mediated immunity (CMI) in ulcerative colitis (UC) and Crohn's disease (CD), but the factors involved are unknown. We have investigated the effect of spontaneous suppressor cell activity (SSCA) and indomethacin sensitive suppression (ISS) on lymphocyte transformation (LT) in relation to lymphocyte populations (LP) and nutrition in 24 controls (CO), 14 patients with UC and 31 patients with CD. Lymphocyte populations were estimated using OKT monoclonal antibodies. Lymphocyte transformation with phytohaemagglutinin (PHA) and Concanavalin A (Con A) were carried out in parallel (1) control LT; (2) 24 hour preincubation (SSCA assay); (3) with 1 mg/ml indomethacin (ISS assay).

Seventeen CD patients were normally nourished (nCD) and 14 malnourished, being <90% of ideal body weight. The percentage OKT3 cells, and the OKT4:OKT8 ratio were normal in CD, but in UC the ratio was reduced (CO 1:93±0:07 vs UC 1:12±0:19, p<0:001). Control LT responses were reduced in maLCD (PHA p<0:01, Con A p<0:01), but not in nCD; in UC responses to Con A only were reduced (p<0:05). There were small increases in ISS in both UC and CD. In UC and nCD there were small reductions in SSCA. In maLCD SSCA was increased (PHA p<0:05, Con A p<0:01), and was partially responsible for the reduced control LT of maLCD.

In UC, LT is reduced with an abnormal OKT4:OKT8 ratio, but SSCA and ISS are normal. In nCD, LT, SSCA and ISS are normal. In maLCD, LT is reduced, in part due to increased SSCA. Malnutrition underlying abnormal CMI in CD.

Peripheral blood T cell subsets in sclerosing cholangitis (PSC) and ulcerative colitis (UC)

G K SACHDEV, R W G CHAPMAN, AND D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) Previous studies of T cell subsets in patients with ulcerative colitis have produced conflicting results. One explanation may be methodological because subsets have been evaluated using mononuclear cell suspensions. T cell subsets have now been re-examined using whole blood smears.

Patients with UC (n=40, remission 27, active 13), and PSC with UC in remission (eight) were compared with normal healthy control subjects (15) and patients with the irritable bowel syndrome or peptic ulcers (17). Blood smears were air-dried, fixed with acetone-methanol and stained with monoclonal antibodies: Dako-T1 (panT), Dako-T4 (helper), Dako-T8 (suppressor-cytotoxic, CR23/43 (la).

Patients with active UC showed a significantly (p<0:01) lower proportion of T8+ cells (16%) than those in remission (25%), the healthy controls (27%) or disease controls (24%). This difference was related to disease activity and not to length of history or therapy. Patients with PSC, whose UC was in remission, had significantly fewer T8+ cells than healthy controls (19-2, p<0:02). There were no differences between the groups for T1+, T4+ or CR23/43+ cells.

We conclude that reduced proportions of peripheral blood lymphocytes of suppressor-cytotoxic phenotype are associated with active UC and PSC regardless of activity of the UC.

P77 Peanut lectin binding and dysplasia in multicolon biopsies from patients with ulcerative colitis complicated by carcinoma

J B FOZARD, S B GRIFFITHS, M F DIXON, A R AXON, AND G R GILES (University Department of Pathology, Department of Surgery, St James's University Hospital, Leeds, and Gastroenterology Unit, Leeds General Infirmary, Leeds) The demonstration of dysplasia in the mucosa of patients with ulcerative colitis (UC) is important in cancer surveillance and may determine the need for surgery. There are problems in the interpretation of dysplasia especially in the presence of inflammatory changes. In a preliminary study using an immunoperoxidase technique we assessed 11 lectins for the identification of dysplasia in colorectal specimens from patients with UC peanut lectin binding in all cases of dysplasia.

We have now studied peanut lectin binding and dysplasia in 165 colonic biopsies from patients with UC complicated by carcinoma (n=6) and cancer free controls (n=10). A significant increase in peanut lectin binding was found in biopsies from the cancer group 81/89 (83%) compared with controls 43/67 (64%) p=0:005 x2. Comparable rates of dysplasia occurred in the cancer (32/88, 32%) and control groups (20/67, 30%). High grade dysplasia was absent, however, in the control groups and universally present in the cancer group.

Peanut lectin binding is a sensitive indicator of cancer complicating UC, but lacks specificity. High grade dysplasia indicates the presence of carcinoma.

Detecting premalignancy in the colon

J MATTHEWS, T COOKE (INTRODUCED BY A PARKINS) (Department of Surgery, Charing Cross and Westminster Medical School, London) We have previously reported that in an animal carcinogenesis model the mean DNA content per epithelial cell in the upper regions of the colonic crypts increases as carcinogenesis progresses. We have now studied the DNA content of colonic mucosa in patients with colorectal carcinomas.

Using microdensitometry, DNA content was measured in the cells in the proliferative and functional zones of histologically normal Feulgen stained sections taken adjacent to and distal from colonic carcinomas, and related to stem cell DNA content. DNA content was measured similarly in cytological brushings from the same areas and the percentage of 2N cells calculated.

There was a significant increase in the amount of DNA in the proliferative cells adjacent to the tumours (100%±1:3) compared to distally (91%±2:0, p<0:002). Although a similar increase was seen in the functional cells adjacent to the tumours compared to distally the difference was not significant. In cytological preparations there was an increase in the proportion of dividing or aneuploid cells in the transitionally mucosa (7:3%±1:2) compared with distal mucosa (3:5±0:9, p<0:02) and to the mucosa of patients with non-cancer related bowel problems (2:1%±0:5, p<0:001).

These techniques appear to be reliable in detecting early malignant or pre-malignant changes in the colonic mucosa patients.

111Indium granulocyte scanning in acute graft versus host disease after bone marrow transplantation
The use of bone marrow transplantation to cure aplastic anaemia and certain haemato logical malignancies has been hindered by acute graft versus host disease (GVHD), which affects primarily the gastrointestinal tract in addition to the liver and skin. Because intestinal GVHD displays many of the histological features of acute inflammatory bowel disease we have investigated the value of $^{111}$Indium granulocyte scanning in diagnosis and management.

Ten patients with suspected or definite GVHD after bone marrow transplantation were studied and scans compared with histological grading of rectal histology. Six patients with active GVHD showed extensive abnormal bowel activity on $^{111}$Indium granulocyte scan (both small and large intestinal activity) and five subsequently died. Rectal histology was abnormal in all six cases but in half the cases underestimated the severity of the disease. Three further patients were studied after treatment with methylprednisolone, when GVHD was quiescent and showed just localised ileocaecal involvement while rectal histology was normal. The remaining patient had a normal $^{111}$Indium granulocyte scan and subsequently GVHD was excluded.

$^{111}$Indium granulocyte scanning shows clear differences between active and quiescent GVHD and appears to be a promising non-invasive technique for assessing disease severity and prognosis in this difficult group of patients.

P80
Colonic permeability to $^{51}$Cr-EDTA in inflammatory bowel disease

R T Jenkins, D B Jones, R L Goodacre, R H Hunt, and J Bienenstein (Intestinal Disease Research Unit, Departments of Pathology and Medicine, McMaster University, Hamilton, Ontario, Canada) The purpose of this study was specifically to measure colonic permeability to $^{51}$Cr-EDTA in Crohn’s disease (CD) and ulcerative colitis (UC) after rectal administration. Five volunteers (four men, one woman; aged 21–43 years) served as the control group. Seven patients (four men, three women, aged 22–44 years) with colitis (one ileocolonic CD, one colonic CD, and five subtotal or total UC) also were studied. No bowel preparation was used. After normal evacuation of the bowel just before the test, 25 uCi of $^{51}$Cr-EDTA in 30 ml of normal saline (pH 6.2, 280 mOsm/kg) was instilled into the rectum via a 30 cm, 8F, paediatric feeding tube, while the patient was supine in the left lateral position. Urine was collected for 24 hours. Volunteers were requested to retain the enema for at least two hours. Food and drink were allowed ad libitum. In the control group, urinary excretions of the probe ranged from 0·23–1·42%/24 h (mean 0·69%/24 h, SD 0·51%/24 h). In the patients with colitis, the 24 hour urinary excretions of the probe ranged from 2·95 to 21·57%/24 h (mean 8·17%/24 h, SD 6·49%/24 h). The difference between the control group and patients was significant (p<0·03). This study emphasises that colonic absorption of $^{51}$Cr-EDTA does occur in health and that increased permeability may be found in patients with extensive colitis.

P81
An audit of ulcerative colitis in a district general hospital

H W Jones, J Grogono, and A M Hoare (Wycombe General Hospital, High Wycombe, Bucks) Previous reports have shown a high mortality for ulcerative colitis (UC) in district hospitals. We have carried out an audit of all patients with UC in one health district (pop 270 000) between 1975–1984. The incidence and prevalence were 6·7 and 70/100 000 respectively. Ninety-six patients required 114 admissions with acute colitis. Before admission 3·7% were undiagnosed. Nineteen per cent required emergency surgery. There were no deaths from acute colitis suggesting an improved prognosis for colitis in district hospitals. Three hundred and two patients were followed for 1151 patient years. Colonoscopy performed routinely eight to 10 years after diagnosis detected two Dukes’ A carcinomas and one severe dysplasia. Seventeen per cent of patients initially assessed as having distal colitis were found to have extensive disease including the two with malignancy. Of 99 patients lost to follow up two represented with carcinomas, one died, being the only colitis related death. Therefore, close follow up and routine colonoscopy even of patients with apparent distal disease appears worthwhile. In this district the workload to examine all patients 10 years after diagnosis, and subsequently those with extensive disease biannually, requires an estimated 30 colonoscopies/year.

P82
Clinical importance and complications of the early postoperative water-soluble contrast enema

I G Haynes, M Goldman, S H Silverman, J R Lee, J Alexander-Williams, and M R B Keighley (The General Hospital, Birmingham) The early postoperative water-soluble contrast enema (WSCE) is a well established technique to assess the integrity of large bowel anastomoses. We have assessed the safety and accuracy of a WSCE from a prospective series of 117 consecutive patients undergoing colorectal operations.

Twenty four radiological leaks (24%) were detected and 14 clinical leaks (12%) occurred. In four patients (3%), however, with clinical leaks, the anastomosis was radiologically intact. The overall accuracy of a WSCE was 84·6% (false positive 11·9%, false negative 3·4%; sensitivity 71%; specificity 86%).

Septicaemia occurred in five patients (4·2%) after WSCE, one of whom died and only one patient had a radiological leak. Fifty two patients (44%) had a stapled anastomosis, and in 12 patients (23%) the ring was disrupted on plain radiograph. All the clinical leaks after stapled anastomosis were identified by this non-technique.

This study of postoperative WSCE indicates that the investigation is potentially dangerous and does not always identify clinically important anastomastic dehiscence.

P83
An analysis of anal sphincter competence by measurement of anal compliance

C P Gibbons, A Trowbridge, J J Bannister, and N W Read (Departments of Surgery, Physiology and Medical Physics, University of Sheffield, Sheffield) The circular smooth muscle of the anal sphincter is required to contract sufficiently to close the anal canal in order to preserve continence, but also to stretch sufficiently to allow the passage of a stool. These functions depend upon the elastic properties of the sphincter, which have been little investigated. Anal distensibility was assessed in 14 normal men and 11 normal women by measuring sphincter pressures via perfused catheters.
Patients with pruritis ani leak liquids from the anal canal more readily than normal subjects

N S AMBROSE, A ALLAN, S SILVERMAN, AND M R B KEIGHLEY (Department of Surgery, The General Hospital, Birmingham) We have assessed the physiological abnormalities in the anorectum of 20 patients with pruritis ani compared with 12 age matched controls.

A saline infusion (1500 ml) test showed that leakage started after infusion of 425 ml in patients with pruritis ani, compared with 1500 ml in controls (p<0.001).

The anal canal high pressure zone was greater in patients (4 cm) than controls (3 cm). The resting anal canal pressures were also greater in patients (100 cmH2O) than controls (82 cmH2O). A similar trend was found with regard to the maximum squeeze pressures (280 cm of water and 213 cm of water respectively). The degree of perineal descent was 1.5 cm in patients compared with 1.4 cm in controls. The rectoanal inhibitory reflex was absent in five of the patients (25%) compared with only one control (8%), however, the percentage reduction of anal pressure after 50 ml inflation of a rectal balloon was greater in the patients with pruritis ani (40%) compared with controls (23%).

Results indicate that patients with pruritis ani leak liquids through the anal canal more readily than controls, despite apparently normal sphincter pressures.

P85
Partial purification of a high molecular weight hepatotropic factor from human serum

A C SELDEN, R JOHNSTONE, S GUPTA, H DARBY, AND H J HODGSON (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) Several circulating low molecular weight hepatotropic factors have been associated with liver regeneration after partial heptectomy including insulin, glucagon and epidermal growth factor (EGF). In contrast, we have partially purified a high molecular weight (approx 150 000 daltons) factor from human serum taken 24 hours after partial hepatic resection. Hepatotropic activity was shown on rat hepatocytes cultured in supplemented Williams E media by 3H-thymidine incorporation into DNA. The hepatotropic factor, prepared by gel filtration and heparin-Sepharose affinity chromatography, or EGF and insulin, were added 20 hours postplating of the cultures.

The 'hepatotropic factor' stimulated DNA synthesis in a dose dependent manner (161 µg/ml, 0.42x10^6 dpm 3H/mg protein, 320 µg/ml, 0.54x10^6 dpm 3H/mg protein), to a greater extent than dexamethasone alone (0.29x10^6 dpm 3H/mg protein). At concentrations studied the factor was 20% as potent as optimal concentrations of EGF plus insulin. A similar high molecular weight hepatotropic factor from rat serum after partial heptectomy reached 60% the potency of EGF+insulin, suggesting either partial species specificity, or differing time-relationships of production of these factors after hepatic resection in different species.

P87
HBV infection and alcohol abuse: a synergistic effect leading to a more severe liver disease or a casual association?

M CHIARAMONTE, A FLOREANI, D MARTINES, M SALVAGNINI, E PORNARO, AND R NACCARATO (Department of Gastroenterology, Policlino Universitario, Padova, Italy) Eighty six (77 men) heavy drinkers – 29 HBsAg+ve, 13 antiHBs/antiHBC+ve, 14 antiHBC+ve, 30 negative for any HBV marker – were studied to verify whether: (1) the HBV can be responsible for chronic hepatitis in alcoholics; (2) the concomitant presence of HBV infection and alcohol abuse enhances the severity of the disease. Histological features of ACH were present...
in 12 patients (14%) (six HBsAg+ve, five antiHBe+ve and/or antiHBs+ve and one HBV negative) and of CPH in 13 (15%) (six HBsAg+ve, three antiHBe/anti-HBs+ve and four HBV−ve); four HBsAg+ve patients had signs of acute hepatitis superimposed on cirrhosis. Thirty patients had cirrhosis (11 HBsAg+ve and eight antiHBV+ve) and 27 steatosis (two HBsAg+ve, 10 antiHBV+ve and 15 HBV negative). Liver tissue HBeAg was detected by indirect immunofluorescence in 50% of HBsAg+ve patients (but without relationship with serum HBeAg/antiHBe positivity), in 33% of antiHBV+ve patients and in one of 30 HBV serum negative patients. The clinical course had been very severe in HBsAg+ve patients: four aged 25, 31, 43, 44 years, died of liver failure, while none of the HBsAg negative died during a comparable follow up period. The prevalence of ‘severe’ liver disease (cirrhosis or ACH) was 80% in the HBsAg+ve, 61% in antiHBs/antiHBe+ve and 33% in HBV negative.

We conclude that (1) the HBV has a putative aetiopathogenic role in chronic hepatitis in alcoholics; (2) alcohol abuse enhances HBV pathogenicity and – vice versa – the course of alcoholic liver disease is accelerated by the HBV infection.

P88
Assessment of portal vein patency: value of ultrasound scanning

N RABY, J KARANI, P POWELL-JACKSON, H MEIRE, AND R WILLIAMS (Liver Unit, King’s College Hospital, and School of Medicine and Dentistry, Denmark Hill, London)

The value of ultrasound scanning (US) for estimating portal vein (PV) patency has not been assessed previously in a large series. In the present study the accuracy of US was estimated either by comparison with the findings at operation (21 patients) or with the findings after aortoportography (94 patients). In the first group, US was accurate in 18 (86%). Non-visualisation of the PV by US in one and misdiagnosis of PV occlusion in two was attributed in each instance to distortion of hepatic anatomy by shunt surgery in two and a Kasai operation in one. In the second group, confirmation of US findings was obtained by aortoportography in 73 (78%). Non-visualisation of the PV by US could be explained in eight of 11 patients as due to portal vein thrombosis (two), hepatic malignancy (four), aberrant PV (one) and previous shunt surgery (one). Misinterpretation of USS findings in five could be attributed to cavernous transformation of the PV (two), hepatic malignancy (two), and previous Kasai operation (one). In conclusion, the accuracy of US for estimating PV patency is high but in cases complicated by previous Kasai operation or shunt surgery, aortoportography should also be carried out.

P99
Comparison of lactulose and lactitol on ileal and colonic pH

D H PATIL, D WESTABY, Y R MAHIDA, K R PALMER, R REES, M L CLARK, AND D B A SILK (Departments of Gastroenterology, Central Middlesex Hospital, London, and St Bartholomew’s Hospital, London)

Lactulose is an unabsorbed disaccharide with a defined laxative threshold. It has superior taste properties to lactose and has been suggested as an alternative to lactulose for treatment of chronic hepatic encephalopathy. The aim of the present study was to compare the effects of these two sugars on luminal pH in the terminal ileum, colon and rectum of five normal subjects. The luminal pH was recorded every one to two hours using a pH-sensitive radiotelemetering device, either after ingestion of a normal diet, or this supplemented with sufficient lactulose or lactitol to produce 2-4 semiformed stools daily. Neither sugar had an effect on terminal ileal pH (basal 7.48±0.40; lactulose 7.20±0.48; lactitol 7.02±0.31, mean±SD). The pH of the right colon (basal 6.36±0.32) was significantly lowered during ingestion of both lactulose (5.1±0.89) and lactitol (5.78±0.45; p<0.05 or less). There was no significant difference between the acidification properties of the two sugars. Neither lactulose or lactitol had a significant effect on the pH of the left colon or rectum. If the mode of action of lactulose in the treatment of hepatic encephalopathy is dependent upon its ability to lower right sided colonic pH, then our data lend support to the suggestion that lactitol may also have a role to play in the treatment of this condition.

P90
Effects of dietary protein on plasma and CSF amino acid levels: correlation with the degree of encephalopathy

S A JENKINS, N B ROBERTS, J N BAXTER, G SKERRITT, AND R SHIELDS (Departments of Surgery and Veterinary Anatomy, University of Liverpool, Liverpool)

There is little information on the precise relationship between diet and the development of hepatic encephalopathy (HE) after portocaval shunting (PCS). Therefore, we studied the effects of varying protein diets on plasma and CSF amino acid profiles and the development of HE in dogs with a PCS. Fasting blood and CSF samples were taken for amino acid and ammonia estimations from four dogs with a PCS at the end of 28 days of respectively protein free (control period), 15% and 40% protein diets. The degree of HE was assessed at the time of sampling. Normal fasting ranges of CSF and plasma amino acids were determined in dogs without a PCS. The degree of HE increased with increasing protein intake. There was a marked decrease in plasma levels of branched chain amino acids in non-shunted dogs which did not alter with increasing protein intake. In contrast, plasma phenylalanine, glycine and ammonia levels increased with higher protein intake. The marked encephalopathy at the end of the 40% protein regimen was associated with significant increases in CSF ammonia (52 to 316 μmol/l), glutamine (115 to 2919 μmol/l), phenylalanine (51 to 75 μmol/l) and glycine (22 to 172 μmol/l) (Students t test; p<0.05). However, CSF, GABA and tryptophan showed no consistent change. The results suggest; (1) portocaval shunting maintains low levels of branched chain amino acids irrespective of dietary protein intake; (2) the effects of a high protein diet on CSF amino acids and ammonia may have important implications in the management of patients with HE.
and 30 normal subjects. Among the cancer patients studied there were 25 with hepatocellular carcinoma (HCC), 20 cholangiocarcinoma and 36 with secondary liver neoplasms and two with angiosarcomas. The control patients included 10 liver cirrhosis, six iatrogenic biliary stricture, three haemangiomata, two sclerosing cholangitis, two hydatid disease, two intraparenchymal cholelithiasis, two liver cyst, two adenoma and one liver sarcoidosis.

The CA-50 RIA test was positive in 15 (60%) HCC, 14 (70%) cholangiocarcinoma and 26 (72%) of those with secondary liver neoplasms. The test was negative in the two patients with angiosarcoma, all control patients and in all normal subjects. Therefore the CA-50 RIA test could help in the differential diagnosis of pathological liver conditions.

Expression of oncogene related proteins in human malignant liver neoplasms

N A HABIB, H NIMAN, A THOMPSON, AND C B WOOD (Department of Surgery, Royal Postgraduate Medical School, London, and Department of Molecular Biology, Scripps Research Centre, La Jolla, USA) Protooncogenes are responsible for normal cell growth and their conversion into activated cellular oncogenes are associated with cancer. We investigated the expression of ras-oncogene product in human liver with the use of monoclonal antibodies raised against c-Ki-ras oncogene normal product (Mo-EP). Using the peroxidase-anti-peroxidase technique, liver tissue was stained with Mo-RAP to a concentration of 1:200. The patients studied were five normal, 10 hepatoma and 20 colorectal liver secondaries. Positive staining in the cytoplasm was found in six of the 10 hepatomas and 16 of the 20 liver secondaries. The remaining cancer patients and the five control patients (apart from two patients specific staining in the connective tissue) had negative hepatocytes staining. These findings suggest that liver tissue may express ras-oncogene in carcinoma and this may offer new diagnostic and therapeutic applications.

Lack of osteomalacia in chronic active hepatitis on maintenance corticosteroid therapy

A J STELLON, J COMPSTON, AND R WILLIAMS (Liver Unit, King’s College Hospital, London SE5, and Department of Histopathology, St Thomas’s Hospital, London SE1) Subnormal 25-hydroxyvitamin-D (25-OHD) levels have been reported to occur in 45-60% patients with chronic active hepatitis (CAH), although the number that developed osteomalacia is uncertain as diagnostic iliac crest histology was performed in few patients. We report serum 25-OHD levels and iliac crest histology to determine the incidence of osteomalacia in 36 patients, aged 20-66 years, 34 women, with biopsy-proven CAH, in biochemical and histological remission, of whom 23 had cirrhosis on biopsy. All had received prednisolone therapy for one to 12 years (median 3-6 years) and the maintenance dose ranged 5-12.5 mg/day (median 10mg). All patients had an iliac crest biopsy to determine total trabecular bone volume (TBV), mean osteoid seam width (MOSW) and mineralisation lag time (MLT). Osteomalacia was defined as MOSW >15 μm coupled with a MLT >100 days. 25-OHD levels were low in four (11%) patients, TBV was significantly lower in the patients compared to age and sex-matched controls (19.2±4.6 vs 23.5±5.8 respectively; p<0.001). No patient was found to have an MOSW >15 μm and the mean values were not significantly different from controls (8.4±1.2 vs 9.59±2.36 respectively; p=NS) but MLT was significantly prolonged in the patients (28.4±310 vs 13.7±8.4 respectively; p<0.01). Low TBV and absent osteomalacia suggests that osteoporosis is the metabolic bone disorder associated with steroid-treated CAH.

Prophylactic chemotherapy after operations for hydatid disease – an animal study

D L MORRIS, JANET B CHINNERY, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) There is approximately a 10% risk of recurrence after operation for hydatid cyst (Echinococcus granulosus). The surgical treatment of recurrent disease is associated with considerable morbidity and whilst chemotherapy with Mebendazole, and more recently Albendazole has been investigated in such patients, prevention of recurrence would have great advantages.

In order to study the effect of Albendazole on the development of cysts, 25 gerbils were given intra-peritoneal injections of live E granulosus protoscoleces. Nine gerbils remained as untreated controls. Seven received Albendazole 10 mg kg orally for one week before injection and eight received the same dosage for one week after infection. The animals were killed at six months. All control animals developed peritoneal cysts. They had a mean number of 44-1 (SD16-5) cysts per gerbil while in eight gerbils which received Albendazole after infection, two had no cysts and the mean number of cysts was 7.6 (SD 8.0) (p<0.01). The cysts which did develop in the treated animals were of similar size to controls. There was no significant reduction in number of cysts in the animals treated before infection (59±1). We conclude that even a short postoperative course of Albendazole is likely to significantly reduce the number of spilled protoscoleces which are able to implant and grow into cysts.

The British Society of Gastroenterology

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and liver transplantation should be considered in stage D.

P96
Long term prognosis of Budd-Chiari syndrome

S GUPTA AND H J HODGSON (Department of Medicine, Royal Postgraduate Medical School, London) The Budd-Chiari syndrome is commonly considered a serious condition with progressive deterioration and a high mortality. It is, however, an heterogeneous condition, and we have analysed the histories of 18 patients seen over 20 years to elucidate determinants of prognosis.

In all patients diagnosis was based on liver biopsy and/or hepatic venography. In seven men and 11 women, mean age 37.6 (19-60 years range), symptoms had been present on average for 6.6 months before diagnosis. Patients were followed for 4-7 years (range 0.5-19). Eight patients died (44%), two after surgery, two because of associated tumours, and four from complications of hepatic failure. Actuarial analysis showed a one year mortality of 22.9%, and three years of 51.1%, but no further mortality beyond this period. A poor prognosis was associated with an associated malignancy, and bleeding from oesophageal varices, but in the absence of these features the prognosis is unexpectedly good. The 10 survivors all lead normal lives with control of symptoms by medical means, though in two surgical therapy (side-to-side shunt or removal of hepatic venous webs) has been necessary. Many patients with Budd-Chiari syndrome have only mild symptoms and a good prognosis.

P97
Liver biopsy in patients with impaired coagulation – which route?

M V TOBIN AND I T GILMORE (Gastroenterology Unit, Royal Liverpool Hospital, Liverpool) Histology is crucial in the investigation of hepatic disease but there is still a significant morbidity and mortality associated with conventional liver biopsy. Its safety, however, has usually been evaluated in patients with normal coagulation and the complication rate in those with prothrombin times greater than 15 seconds or platelet counts below 80 x 10⁹/l is unknown.

In our unit during the past three years, in patients with impaired coagulation, we have preferred the recently described ‘plugged’ biopsy to the transvenous approach. Sixty five patients with prothrombin times prolonged by up to eight seconds or platelet counts as low as 20 x 10⁹/l have been biopsied and the needle track filled with absorbable gelatin sponge. The technique is straightforward and there have been no complications. Specimens have all been satisfactory for histological examination and superior to those taken transvenously. Our results are sufficiently encouraging to recommend its use in this high risk group in preference to the laparoscopic or transvenous approach which both require more expertise, equipment and time.

P98
Long-term oral contraceptive use and serum total cholesterol and total bile acids

P R BAKER, J S BUMBRA, A D REID, P E PREECE, AND J D E KNOX (University Departments of Surgery and General Practice, Ninewells Hospital and Medical School, Dundee) Oral contraceptive steroids (OC) increase the cholesterol saturation index of bile and are associated with raised serum total cholesterol concentrations. Changes in serum bile acid levels might also be expected, especially after several years use of OC comprising ethinylestradiol (EE) and a progestogen. Serum concentrations of total cholesterol (CHOD-PAP method) and total bile acids (TBA; Sterognost-3xFlu assay) were therefore determined in 10 women (27 ± 4.7 years (mean ± SD) with well documented long-term EE/progestogen OC intake and compared with levels in 10 age-matched women (26 ± 4.9 years) from the same general practice who had never taken OC (NON-OC). The OC were taken, as prescribed, continuously for 3-12 years (mean 5.6 years), and total oestrogen and progestogen intakes were estimated as 25-156 mg and 93-2948 mg respectively, and all were currently on 30 µg EE and 50-250 µg L-Norgestrel. Blood was taken between 1800 and 1845 hours after a six hour fast and serum obtained within one hour. Total cholesterol (µM) were significantly higher in the OC group (5.8 ± 0.57 (mean ± SD) vs 4.7 ± 0.67; p<0.05, t-test) and four of these women had values >5.7 (suspicion limit) compared with only one in the NON-OC group. Serum TBA (µM) was lower in women on OC (3.7-1.9 vs 6.1-2.8) although the difference was of borderline significance (Mann-Whitney U = 24, z = 1.968 (corrected for ties); t=2.25). The TBA/cholesterol molar ratio was significantly lower in the OC group (0.7 ± 0.4 x 10⁻³ vs 1.3 ± 0.7 x 10⁻³; p<0.05, Mann-Whitney) and the two constituents exhibited a negative correlation (rho=0.51, p<0.025). There was, however, no correlation between total cholesterol or TBA and total duration or total amount of OC steroid intake. Oral contraceptive steroid intake over several years appears to result in a relatively large increase (23%) in serum total cholesterol and a decrease in serum total bile acids which might reflect a change in the output of bile acids by the liver.

P99
Biopsy findings in liver allograft rejection

S HUBSCHER, D CLEMENTS, E ELIAS, AND P MCCUMSTER (Queen Elizabeth Hospital, Edgbaston, Birmingham) It is difficult to distinguish liver transplant rejection from other causes of graft dysfunction on the basis of histological criteria alone. Early studies, based mainly on necropsy findings, reflect this problem and the histological features which characterise rejection remain the subject of controversy.

During the past 12 months we have routinely carried out needle biopsies in the assessment of abnormal liver function after transplantation. In all cases a diagnosis of rejection was based on excluding other known causes of graft dysfunction by microbiological, serological and radiological criteria. Changes ascribed to rejection were seen in 15 biopsies from five patients. The features of acute rejection were (1) a mixed portal inflammatory infiltrate and (2) infiltration of bile duct epithelium by polymorphonuclear leucocytes. In one patient this was followed by complete loss of small bile ducts and the need for retransplantation. In a second patient there was chronic bile duct damage resembling that seen in graft-versus-host disease. In the other three cases there was clinical and histological improvement following immunosuppressive therapy.

We conclude that liver biopsy is useful in the diagnosis and management of rejection after liver transplantation.

P100
Increased permeability to proteins of hepatic tight junctions in α-naphthylisothiocyanate (ANIT)-treated rats

K S KAN, P J LOWE, AND R COLEMAN
(Department of Biochemistry, University of Birmingham, Birmingham) The movement of proteins from blood to bile has been studied using isolated perfused liver operating under one pass conditions. After a one minute perfusion pulse of horseradish peroxidase (HRP) peaks were observed in bile, at five, and at 20–25 minutes (abolished by colchicine and probably representing a vesicle mediated transcytosis). The first HRP peak was substantially increased in rats pretreated with ANIT, known to increase paracellular permeability, probably through an effect on tight junctions. There was no decrease in bile flow within the time-period of the present experiments (until 15 hours), and thus the effects represent one of the earliest stages in ANIT-cholestasis.

Rats were treated with ANIT 0–15 hours before pulsing with HRP. Biliary concentration, in the five minute peak, of copulsed inulin (MWt 5000) rose steadily over the dose period, but the peak of HRP (MWt 40 000) and of ovalbumin (MWt 40 000) began to rise only after 10 hour exposure to ANIT, suggesting that the extent of ANIT-increased permeability is dependent upon the molecular weight. The five minute HRP peak was increased after only two hours of ANIT exposure in phenobarbital-treated rats suggesting that ANIT metabolites, rather than ANIT alone, may be involved.

COLORECTAL
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P101
Laparotomy: still a valuable investigation in patients with bleeding from the intestine

S BREARLEY, P C HAWKER, N J DORRICOTT, R LEE, N S AMBROSE, P W DYKES, AND M R B KEIGHLEY (General Hospital, Birmingham) Bleeding lesions of the small intestine and colon are often difficult to diagnose despite the availability of a wide range of diagnostic techniques. In recent papers, laparotomy has not been recommended and particularly good results have been claimed for selective mesenteric angiography.

Sixty three patients who had had either colonoscopy or mesenteric angiography while being investigated for intestinal bleeding were reviewed. Twenty six had had trivial bleeding and were not considered further. The remaining patients could be divided into two groups, 14 with occult bleeding and 23 who had had major intestinal bleed. Colonoscopy was diagnostic on six of 37 occasions (two of 15 following occult bleeding and four of 22 after major haemorrhage). Angiography was diagnostic on three of 14 occasions (occult bleeding none of three, major bleeding three of 14). Thirteen undiagnosed patients had a laparotomy which was diagnostic in nine (occult bleeding three of three, major bleeding six of 10). Patients with intestinal bleeding should have upper and lower gastrointestinal endoscopy. Undiagnosed patients who continue to bleed should have a laparotomy with an endoscopist available to undertake on table panendoscopy. Angiography should be reserved for the few patients still undiagnosed after laparotomy and should be carried out in centres with special expertise in the technique.

P102
Modified oxygen electrode as a probe for detecting local blood flow in canine colon

C PIASEcki AND S LAKE (INTRODUCED BY R POUNder) (Department of Anatomy, Royal Free Hospital School of Medicine, London) There is a need for simple, fast, non-invasive probing of blood flow in areas of – for example ½ sq cm. Postanastomotic colonic leakage might thus be prevented if local ischaemia was detectable peroperatively. A Clark type surface oxygen electrode was modified to perform this task. It does not measure PO2 because its oxygen consumption is high. Instead, it depletes the tissue of oxygen, the maintenance of which is dependent on inflow of blood. Thus the instrument's reading varies with blood flow. A 95% response is obtained in 20 seconds of application, thus sites can be probed at 15 second intervals.

The instrument was tested in six anaesthetised dogs. Electromagnetic blood flow in the inferior mesenteric artery was compared with probe reading on colon, at five levels of graded arterial constriction. A semi-linear relationship emerged (r=0.91; p<1%), showing dependence on blood flow. The electrode was more sensitive to flow changes at low flows that at high flows.

Being cheap, sterilisable, and simple to use, the instrument may prove valuable in detecting and grading areas with reduced flow.
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motes the formation of carcinogens from benzo(a)pyrene. We are interested in the adenoma-carcinoma sequence and have measured PGE₂ synthesis in biopsies from polyps and cancers at colonoscopy. Normal mucosal samples were obtained at negative procedures. Biopsies were vortexed to stimulate PGE₂ synthesis and released PGE₂ measured by RIA. Results were (mean±SD in pg PGE₂/mg wet weight); normals 102.8±24.3 n=11, polyps 162.1±27.7 n=6; (p<0.01 vs normal), cancers 177.1±13.1 n=7; (p<0.001 vs normals, NS vs polyps) and uninvolved mucosa of tumour bearing colons 117.3±32.6 n=12 (p<0.002 vs polyps and cancers, NS vs normals). We conclude that like other premalignant conditions of the colon, polyps synthesise increased quantities of PGE₂ and that this may be a factor in the transformation of benign polyp to colonic cancer.

P105
In vitro binding and in vivo localisation of an anti CEA monoclonal antibody (C46)

N C ARMITAGE, K C BALLANTYNE, L DURRANT, R C HARRISON, A M L RILEY, I O ELLIS, A C PERKINS, AND J D HARDCASTLE (Department of Surgery, Pathology and Medical Physics, University Hospital, Nottingham and Amersham International, Bucks) Antitumour monoclonal antibodies have been shown to localise in colorectal cancer by several workers. The directly measured tumour:non-tumour (T:NT) uptake in resected specimens after pre-operative injection of radio-labelled antibody has been only 2.5-3.3:1. A monoclonal antibody C46, raised against carcinoembryonic antigen was studied for in vitro binding and in vivo localisation to colorectal cancer.

Binding was measured by flow cytometry of disaggregated tumour cells from 15 primary and three metastatic/recurrent tumours and by immunoperoxidase staining in 18 cancers. Eight patients (seven primary, one recurrent) were injected preoperatively with ¹¹¹In-labelled C46 and tumour and normal tissue from the resected specimens counted.

Binding of C46 was increased 10-fold, median fluorescence 463F1U (33-2203) compared with normal immunoglobulin 43F1U (24-86) (U=20.5, p<0.0001). Immunohistologically intense staining was seen in 15/18 sections, moderate staining in 2/18 and only one section did not stain. The T:NT uptake in resected specimens was mean 5.8±1.7:1 for primary cancers (seven) and 4.6:1 for the recurrence. All patients gave positive preoperative gamma camera images.

The high affinity and high T:NT ratio of 5.8:1, considerably greater than previously reported, increases the prospects for effective targeting of antitumour agents with monoclonal antibodies.

P106
Duodenal bile acid profiles in patients with colorectal polyps

R J MOORHEAD, JOAN DONALDSON, AND D MCKELVEY (Department of Surgery, The Queens University of Belfast, Belfast) It has been reported that patients with colorectal adenomas have increased concentrations of secondary bile acids in duodenal bile. To investigate this finding we have carried out an analysis of duodenal bile acids using gas liquid chromatography, in 38 patients with histologically proven adenomas and compared them with a group of controls matched for age and sex.

We have shown that the levels of chenodeoxycholic acid were significantly higher in those with polyps compared with controls (mean percentage±SD, 30.5±10.6; 26.5±9.0; p<0.04). The levels of cholic acid and deoxycholic acid did not differ significantly between the two groups. (Cholic acid: 47.5±13.0; 50.8±14.1; deoxycholic acid 18.7±7.9; 22.2±12.7). We have also shown an unidentified bile acid which was significantly more prominent in the polyp group compared with the controls (2.9±4.2; 0.9±1.6; p<0.02). The levels of chenodeoxycholic acid and of this unidentified bile acid correlated with the increasing malignant potential of the adenomas with respect to size, type and degree of dysplasia.

We have confirmed that the duodenal bile acids of patients with colorectal adenomas are abnormal when compared with controls. Contrary to the findings of the previous study we have shown the levels of chenodeoxycholic acid to be abnormally elevated in those with polyps, and have been unable to detect any significant differences in levels of deoxycholic acid. Further work is being done to identify the unknown bile acid.

P107
ABSTRACT WITHDRAWN

P108
Influence of sialomucin at the resection margin on survival of patients with colorectal cancer

P M DAWSON, N A HABIB, R C N WILLIAMSON, AND C B WOOD (Department of Surgery, Royal Postgraduate Medical School, London, and Bristol Royal Infirmary, Bristol) There is strong evidence to suggest that a predominant sialomucin production in the colonic mucosa represents a preneoplastic stage in the carcinogenic process. We therefore studied the relation between sialomucin at the resection margin and survival in patients with colorectal cancer. In a multicentre prospective trial, 204 patients have been followed for a mean of 14.8 months (SD 7.3 months). The presence or absence of sialomucins at the resection margin was studied histochemically using the High iron diamine-alcian blue (HID-AB) stain. There were 32 deaths relating to tumour recurrence: 15 deaths in the sialomucin positive group (n=50) and 17 deaths in the negative group (n=137) (p<0.01).

Percentage survival was correlated with time and with the presence or absence of sialomucin in the resection margin. Regression analysis predicts 63.2% five year survival for patients with no sialomucin and 28.4% five year survival with sialomucin present. There was no significant statistical correlation between the sialomucin staining at the resection margin and Dukes' stage, tumour site or differentiation. Sialomucin production in either resection margin appears to be of poor prognostic significance.

P109
Incidence of colorectal cancer and polyps in a health care district: experience at one year of registration

M PONZ DE LEON, A ANTONIOLI, S BONILABII, K ARDUINI, A MERRHIGI, G P RIGO, M PULVERENTI, G GIBERTINI, P DI DONATO, AND F MANENTI (Istituto di Patologia Medica, Cattedra di Gastroenterologia, Divisione di Chirurgia generale, Università di Modena, Italy) From January 1984 a 'tumour registry' for colorectal cancer and polyps has been instituted in a predominantly urban population (263 546 inhabitants) of northern Italy. Based on the experience of the first year of registration, the purposes of this report were three-fold: (1) to determine the incidence of colorectal tumours in
a rather homogeneous population; (2) to find out possible associated risk factors; (3) to ascertain if the data from registration could fit into the 'poly-cancer theory'.

The observed incidence of colorectal cancer was 52.8 new cases/100 000/1984 (53.4 in men, 52.2 in women). The incidence of polyps was 59.6 cases (83.4 in men, 37.3 in women). The incidence increased with age either for cancer or for polyps; however, polyps were more frequent than cancer until the sixties and the peak of incidence of polyps anticipated that of cancer by a five years period. Both cancer and polyps had a similar distribution in the large bowel, more than 60% being located in the left distal portion. No dietary (including alcohol) or occupational factor was clearly associated with colorectal cancer or polyps. Smoking was more frequent in patients with polyps than in those with cancer (46.6% vs 27.6%, \( \chi^2 = 5.61, p = 0.01 \)), presumably because of the male preponderance in the former group.

We conclude that the incidence of colorectal cancer in northern Italy is higher than that of many other European countries and comparable to that observed, on average, in the United States. No obvious risk factor could be detected during the first year of registration. The earlier rise of incidence of polyps – as compared to cancer – and the similar distribution in the various tracts of the large bowel lend further support to the 'poly-cancer sequence'.

**P110**

Prospective comparison of ultrasonic scanning and static and dynamic isotope imaging in the pre-operative diagnosis of liver metastases from colorectal cancer

P J Finan, S H Leveson, G R Giles, P A Wiggins, P J Robinson, and H Irving (Departments of Surgery and Diagnostic Imaging, St James's University Hospital, Leeds) The pre-operative detection of hepatic metastases from colorectal cancer is of importance for accurate staging and planning of adjuvant therapy. Assessment has relied previously on a variety of imaging techniques including static isotope scanning ultrasound and computed tomography. Isotopically measured liver blood flow ratios have previously been described for the detection of hepatic metastases. We wish to present a prospective comparison of ultrasonic imaging together with static and dynamic scintigraphy in patients undergoing surgery for colorectal cancer; the results being correlated with the findings at subsequent laparotomy.

Forty-five patients have been fully evaluated of whom 10 had metastatic disease at laparotomy. The sensitivities for ultrasound, static and dynamic scintigraphy were 50%, 50%, and 70% respectively. The specificity for these three methods was 91%, 100%, and 66%. When either static scanning or ultrasound was used in combination with dynamic scintigraphy, the sensitivity was increased from the original 50% to 80%.

It is known that at least 30% of patients with no evidence of liver metastases at surgery will subsequently develop overt disease and it has been shown that dynamic scintigraphy will identify patients harbouring occult metastases. Based on this study it is apparent that a combination of ultrasound or static isotopic imaging used in combination with flow scintigraphy increases the accuracy of either of these diagnostic procedures in the detection of metastatic colorectal disease.

**P111**

Diagnosis and surgical management of intractable constipation

A M Roe, D C C Bartolo, and N J McC Mortensen (University Department of Surgery, Bristol Royal Infirmary, Bristol) Intractable constipation presents a clinical problem in diagnosis and management. We have investigated 52 patients using a protocol involving transit studies, manometry (anul sphincter pressures, rectal compliance and rectosigmoid motility), EMG measurements of volitional pelvic floor activity, and proctographic techniques in order to identify those patients who may be helped by surgery. Twenty-eight patients (27 women, one man) had slow transit and seven patients have had nine procedures: two had internal sphincterotomy without objective improvement and subsequently had a colectomy. A further four had a colectomy and ileorectal anastomosis (IRA) with satisfactory results. One had a puborectals division. Twenty-four patients (17 women, seven men) had normal transit but symptoms of obstructed defaecation. Dynamic protograms showed rectal intussusception in five, treated by rectopexy with good results in four. One patient had a rectopexy and IRA and one an excision of anterior mucosal prolapse. A combination of transit studies and a dynamic protogram were the most helpful investigations.

**P112**

Anorectal myectomy; a valuable treatment for chronic constipation

N D Heaton and E R Howard (King's College Hospital, Denmark Hill, London) Partial excision of smooth muscle from the internal anal sphincter and rectum (anorectal myectomy) has been suggested as a technique for the management of severe chronic constipation.

We used a modified technique in the treatment of 53 new cases who had failed to respond to treatment with laxatives and anal stretch, (age range two months to 66 years, mean 8.5 years; men 31, women 23). There were no clinical features of congenital aganglionosis (Hirschsprung's disease) in these patients.

The rectored strips of smooth muscle were assessed with neurohistochemical techniques, using acid phosphatase staining for ganglia, and assessing nerves for acetylcholinesterase activity and catecholamine fluorescence. Significant abnormalities were detected in 34 cases — hypoganglionosis (32), hyperganglionosis (one), and angangiongiosis (one). There were minor abnormalities in five cases. Fourteen showed a normal pattern of innervation.

Postoperative assessment in 48 patients (follow up two months to five years; mean 14 months) showed an excellent result in 26 (54%) and a significant improvement in eight (17%). A poor result was found in 14 patients (29%) and eight of these have subsequently undergone a large bowel resection.

Anorectal myectomy is valuable in the diagnosis of neuronal disorders of the hindgut, and is a useful therapeutic manoeuvre in a significant number of patients.

**P113**

Impaired repairment of the pelvic floor musculature by intra-abdominal pressure in faecal incontinence

N R Womack, J F B Morrison, and N S Williams (University Department of Surgery and Physiology, The General Infirmary, Leeds) Patients with idiopathic
faecal incontinence (IFI) often report exacerbation of symptoms with activity that raises intra-abdominal pressure. Normally neural reflexes generate a compensatory increase in the activity of the pelvic diaphragm when intra-abdominal pressure (IAP) rises. To assess the integrity of these reflexes in incontinence 15 patients with IFI (12 women, three men, age 62±14 years) were compared with 15 age and sex matched normal subjects (12 women, three men, mean age 59±17 years; p=NS).

Intra-abdominal pressure, measured via an intrarectal balloon, was raised by a series of forced expirations to graded preset levels. Activity in the puborectal muscle was recorded using a concentric EMG needle, and the signal rectified and integrated. In each subject there was a positive linear correlation between muscle activity and IAP (R=0.67-0.98, median 0.88). Extrapolation of the regression line allowed measurement of the rise in IAP that was necessary to increase muscle activity. Since these muscles are tonically active this increase in activity depends on the sensory side of the reflex mechanism. In the control group recruitment occurred at 0.2±2.0 cm water, whereas in the IFI group recruitment required a significantly higher rise in IAP of 7.6±5.0 cm water (p<0.01 Mann Whitney U test). This deficient response of the pelvic floor muscles to raised IAP in IFI explains the increase of symptoms with activity. It also suggests that IFI may not be entirely motor in origin, as has been postulated, there also being a deficient sensory input.

P114 Experimental support for a simple model of defecation

J J BANNISTER, C P GIBBONS, E A TROWBRIDGE, AND N W READ (Departments of Surgery and Medical Physics, Royal Hallamshire Hospital, Glossop Road, Sheffield) A simple model of the forces involved in the passage of a stool, through the anal canal, predicts that small stools will be more difficult to pass than large stools and that a linear relationship will be found between the intrarectal pressure required to pass a stool and the reciprocal of the radius of the stool. To test this model, in seven volunteers (four men, three women) the intrarectal pressure was measured whilst the subjects passed five incompressible spheres of known diameter. The smallest sphere (diameter 0.5 cm) was passed by only two subjects, the largest (diameter 2.0 cm) by all seven. Analysis of the pressure traces for the spheres, that were passed, shows that the intrarectal pressure and the time required to pass the largest sphere were significantly less than those required to pass the smallest (diameter 0.5 cm or 1.0 cm) (p<0.01). Plotting the peak intrarectal pressure, to pass each sphere, against the reciprocal of the radius gave linear correlation coefficients of 0.75-0.98 (median 0.82).

These findings support our simple analysis of defecation and confirm the clinical impression that the size of the stool is an important contributory factor in difficulties in defecation.

P115 Urological abnormalities in patients with slow transit constipation

J J BANNISTER, W T LAWRENCE, D G THOMAS, AND N W READ (Department of Surgery, Royal Hallamshire Hospital, Sheffield, and Department of Urology, Lodge Moor Hospital, Sheffield) In a study of 24 young women with severe slow transit constipation, it was noted that a surprisingly high number (75%) had symptoms of urinary dysfunction, including hesitancy, frequency, urgency, stress incontinence and symptoms of urinary infection. In 10 patients a combined radiological and manometric, urodynamic and anorectal evaluation was performed. The urodynamic assessment showed that all the subjects required bladder volumes larger than the normal range (150-300 ml) to stimulate the first desire to micturate (p<0.01) and their bladder capacity exceeded the normal range (300-500 ml) in all except one subject (p<0.01). Detrusor contraction was normal with no evidence of instability, the rate of micturition was normal with no radiological evidence of impaired bladder neck opening. The anorectal studies revealed that the constipated subjects required larger rectal volumes than normal to stimulate the desire to defecate (200±50 ml vs 110±10 ml (Mean±SEM); p<0.05) and that their maximum tolerated volume was also larger (380±30 ml vs 290±20 ml (Mean±SEM); p<0.05), other modalities of rectal sensation and compliance were normal. The similar findings in the bladder and anorectum suggest an analogous sensory defect in both organs, raising the possibility of a common abnormality in their intrinsic innervation.

P116 Investigation of colonic motility patterns in the irritable bowel syndrome using radiotelemetry

J R REYNOLDS, A G CLARK, D F EVANS, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) An un tethered pressure sensitive radiotelemetry capsule and portable receiving apparatus have been used to measure colonic motility for 24 hours in ambulatory subjects. Twenty one patients with irritable bowel syndrome (mean age ±SD 34±7-9 years) were compared with 10 healthy volunteers (24±5-67 years). All patients complained of abdominal pain with constipation in nine and diarrhea in 12. Data were analysed using a microcomputer and a motility index derived for three periods: interfood (IF), postprandial (PP) and night (N). Significant differences between IF, PP and N were found in controls (7.52±5-91, 13-14±1-47 and 1.86±0.66 p<0.01) and patient group (10-65±1-35, 18-16±2-04, and 6-01±0-8 p<0.02). Night time activity in the patient group (6-01±1-08) was significantly higher than control (p<0.05) and there was a similar trend, though not significant, in the interfood periods. Postprandial activity was significantly greater in patients with diarrhea (20-52±3-01 p<0-05) whereas no difference was found in the PP response in the constipation group (15-54±2-59). This non-invasive method has identified a sub-group of 30% of patients who have periods of relative colonic hypermotility studied in their normal environment and subject to usual daily stress.

P117 Management and differential diagnosis of perianal hidradenitis

B J HARRISON AND L E HUGHES (Department of Surgery, University of Wales College of Medicine, Cardiff) Perianal skin is prone to involvement with hidradenitis suppurativa and is characterised by the development of recurrent skin nodules which progress to multiple chronically discharging sinuses. Nalit cleft and buttock skin may be affected, superficial fistulae involving the distal anal canal have been described.

Since 1979, 15 patients with perianal hidradenitis in whom conservative measures had failed required wide excision of perianal skin. In all cases active disease involving the axillae and/or puboinguinal...
region was present. The wounds were allowed to heal by granulation with the aid of silastic foam dressings and satisfactory results were obtained in all cases. Follow up of 12 patients (mean 2.5 years) has revealed no evidence of recurrent disease.

Careful examination usually differentiates hidradenitis from other perianal disease. Anorectal Crohn's and perianal fistulae are conditions commonly causing diagnostic difficulty. In the former, cavitating ulcers are found within the anal canal, in the latter, inflammation rarely spreads to involve the buttocks. Less common problems of diagnosis include primary perianal pilonidal sinus, postnatal pilonidal sinus, Paget's disease, Bowen's disease and colloid carcinoma.

A normal anal canal and hidradenitis at other sites are the most important clinical features in diagnosis.

P118
Are bile acids involved in the regulation of mouth-to-caecum transit time (MCTT) in man?

R Penagini, R C Spiller, D B A Silk, and J J Misiewicz (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Bile acids can affect water and electrolyte movements in the human jejunum and ileum. After cholecystectomy, the postprandial peak luminal and blood concentration of bile acids is markedly lowered.

To test if this could delay intestinal transit we studied 10 patients two to four months after cholecystectomy (C) and compared them with 10 healthy controls (N). MCTT was measured in all subjects after a standard liquid 440 kcal (1842 kJ) meal containing lactulose 15 g, using the hydrogen breath test. Blood samples were collected at 0, 30, 60, 120, 180, 240 min (8 C and 8 N) for measurements of total bile acids (enzymatic method) and cholyglycine (RIA); peak incremental response (PIR) and area under the curve (AUC) were calculated. Analysis of results was done with the Mann-Whitney U test. MCTT (mean±SEM) was 65.0±7.6 min in N vs 41.2±5.3 in C (p<0.05). Cholyglycine PIR was 2.17±0.48 μmol/l in N vs 1.11±0.23 in C (p<0.05) and its AUC 306.15±53.7 in N vs 204.12±36.1 in C (p<0.02), while total bile acids PIR was 17.2±1.91 μmol/l in N vs 10.75±1.1 in C (p=0.025) and the AUC 2328.86±328.26 in N vs 2893.39±208.77 in C (p=ns).

Contrary to our hypothesis patients after cholecystectomy appear to have a faster MCTT than healthy controls. As AUC of total bile acids was the same in C and N with lower AUC for cholyglycine in C, higher concentrations of dihydroxy bile acids may be the responsible factor. Rapid MCTT may be relevant to the pathogenesis of post-cholecystectomy diarrhea.

P119
Morphological and biochemical studies on rat pancreatic ducts maintained in tissue culture

S Arkle and B E Argent (Introduced by A Allen) (Department of Physiological Sciences, University Medical School, Newcastle Upon Tyne) Recently, we have developed a technique for the isolation of viable small interlobular ducts from the pancreas of copper deficient rats. Copper deficiency causes a non-inflammatory atrophy of pancreatic acinar cells while the duct cells remain structurally and functionally intact. When isolated ducts were maintained in tissue culture their cut ends sealed within eight hours. This process was accompanied by an overall swelling of the duct, a marked dilatation of the lumen and a flattening of the epithelium against the surrounding connective tissue layer. Secretin (0-1 nmol to 1 μmol) caused a dose related increase in cyclic AMP content and, usually, further swelling of the ducts. Puncture of the cultured ducts caused a fall in duct size, largely accounted for by a reduction in lumen volume, and also increased the height of the epithelium.

Taken together these observations suggest that the duct swelling which occurs during maintenance in culture is because of an increased luminal pressure, resulting from fluid secretion into the closed luminal space.

P120
Cholesterol absorption by the human gall bladder

M R Jacyna, P E Ross, D Hopwood, and I A D Bouchier (Department of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland) Although guinea pig gall bladder is known to absorb significant amounts of luminal cholesterol, there are no data currently available relating to the human gall bladder. Consequently a modified Ussing Chamber was used to investigate cholesterol absorption and transport in human gall bladder mucosa using artificial biles of varying cholesterol saturation. Uptake and transport of cholesterol was determined by tissue and serosal fluid content of 1-(4-C)-cholesterol used as tracer in the artificial bile solutions while (3H)-Dextran was used to correct for adherent bile on the mucosal surface. Tissue viability during experiments was established by using electron microscopy to confirm ultrastructural integrity and also by serial measurements of transmural potential difference and diffusion potentials.

In 33 human gall bladders studied so far, cholesterol was absorbed from the lumen and transported into the serosal fluid. During this process, almost 15% of the absorbed cholesterol was esterified. Absorption and transport rates increased with increasing cholesterol saturation, reaching a maximum value (of approximately 3.5 nmol/cm²/min) when bile became supersaturated. These results show absorption and esterification of biliary cholesterol which may be important in the pathogenesis of human gall bladder disease.
body T204 (directed to the sulphated tyrosyl region of CCK) and antibody 1703 (binding to C-terminal CCK-peptides containing at least 14 amino acid residues). No CCK-LI was demonstrable in fractionated basal plasma. Chromatography revealed four peaks in fat stimulated plasma. Peak I eluted in the void volume and comprised 1-10% of CCK-LI, peak II eluted at 35% and comprised 3-35%, peak III eluted at 50% and comprised 24-62%, and peak IV eluted at 75% and comprised 15-45% of CCK-LI. No additional peaks were detected by antibody 5135, directed to the C-terminus of CCK and gastrin.

We conclude that CCK in plasma after fat stimulation is heterogeneous. From the cross reactivity pattern it is also concluded that the small form of CCK is different from CCK-8.

P122
Cholecystokinin octapeptide-like material is produced from larger forms during circulation in man
C J SPRINGER and J CALAM (Hammersmith Hospital, London) Cholecystokinin in plasma exists in forms containing 58, 39 (CCK39), 33 (CCK33), and eight (CCK8) amino acid residues but the relationships between different forms is ill understood. In this study we have shown that CCK8-like material is formed from CCK33/39 during circulation.

Six fasted normal volunteers received intravenous natural porcine CCK (Kabi Diagnostics) at a measured rate of 0.7-2.5 pmol/kg/min for 15 minutes. CCK forms were separated on Sephadex-G50 and measured by C-terminal specific radioimmunoassay. CCK in infusates eluted chiefly in the characteristic position of CCK33 and CCK39 (CCK33/39). A second peak, eluting between CCK33 and CCK8, accounted for 0-15% and CCK8-like material accounted for less than 3% of immunoreactivity. During infusions CCK33/39-like immunoreactivity appeared in plasma and rose to a mean concentration of 49 pmol/l at the end of the infusion. In addition, CCK8-like material was detected during all infusions, rising about 3 minutes later than CCK33/39 to a mean concentration of 48 pmol/l at the end of the infusion. A steady state was not achieved but both forms became undetectable (<10 pmol/l) 11 minutes after the infusion. The CCK-8-like material seen in normal human plasma may be the product of post secretory cleavage of larger forms.

P123
Methods to assess 'enzyme induction' in patients with idiopathic pancreatitis
L N SANDLE, D W K ACHESON, L P HUNT, A H GOWENLOCK, AND J M BRAGANZA (Departments of Biochemistry and Gastroenterology, and Faculty of Medicine Computation Group, Royal Infirmary, Manchester) Recent studies suggest that pancreatitis may be facilitated by an imbalance between enzyme induction and available antioxidants. There is a need to assess this induction/antioxidant axis. We have compared the information on induction provided by various tests done in the same week on 11 patients with idiopathic recurrent pancreatitis, without overt liver disease. The last attack of pain in these patients occurred between one week and 12 months before the tests: the time since their first symptoms varied widely, between two months and 13 years.

The group displayed: (1) rapid theophylline clearance, indicating induction of cytochromes P450 (median 179, vs 74 ml/kg/h in controls, p<0-005); (2) accelerated early-phase disappearance of sulphobromophthalein, suggesting induction of ligandin (mean k, 23-0, vs 14-3%/min in controls, p<0-025); (3) increased D-glucaric acid excretion in 'spot' samples of urine, reflecting heightened 'phase II' reactions (median 3-7, vs 2-9 mmol/mmol creatinine in controls, p<0-025), (4) increased post-secretin bilirubin output, suggesting induction of haem oxygenase as well as 'phase II' reactions (median 8363, vs 4000 u/ml in controls, p<0-025). Theophylline clearance was increased in nine of the 11 patients: none of the other induction 'markers' achieved this sensitivity.

The theophylline test is thus the obvious choice to assess the induction component of the induction/antioxidant axis in pancreatic disease.

P124
Modified sham feeding induces gall bladder contraction by an atropine-sensitive, CCK-independent mechanism
W P M HOPMAN, G M P HOUBEN, M C A VERMEULEN, J B J M JANSEN, G ROSENBUSCH, AND C B H W LAMERS (Departments of Gastroenterology-Hepatology, and Department of Radiology, Universities of Nijmegen and Leiden, The Netherlands) This study was undertaken to determine whether modified sham feeding induces gall bladder contraction, to assess the relative contribution of the cephalic phase to postprandial gall bladder contraction, and to elucidate the mechanism of cephalic stimulation of gall bladder contraction. On separate mornings eight fasting healthy volunteers (four men, four women, 20-65 years) underwent the following studies: sham feeding during 30 minutes, sham feeding after atropine (0-015 mg/kg as bolus followed by infusion of 0-005 mg/kg/h), and ingestion of the same meal in 30 minutes. Gall bladder volumes were measured by ultrasonography and plasma CCK by a sensitive and specific radioimmunoassay. Sham feeding induced a significant gall bladder contraction of 33±4% of the original volume (p<0-005). After ingestion of the meal gall bladder contraction was 67±47% (p<0-0001). Gall bladder contraction after modified sham feeding was abolished by atropine. Plasma CCK concentrations were not affected by sham feeding, whereas ingestion of the meal increased plasma CCK from 2-3±0-6 to 4-6±1-1 pm (p<0-001).

We conclude that modified sham feeding induces gall bladder contraction by an atropine-sensitive, CCK-independent mechanism. The extent of gall bladder contraction after modified sham feeding was about half of that after ingestion of the meal.

P125
Diagnosis and management of pancreatic duct injuries in children: a report on four cases
R I HALL, M I LAVELLE, AND C W VENABLES (Departments of Surgery and Radiology, Freeman Hospital, Newcastle upon Tyne) Major pancreatic injuries in children are difficult to diagnose and may go unrecognised for very long periods. Of crucial importance is the identification of those patients with damaged pancreatic ducts, because they require urgent surgical treatment. We have encountered four children, aged three to 13 years, with major pancreatic injuries. Although three had sustained the type of bicycle and sledging accidents associated with pancreatic injury, the diagnosis was delayed in all children for periods of up to one year. All children complained of persistent abdominal pain and vomiting. Traumatic pancreatitis was suggested by raised serum amylase concentrations in each case. Ultrasound scans identified pseudocysts in three, although the location was incorrect in one. Computed tomography scanning suggested a
lacerated pancreas in one, but was unhelpful in another. ERCP was performed under general anaesthetic in all patients. The presence and location of the duct injury was correctly identified in every case. Distal injuries (two) were treated by distal pancreatectomy, proximal lacerations (two) were internally drained into Roux-en-Y loops. All patients recovered. ERCP should be performed in all children with traumatic pancreatitis and any duct injury identified must be treated by urgent surgery.

P126 Evidence for an inhibitory effect of bombesin on pancreatic polypeptide secretion in man

A J L DE JONG, J P M BLAuwHOF, M C A VERMEULEN, AND C B H W LAMERS (Departments of Gastroenterology-Hepatology, Universities of Nijmegen and Leiden, The Netherlands) Bombesin containing nerves have been demonstrated in the pancreas. Because infusion of bombesin stimulates the secretion of pancreatic polypeptide (PP), it is possible that bombesin is involved in postprandial PP secretion. To determine the interactions between bombesin and food in the regulation of postprandial PP secretion, we have studied the effect of increasing doses of bombesin (1.25 and 5 ng/kg/min for two hours) on postprandial PP secretion in six healthy volunteers (four men, two women, 20-26 years). Thirty minutes after the start of the bombesin infusion the subjects ingested a liquid test meal. As expected the meal induced significant increases in plasma PP from 17±3 to 47±8 pm (p<0.01). Infusion of bombesin did not stimulate, but rather inhibited and even abolished postprandial PP secretion in a dose-related manner. Integrated postprandial plasma PP secretion during saline infusion was 1850±362 pm/90 min, 1245±542 pm/90 min (ns) during 1 ng/kg/min, 668±218 pm/90 min (p<0.05) during 2.5 ng/kg/min, and 426±478 pm/90 min (p<0.01) during 5 ng/kg/min bombesin. Infusion of the three doses of bombesin without the meal induced small, non-significant increases in plasma PP. After stopping the bombesin infusion, however, a steep, dose-dependent increase in plasma PP was found (13±5 pm after 1 ng/kg/min, 29±7 pm after 2.5 ng/kg/min bombesin; p<0.05).

The findings of the present study suggest that bombesin stimulates the secretion of an inhibitor of PP release. The nature of this inhibitor is at the present time unknown.

P127 Partial purification of pancreotide

A H HARPER, A J C HODD, J M MUSHENS, J R SMY, C SNELL, P SNELL, AND R K VEITCH (Department of Pharmacology, Sunderland Polytechnic, Medical School, Newcastle University, and MRC Neuroendocrinology Unit, Newcastle General Hospital, Newcastle) Pancreotide is an aqueous alcohol peptide extract of distal but mucosa prepared by precipitation onto bile salts at pH 3.9. Pancreotide iv in chloralose-anaesthetised cats inhibits secretion of pancreatic juice (antisecretin effect) and gastric pepsin secretion. In cats and guinea pigs gall bladder contractility is also inhibited (anticholecystokinin effect).

Reprecipitation of crude pancreotide from aqueous alcohol at pH 4-1 followed by extraction with acid alcohol and precipitation with acetone, increased the specific activity six-fold and reduced the bile salt content by 85%. When these partly purified preparations were subjected to isoelectric focusing with ampholines in Ultrodex gel, two peaks of antisecretin activity were revealed. One at pI 8-1-8-3 contained approximately 1/3 of the recovered activity, and the other at pI 4-8-5-1 contained in addition all the recovered anticholecystokinin activity. Both fractions inhibited pepsin secretion. The material at pI 8-1-8-3 cross reacted strongly with antibodies to PYY (S R Bloom, personal communication). Furthermore, when injected iv into cats it produced a small pressor response, whereas the pI 4-8-5-1 material produced a small depressor response.

The activities at pI4-8-5-1 do not coincide with those of characterised peptides of the distal gut and include all the effects of pancreotide.

P128 Preliminary evaluation of a modified PABA test

W H BRADBURY, A R W FORREST, C D HOLDsworth, A ROB, AND J R WORTHERS (Department of Clinical Chemistry and Gastrointestinal Unit, Royal Hallamshire Hospital, Sheffield) The combined BT PABA/14C test is accepted as a specific and sensitive test of pancreatic function. The usual analytic method for urinary PABA is, however, subject to drug interference. We have investigated anthranilic acid, the orthoisomer of PABA as a substitute for 14C PABA in the BT PABA/14C test. Anthranilic acid is absorbed and metabolised independently of pancreatic chymotrypsin.

The test has been evaluated in normal volunteers, patients with known pancreatic steatorrhoea and patients with suspected pancreatic disease.

After fasting, BT PABA 1 g and anthranilic acid 340 mg was taken with water. Urine was collected for six hours and both isomers were measured by high performance liquid chromatography (HPLC) using a previously unpublished method. An excretion ratio (% PABA recovery/anthranilic acid recovery) was calculated.

The test clearly distinguished between normal subjects (excretion ratio 0.63-1.14) and patients with known pancreatic steatorrhoea (excretion ratio 0.13-0.43). Patients found to have no evidence of pancreatic disease had excretion ratios in the range of the normal subjects. Those with equivocal Lundh tests had excretion ratios of 0.467-0.837. This modified test may become a useful alternative to the BT PABA/14C test, and eliminates problems with both drug interference and the administration and counting of 14C.

P129 Absorption of omeprazole in Zollinger-Ellison syndrome is accelerated by alkalali

C B H W LAMERS, L TEUNISSEN, AND J B M J JANSSEN (Departments of Gastroenterology and Hepatology, Universities of Nijmegen and Leiden, The Netherlands) Omeprazole is a potent inhibitor of gastric acid secretion in patients with Zollinger-Ellison syndrome. As omeprazole is inactivated by acid, an enteric-coated preparation has been developed from which the drug is released only when the pH is greater than six. About half of patients with Zollinger-Ellison syndrome, however, show low inhibition of gastric acid secretion in the first hours after ingestion of the drug. We have measured the absorption of 80 mg omeprazole ingested either as enteric-coated preparation together with 250 ml saline or as enteric-coated preparation together with 250 ml (40 mmol) sodium bicarbonate or as uncoated preparation with sodium bicarbonate in six patients with Zollinger-Ellison syndrome (three men, 35 women; 35-63 years). Plasma samples for omepra-
zole were obtained at regular intervals for three hours. There was a wide variation in omeprazole absorption with the enteric-coated preparation and saline (AUC 0–18.8, median 0–6 μmol/l/3h). Ingestion of enteric-coated omeprazole with sodium bicarbonate resulted in significantly greater absorption (AUC 2.1–23.1, median 14.3 μmol/l/3h; p<0.05). Omeprazole absorption after uncoated omeprazole with sodium bicarbonate (1.4–31.2, median 4.3 μmol/l/3h) was slightly greater than that with the enteric-coated preparation and saline (p<0.10), but not significantly different from that with enteric-coated omeprazole and sodium bicarbonate. The acid inhibitory effect of omeprazole was related to the absorption of the drug. In tests with an AUC of more than 0.2 μmol/l/h acid inhibition was greater than 80%, whereas in tests with an AUC of less than 0.2 mmol/l/h inhibition was smaller than 30%.

We therefore conclude that addition of alkali accelerates absorption of omeprazole in patients with Zollinger-Ellison syndrome resulting in early inhibition of acid secretion.

P130
Ultrasonography in choleodocholithiasis – a new look
M TOBIN, R M MENDELSON, G LAMB, AND I T GILMORE (Gastroenterology Unit and Department of Radiology, Royal Liverpool Hospital, Liverpool) Ultrasonound (US) diagnosis of common duct stones has been disappointing. To assess its accuracy in a specialist centre and its role as a screening test in selecting patients requiring direct cholangiography, US was done by one of two experienced operators immediately before endoscopic cholangiography (ERC) in 104 consecutive patients referred for suspected biliary disease.

Of 36 patients with choleodocholithiasis on ERC, US showed stones in 20, common duct dilatation in a further 10, and failed to visualise the common duct in five. The sensitivity was 64.5% and 55.5% for calculus visualisation and 97% and 83% for an abnormal common duct, excluding and including technical failures respectively. Of 39 normal cholangiograms, US agreed in 37 (95%), was technically unsatisfactory in one, and incorrectly diagnosed a calculus in one. One further false positive US for calculus occurred in 16 patients showing ERC dilatation only. Using US visualisation of common duct calculus, dilatation or technical failure as criteria for proceeding to ERC would have resulted in the omission of only one patient with calculi and 14 ‘unnecessary’ cholangiograms. Ultrasound is a sensitive screening test in suspected choledocholithiasis. A normal US virtually excluded choledocholithiasis in this series.

P131
Electrohydraulic lithotripsy of gall stones, and in vitro study
J D HARRISON, D L MORRIS, JULIE HAYNES, AND D C WHERRY (Department of Surgery, University Hospital, Nottingham) Electrohydraulic lithotripsy is widely used in the endoscopic management of urinary tract calculi. Its role in the management of gall stones has received little attention.

An electrohydraulic generator and probe (ACM) with variable voltage, plus length and number of pulses used to fragment 12 mixed pigment/cholesterol gall stones recently removed from five patients in 0.9% saline. Two stones (6×7, 5×4 mm diameter) were fragmentated at 60 volts (V), two required 80 V (9×7, 7×5 mm), two were fragmented at 100 V (13×12, 12×13 mm) while two were not affected until 120 V was used (12×8, 15×13 mm). In only one stone did we fail to achieve fragmentation (28×21 mm). Three stones (7×5, 5×6, and 7×6 mm) were then fragmented within human and ovine bile ducts at 60, 60 and 120 V without obvious macroscopic evidence of damage to the ducts.

Direct control of the end of the probe with bile duct or gall bladder wall produced a perforation even at 60 V, but both were resilient to shock waves (rather than spark effect).

Most gall stones may be fragmented by the electrohydraulic lithotripter. This instrument may be useful to both endoscopist and surgeon for impacted bile duct calculi.

P132
Results of endoscopic stenting in malignant stricture of the biliary tract
J STOKER, J DEES, M VAN BLANKENSTEIN, AND G A J NIX (Departments of Internal Medicine and Radiology, University Hospital Rotterdam, Rotterdam, The Netherlands) In 1983–1984 endoscopic placement of a biliary stent (EPS) by the Huibregtse-technique was attempted in 123 patients suffering from malignant stricture. The results were assessed in relation to the localization of the stricture, a comparison between common duct and perihilar strictures being found to be relevant. Stenting was successful in 97 cases (79%). In common duct strictures the failure rate was 11.8%. After successful stenting early complications were seen in 10% and there was a satisfactory drainage in 94%. In hilar tumours these percentages were 42, 29 and 73 respectively. Early complications included haemorrhage, requiring transfusion in five patients and cholangitis in 11. Mean survival in 79 patients who were only treated by stent drainage was 18-6 weeks. Late complications were recurrent jaundice in 33 patients, and fever in four patients. Only eight patients were referred for stent replacement.

We conclude that (1) EPS is an effective and safe treatment for malignant strictures of the common bile duct. It is less successful in hilar strictures which may be more amenable to percutaneous drainage. (2) Patients and their doctors should be alert to the necessity of prompt stent replacement if fever or jaundice recur.

P133
Randomised trial comparing endoscopic and percutaneous prostheses in poor risk patients with malignant obstructive jaundice
A G SPEER, P B COTTON, A HATFIELD, R R MASON, R C G RUSSELL, J LEUNG, T P YIN, J LENNARD-JONES, J BAILIE, AND K MCCRAE (Departments of Gastroenterology, Radiology and Surgery, The Middlesex and London Hospitals; Cancer Research Campaign Centre, King’s College Hospital, London) Bypass surgery for palliation of biliary obstruction due to malignancy has a high mortality in poor risk patients. We have compared the insertion of a prosthesis via the percutaneous transhepatic method (PTE) or endoscopically (EP) in a prospective randomised trial. Seventy five patients with primary tumours (pancreatic and cholangiocarcinoma) who were judged to be unsuitable for surgery were entered. Analysis was according to a sequential block design. The results are presented on a strict intention to treat basis. The two groups of patients were well matched apart from the incidence of hilar stricture – EP – 49%; PTE – 28%.

Criterion for significance (p≤0.016) was achieved for 30 day mortality using log rank analysis stratified according to site of lesion. The significantly increased early mortality and risk of complications of PTE were related to puncturing the liver –
haemorrhage, biliary peritonitis and abscess formation. The endoscopic method is now the preferred route for insertion of biliary prostheses. The relative merits of prostheses and bypass surgery in fitting patients are being compared in another trial.

ENDOSCOPY
P133–135

P134
Balloons against bougies for dilatation of benign oesophageal stricture – a randomised prospective trial
J C COX, R K WINTER, R JONES, J F DYET, D R SUTTON, AND J R BENNETT (Hull Royal Infirmary, Hull) Balloons have been advocated as safer and more effective than bougies for dilating oesophageal strictures, but there is no evidence to support this.

Twenty-six patients, aged 30–90 years, were randomly allocated to dilatation by bougie or balloon to a predetermined diameter. Stricture size was measured before, one week and one month afterwards using the barium sphere technique. Patients' acceptance of each technique was assessed by a simple scoring system.

All dilatations were achieved without complications. There was no significant difference in the mean change from the initial measurement between the two groups at one week or one month. In 12 patients measured at three months, four months, and five months after dilatation the diameter diminished more rapidly in the balloon group than in the bougie group (p<0.1). Two patients in each group required repeat dilatation because of dysphagia. There was no significant difference in the patients' acceptance score between the two groups.

Balloon dilatation appears to be a safe treatment for benign oesophageal strictures, but is neither more effective nor more acceptable to patients than bougienage.

P135
Endoscopic injection of adrenaline in bleeding peptic ulcers
J W C LEUNG AND S C S CHUNG (Combined Endoscopy Unit, Departments of Medicine & Surgery, The Chinese University of Hong Kong, Hong Kong) Early endoscopy frequently reveals active bleeding lesions in patients with upper gastrointestinal haemorrhage. We report a simple method of endoscopic haemostasis in bleeding peptic ulcers using local injection of adrenaline. Between November 1984 and April 1985, 206 patients were admitted with upper gastrointestinal haemorrhage. Twenty-one patients (15 men, three women, mean age of 48 years) had an actively bleeding ulcer (17 DU, four GU) on endoscopy. Mean haemoglobin on admission was 9.5 g/dl, and 15 patients required blood transfusion (mean=5 units, range 1–12). Using a needle injector through an endoscope, aliquots (0.5–1 ml) of 1:10 000 adrenaline (volume=1–6 ml, mean=3.2 ml) were injected submucosally around the bleeding site. No complication was observed. Initial haemostasis was achieved in all. Three patients rebled at four hours, three days and four days later, and two (one GU, one DU) required emergency surgery and the third (DU) improved with conservative treatment. Thus definitive haemostasis was achieved in 19/21 patients (90.5%). Repeat endoscopy at eight weeks showed healed ulcer in 13 patients, while six patients are awaiting reassessment. Local injection of bleeding ulcers with adrenaline is a simple, effective and economical method for haemostasis in patients with bleeding peptic ulcers.

The British Society of Gastroenterology

The dangers of surgical treatment for perianal Crohn's disease
M R B KEIGHLEY AND R N ALLAN (Department of Surgery, General Hospital, Birmingham) We have examined 202 consecutive patients with Crohn's disease to determine the current status of perianal disease together with the influence of surgical treatment on outcome. The mean duration of follow up was 7–6 years (range: 1–36 years) and all except 35 patients (17%) had undergone some form of intestinal resection.

One hundred and ten patients had evidence of perianal disease at some time in their illness (54%). The principal lesions were skin tags (n=75), anorectal abscesses (n=53), fistulae (n=52), fissures (n=35) and stricture (n=19). Seven fissures were treated by dilatation but only four were improved and one became incontinent. Twelve fistulae were laid open but only one resolved and six became incontinent. Fifteen abscesses were drained but only five resolved and four developed a fistula. None of the six strictures treated by dilation were improved. Proctectomy was performed in 36 patients: 19 of 27 with perianal disease had a persistent perineal sinus (70%), compared with none in the nine having proctectomy and no perianal disease (10%: p<0.01). Seventeen of the 19 patients with an unhealed perineal sinus had a rectal stricture.

These results imply that local surgery should be avoided for perianal Crohn's disease and that proctectomy for rectal stricture is usually associated with a persistent perineal sinus.

T2
Segmental colonic function in experimental steatorrhoea decreased capitation of the proximal colon
R C SPILLER, M L BROWN, AND S F PHILLIPS (Mayo Clinic, Rochester, Minnesota, USA) In steatorrhoea, long chain fatty acids impair colonic absorption, however, the importance of altered colonic transit in the associated diarrhoea is unknown. After passing an orocaecal manometry tube, we have infused the normal unprepared colon (n=6) at 2.5 ml/min with a solution simulating postprandial colonic inflow in steatorrhoea [oleic acid emulsion (OA), 5 g/100 ml]. Seven control subjects received 0.9% NaCl; both solutions also contained 2.5 g/l lecithin, 10 mmol/l Na taurocholate, and 20 mmol/l glycerol (all adjusted to pH 6.4, 290 mosmol/kg) and were labelled with 1.2 mCi/ml of 111In DTPA. Passage of 111In from ascending (AC) to transverse (TC) and descending (DC) colon and recto-sigmoid (RS) were quantified by serial 1-min gamma scans.

Oleic acid emulsion induced episodic, prolonged (>10 sec), propagated pressure waves (>60 mm Hg) in the AC (mean±SEM, 75±3 mm Hg, 30±2 sec) which were associated with cramps and mass movements of isotope caudally. Such waves occurred 4.1±2.4 times/h during OA infusion, but only once in 33 h with saline, p<0.001. Concomitantly, isotope overflowed from the AC earlier during OA (19±3 vs 39±6 min) and accumulated in the DC and RS more rapidly. reaching >50% infused dose by 10±2±14±8 min (range 34–135), p<0.001 vs saline (all >183 min). Urgent defecation occurred
after 312±20 ml of OA compared with 1049±71 ml of saline (p<0.001). This novel research technique, the 'isotope colo-scintigraphy' which quantifies regional colonic transit, promises new insights into the pathophysiology of diarrhoea.

**T3**

**Randomised trial of vasopressin and vasopressin plus nitroglycerin in the control of acute varical haemorrhage**

A E S Gimson, D Westaby, J Hegarty, A Watson, and R Williams (Liver Unit, King's College Hospital and School of Medicine & Dentistry, Denmark Hill, London) The systemic haemodynamic complications of vasopressin (VP) have been all important limitation to its use in management of varical haemorrhage. Recent studies suggest that nitroglycerin (NG) may reverse these changes and augment the fall in portal pressure. A randomised trial was undertaken to compare the efficacy and complication rate of VP alone (0.4 units/min constant infusion and VP + intravenous NG (40-400 µg/min to maintain systolic blood pressure ≥100 mmHg) for a period of 12 hours. Seventy two bleeding episodes in 57 patients were included: VP alone on 34 and VP + NG on 38 occasions. At the end of the 12 hour period haemorrhage had stopped significantly more frequently in the VP + NG group (26 of 38; 68%) compared with the VP group (15 of 34; 44%, p<0.05). Major complications requiring cessation of therapy were significantly less common in the VP + NG group than in the VP alone group (one and seven respectively, p<0.02). Hospital mortality was similar in both groups. In conclusion, the addition of NG to a VP infusion significantly reduces the complication rate and has been shown to be more effective in the management of active varical haemorrhage.

1983 we have carried out such a study in which patients over 60 years of age admitted to the Nottingham City and University Hospitals with a bleeding peptic ulcer have been questioned about immediate antecedent drug intake. For each patient a community control matched for age and sex was selected from the same general practice list. The same questions were also posed to an age and sex matched hospital control by a trained interviewer (GF) using the same structured questionnaire. Ninety per cent of the 193 community controls so far approached agreed to participate as did all the hospital controls.

Two hundred and thirty of the 289 eligible cases admitted during the two year study period, were directly questioned. Thirty five per cent were users of NSAIDs compared with 14% of 230 hospital controls and 15% of 173 community controls. Patients with bleeding peptic ulcers were nearly four times as likely to be NSAID takers as hospital or community controls (relative risk 3.8, x²=26.1 and 3.7, x²=21.7 respectively, p<0.001 in both cases by McNemar's test). By extrapolation from these results, of about 1000 deaths annually of patients over the age of 60 admitted with bleeding peptic ulcers approximately 200 would be associated with NSAID use.

**T5**

**Gluten sensitive oral ulceration in the absence of coeliac disease**

C O'Mahony, C O’Farrelly, D G Weir, T Finch, and C F Feighery (Departments of Immunology and Clinical Medicine, St James’s Hospital, Dublin, Eire) The clinical management of severe recurrent oral ulceration is often unsatisfactory and such ulceration may continue for life. Symptomatic treatment alone is used unless, as is the case in a small proportion of patients, an underlying systemic illness, such as coeliac disease, is found.

The purpose of this study was to determine if gluten sensitive oral ulceration occurred in the absence of coeliac disease. Nine patients, presenting primarily with severe recurrent oral ulceration, were investigated. All had normal small intestinal biopsies. Three patients had raised alpha-gliadin antibodies, however (raised levels are found in up to 85% of patients with coeliac disease). All three were HLA DR3 – the antigen found in up to 90% of our coeliac patients. A trial of gluten free diet was instituted in these three patients. Two had an excellent response with complete remission of the ulceration and alpha-gliadin antibody levels returned to normal. A subsequent gluten challenge brought an acute relapse in oral ulceration although the small intestinal biopsy remained normal. Alpha-gliadin antibody remained elevated in the non-responding patient and dietary assessment showed non compliance.

Two of the remaining six patients with oral ulceration but negative alpha-gliadin antibodies also went on a gluten free diet but no clinical improvement was noted.

This study shows that in a subpopulation of patients with severe recurrent oral ulceration the lesion responds to gluten exclusion. Thus the clinical spectrum of gluten sensitive disease is wider than is often suspected.

**T6**

**Influence of neuropeptide Y on rabbit ileal mucosa**

K J Moriarty, N B Higgs, M Woodford, J M Allen, S R Bloom, and L A Turnberg (Department of Medicine, Hope Hospital, Salford, and Department of Medicine, Hammersmith Hospital, London) Neuropeptide Y (NPY) has been shown in high concentration in the enteric nervous system and in particular in the submucosal plexuses of the small intestine of a variety of mammalian species including man. This distribution suggests that NPY may play a role in the control of mucosal fluid transport in the intestine and we therefore examined its effect on segments of rabbit ileal mucosa, stripped of muscle coats, and mounted in flux chambers. NPY, added to the serosal aspect of the mucosa in concentrations of 1×10⁻⁹ M to 1×10⁻⁷ M, caused a rapid dose-dependent fall in short-circuit current and electrical potential difference across the mucosa, a significant response being observed at 1×10⁻⁹ M. The maximal decrease in short-circuit current was 1-12±0.19 µmol/cm²/h (p<0.001) and in potential difference was 1-62±0.29 mV (p<0.001) at 1×10⁻⁷ M. A fall in short-circuit current and potential difference is usually associated with enhanced absorption and this response is similar to that induced by opiates, which influence the mucosa indirectly via a presumed neural intermediary, such as NPY. Application of morphine (10⁻⁶ M and 10⁻⁴ M) to the serosal aspect of the mucosa caused a decrease in short-circuit current and potential difference. The response of the ileum to morphine was not however...
influenced by pretreatment with NPY (1-2x10^-7 M).

We conclude that these findings support a role for NPY in the control of ileal ion absorption and suggest that NPY is not the neural mediator of opiate responses in the mucosa.

**BSG/BASL LIVER**

**T7**

**Liver copper content correlates poorly with severity of histological abnormality in Indian childhood cirrhosis (ICC)**

J C TALBOT, M S TANNER, AND M PRADHAN
(Departments of Pathology and Child Health, University of Leicester and King Edward Memorial Hospital, Pune, India)

Among 327 0-14-year-old children with liver disease in Pune, 139 (aged 7-66 months) had liver biopsies diagnostic of ICC. Characteristic features were: peri- cellular fibrosis (96%); hepatocyte ballooning (92%); Mallory's hyaline (91%); foci of polymorphonuclear leucocytes (96%); spotty necrosis (64%); oedema and rhodanidine staining (all). There was disruption of the limiting plate in 99%. Mild bile duct proliferation was seen in only 33%, cholestasis in only 18% (25 cases, including six necropsies), and fat was absent.

Histological features were graded 0 (absent) to 3 (severe). Liver copper, measured by atomic absorption spectrophotometry, was grossly raised (1610-2977 µg/g dry weight, normal <100 µg/g), and correlated with rhodanide (p=0.009) and weakly with oedema (p=0.16), but did not correlate with any other histological feature. Raised hepatic copper in other disorders also did not correlate with histological severity.

Although the histological changes in ICC may result from copper overload, the severity of damage bears no relationship to copper content at the time of examination.

**T8**

**Effects of a long acting somatostatin analogue (SOM 201-995) on the activity of the reticuloendothelial system (RES) in rats**

S A JENKINS, J N BAXTER, AND R SHIELDS
(Department of Surgery, University of Liverpool, Liverpool)

Because the activity of the RES is markedly reduced in cirrhosis, the inability of the liver to detoxify enterically derived endotoxin may accentuate existing hepatic damage. Somatostatin (SMS) has been shown to be effective in controlling acute vasceral haemorrhage and preliminary reports suggest that it is cytoprotective with respect to the liver. The purpose of this study was to investigate the effects of a new long acting analogue of somatostatin (SMS 201-995) on RES function in rats. Male Wistar rats received 2 µg SMS 201-995 bd sub- cutaneously for seven days. A control group of rats received similar injections of the same volume of isotonic saline. Reticuloendothelial system function was assessed by the uptake of technetium sulphur colloid. Cr^51 red cells damaged by acetylphenylhydrazine and colloidal carbon by the liver and spleen. A further study was undertaken to establish whether SMS 201-995 would protect against E.coli endotoxaemia. Administration of SMS 201-995 significantly increased the liver to blood ratio (6.5±0.9 to 27.1±5.1) (p<0.01 Student's t test) and spleen to blood ratio (4.66±1.1 to 29.3±4.4) of sulphur colloid. Similarly, SMS 201-995 stimulated the uptake of colloidal carbon and Cr^51 red cells by the liver and spleen. Furthermore, SMS 201-995 significantly improved survival after intraperitoneal administration of E.coli endotoxin (p=0.004, Log Rank Test). These results suggest that SMS 201-995 may stimulate the RES system and be of value in protecting against endotoxaemia in patients with cirrhosis.

**T9**

**Hepatic infarction after orthotopic liver transplantation**

P POWELL-JACKSON, R J POLSON, R Y CALNE, AND R WILLIAMS
(Liver Unit, King's College Hospital and School of Medicine & Dentistry, Denmark Hill, London)

Although the clinical features of hepatic infarction due to hepatic artery thrombosis (HAT) after orthotopic liver transplantation are well described, the picture that can occur with thrombosis of the portal vein or hepatic veins is less well documented. In 45% (5/11) of cases of hepatic infarction proven by necropsy or reoperation that occurred in 199 patients in our series, thrombosis of vessels other than the hepatic arteries was the cause - portal vein thrombosis in three and hepatic vein thrombosis in two cases. In all cases the clinical picture was characterised by a rapid deterioration of consciousness progressing to coma within 24 hours, hypotension and hypoxia with levels of aspartate aminotransferase >600 IU/l and prothrombin time over 25 seconds prolonged. Death within 12 days of onset of symptoms occurred in 91% (10/11) of these cases and was responsible for 13% (10/75) of all deaths occurring within six weeks of liver grafting. In only four patients (two with HAT) could technical difficulties be identified while possible aetiological factors in the remainder included prolonged hypotension in three and a presumed coagulopathy in one patient with Budd Chiari. In the one survivor of this series, a suitable donor became available within 12 hours of hepatic infarction and retransplantation was successfully carried out.

**T10**

**Increased iron absorption after chronic ethanol feeding in rats**

R MAZZANTI, S K SRAI, M A BOSS, E S DEBNAM, AND P GENTILINI (INTRODUCED BY O EPSTEIN)
(Clinica Medica IV, Universita di Firenze, Italy, and Royal Free Hospital School of Medicine, London)

Alcoholics often have an increased amount of iron in the liver, which may contribute to the development of alcoholic liver disease, however the mechanism is unknown. It has been shown that chronic alcoholism reduces the enterocyte turnover and increases galactose absorption. Whether chronic alcohol intake affects iron absorption is still controversial. The aim of this study was to investigate the effect of chronic alcoholism on whole body iron absorption in rats. Twenty eight adult male Sprague-Dawley rats were pair fed a diet containing either ethanol as 36% of total calories or an isocaloric diet where fat was substituted for ethanol. On the 28th day, four hour fasted rats were given an oral dose of 59Fe (0-5 µCi) and then immediately counted by a whole body counting technique. 59Fe levels were then monitored in the following nine days, using the same technique. Although ethanol fed and control rats had a similar hepatic iron levels (59-5±5.8 vs 60.2±7.41 µg/100 mg dry liver weight (mean±SEM), the 59Fe total body iron content (% of the administered dose) was significantly greater in the ethanol group (75±3) compared with control group (45±4; p 0.001).

These results show that chronic ethanol intake increases iron absorption in rats. This phenomenon may be one explanation of the abnormally high liver iron levels in alcoholics.
T11 The Birmingham liver transplantation programme: our early experience

D Clements, R M Kirby, S Hubscher, W A Jurewicz, M Sealy, E Elias, and P Mcmaster (Queen Elizabeth Hospital, Edgbaston, Birmingham) Our indications for liver transplantation are primary liver tumours without evidence of dissemination, chronic liver disease at end stage (projected life expectancy less than six months), and acute liver failure. Of the patients referred for assessment approximately one quarter undergo transplantation; the remainder being too early in the course of their disease, receive other medical or surgical therapy, or are unsuitable for other reasons.

Twenty five grafts have been carried out in 24 patients. The diagnosis was primary biliary cirrhosis in eight, and primary liver tumour in eight. The other eight patients were grafted for 

T12 Does male sex predispose to the HBsAg carrier state or to chronic liver disease?

M Ciarameone, A Floreani, M Zagolin, E Pornaro, and R Naccarato (Department of Gastroenterology, Policlinico Universitario, Padova, Italy) The male/female differences in response to HBV is a still discussed problem. In the attempt to clarify this point we studied 319 adult HBsAg carriers (aged 15 to 70 years) presented during epidemiological screening or blood testing for suspected liver disease. Two hundred and twenty two were men (M/F=2:3). Out of the men 55% had CALD, 23% had CPH and 22% were healthy carriers, while among women 32% had CALD, 16% had CPH and 52% were healthy carriers. M/F ratio was 0.98 in healthy carriers, 3.4 in CPH and 3.9 in CALD. Age at presentation, prevalence of HBsAg and seroconversion rate to anti-HBe were similar in men and women in each group, while cofactors such as drug addiction, alcohol abuse, Delta infection, infection in adulthood were significantly associated with liver disease and were more frequent in males. Evidence of intrafamilial infection was present in 16% of men and 29% of women and was more frequent in the healthy carrier group (34%), suggesting that, when the HBV infection occurs in the household and/or at early ages the risk of chronicity is the same for males and females. We tested this hypothesis in 86 siblings from high risk families: the HBV infection prevalence was 46-6% in men and 43-5% in women and the HBsAg carrier rate was 34% in men and 38% in women.

In conclusion, the difference in the HBsAg carrier rate between sexes is increasing with the severity of the disease. Other harmful factors (more frequent in men?) and/or the age at infection can partially explain this phenomenon.

T13 The enigma of asymptomatic primary biliary cirrhosis

M R Lucey, J M Neuberger, and R Williams (Liver Unit, King’s College Hospital and School of Medicine & Dentistry, London) Primary biliary cirrhosis in patients without symptoms of hepatic disease (‘asymptomatic PBC’) is well described. Although progression occurs in some cases, these patients are said to have normal life expectancy. In order to consider whether asymptomatic PBC is a benign condition we reviewed the clinical course of 231 patients with PBC followed from 1970 to 1984 of whom 31 (22 women) had no hepatic symptoms, as previously defined, up to the time of diagnosis. At diagnosis the mean age of symptomatic and asymptomatic patients was similar (55 vs 56 years) and disease severity was less in asymptomatic patients; serum bilirubin (median, range) 13 μmol/l, 3-65 (asymptomatic), 35 μmol/l, 4-390 (symptomatic). Life table analysis showed longer survival in asymptomatic patients; actuarial five year survival: asymptomatic 70%, symptomatic 50% (p=0.05). In a median follow up period of 45 months, however, 18 (12 women) patients developed hepatic symptoms and their survival from the onset of symptoms was not different from that in patients with hepatic symptoms prior to diagnosis. These data suggest that many patients with asymptomatic PCB do become symptomatic and they should be considered a presymptomatic group in whom the apparent benign course is a consequence of lead time bias.

T14 Autonomic neuropathy and alcoholic liver disease

F Barter and A R Tanner (Department of Medicine II, Southampton General Hospital, North Tees General Hospital, Cleveland) Autonomic neuropathy (AN) has been assessed in 16 patients with proven alcoholic liver disease (ALD), 14 alcoholics from the community without evidence of liver disease and 30 sex and age matched controls attending for endoscopy. Tests of parasympathetic function were heart rate responses to Vasalva, to deep breathing and to standing. Sympathetic function was assessed by BP response to standing and sustained handgrip. The presence of two or more abnormal tests was taken to indicate AN. Fifty six per cent of subjects with ALD, 14% of community alcoholics and none of the controls had AN. Female alcoholics were more likely to develop this complication (80% vs 28%; p=0.004). There was no significant correlation between symptoms and objective signs of AN. Peripheral neuropathy was documented in 64% of both groups of alcoholics, but not in the controls. Alcoholics with AN were older, had been drinking longer and 91% had an associated peripheral neuropathy. Prospective studies in alcoholics with AN would be of interest since studies in diabetics have shown a high mortality and morbidity associated with objective signs of AN.

T15 Screening for haemochromatosis in the UK: preliminary results

A R Tanner, S Desai, W Lu, and R Wright (Department of Medicine II, Southampton General Hospital, North Tees General Hospital, Cleveland) Recent studies in Europe and North America have indicated that the gene frequency for haemochromatosis in caucasian populations is much higher than previously suspected. In these populations the prevalence of heterozygotes (HO) has varied between 9% and 14% with a homozygote (HH) frequency of 0.3-0.5%. In the present study, serum
A1140

Increased incidence of menstrual abnormalities and hysterectomy preceding primary biliary cirrhosis

A J STELLON AND R WILLIAMS (Liver Unit, King’s College Hospital and School of Medicine & Dentistry, London) Menstrual disturbances have been reported in patients with chronic active hepatitis (CAH) and alcoholic liver disease (ALD) but no studies have been described in women with primary biliary cirrhosis (PBC). In this prospective study menstrual, gynaecological and obstetric histories were obtained from PBC patients and compared both with age-matched control subjects and patients with other types of chronic liver disorders. Histories were obtained from 87 patients, aged 35-70 years, with PBC and compared with a control group of 100 age matched (35-71 years) hospital personnel and 80 age matched (34-73 years) female patients with either CAH (45) or ALD (35). A significantly higher rate of hysterectomy and D & C was found in PBC when compared with control subjects (p<0.025 and p<0.05 respectively) and other patients with chronic liver disease (p<0.005 and p<0.05 respectively). Both hysterectomy and D & C were carried out a mean of 10-7 years and 13-2 years respectively, in the majority of patients, before the diagnosis of PBC. The main clinical indications for hysterectomy in PBC was menorrhagia while fibroids (51%), endometrosis (21%) and endometrial polyps (7%) were the main operative findings. Endometrial hyperplasia was detected macroscopically in 24% PBC patients at hysterectomy and 33% patients in which histological material was obtained at D & C. The findings were consistent with an underlying hormonal disturbance favouring oestrogen excess during the presymptomatic stage of PBC.

T17
Prognostic features in chronic active hepatitis

J J KEATING, A J STELLON, P J JOHNSON, C J O’BRIEN, R D JOHNSON, B PORTMANN, J E HEGARTY, AND R WILLIAMS (Liver Unit, King’s College Hospital and School of Medicine & Dentistry, London) Results relating to survival in chronic active hepatitis (CAH) vary between centres and are more likely to depend upon the nature and stage of the disease than the treatment used. We have, therefore, carried out an analysis of presenting features, histology, frequency of relapse, survival and relation to sex in 106 patients (21 men) with ‘autoimmune’ CAH, 69 patients (28 men) with ‘cryptogenic’ CAH and 29 patients (26 men) with HBsAg seropositive (HBsAg+) CAH. Variceal bleeding and encephalopathy were more common presenting features in the cryptogenic group (p<0.01) while the presence of oedema, ascites and jaundice did not differ between the groups (NS). Cirrhosis was more frequent at presentation in the cryptogenic group (53%) than in the autoimmune (30%) or the HBsAg+ group (35%) (p<0.002). Development of hepatocellular carcinoma (HCC) occurred in five men with CAH and in five men with HBsAg+ CAH. The relapse rate per year in autoimmune CAH was 15% for those treated with prednisolone, 4-4% for those treated with prednisolone and azathioprine and 77% for those in whom treatment was withdrawn. This was similar to the relapse rate in the cryptogenic CAH of 15%, 6-2%, and 72% respectively. The overall five year survival was 87% in the autoimmune CAH group compared with 65% in the cryptogenic group and 80% in the HBsAg+ group (p<0.001) although no significant difference in survival was observed in those presenting without cirrhosis. The response to immunosuppressive therapy is comparable in patients with and without autoimmune markers and the worse prognosis in the cryptogenic group appears related to the higher incidence of cirrhosis at presentation. Development of HCC appears to depend more on the sex of the patient rather than the HBV status.

S Moran Graitron, Peter O’Connor, Monica O’Moore, A Speekenbrink, B Keogh, C T Keane, D G Weir, AND R R O’Moore (Departments of Medicine, Clinical Biochemistry and Microbiology, Trinity College, Dublin, Eire) Bacterial contamination of the upper small intestine (USI) in chronic renal failure (CRF) has been implicated in the causation of uraemic diarrhoea and decreased mental alertness possibly due to bacterial production of dimethylamine and trimethylamine (DMA, TMA).

The incidence and extent of contamination in CRF had been estimated as approximately 40% by the 14C glycycholate breath test (14CBT). Intubation and microbiological culture was carried out in 28 patients with positive14CBT. The controls were 18 patients with contaminated small bowel syndrome and 20 normal subjects. Production of DMA, TMA was monitored serially during digestion of a meal (three hours). After receiving antimicrobial therapy, reassessment of mental alertness (Wechsler), was made in 11, and microbial culture and plasma DMA, TMA levels in six CRF patients.

Twenty four of all 28 CRF patients were contaminated. The 14CBT and anaerobic bacterial counts became normal in all CRF patients after antimicrobial treatment. There was also a significant increase in both weight and mental alertness (p<0.01). Serial plasma and intestinal DMA levels increased significantly during the meal (p<0.001). Plasma DMA concentrations also decreased significantly following treatment.

Our findings suggest USI bacterial contamination may be clinically important and relatively common in CRF. Antimicrobial therapy lead to improvement of symptoms.

T19
Macrophages in the microenvironment of coeliac disease
Involvement of the immune system in coeliac disease is well documented; attention has hitherto been focused on antibody responses and cell mediated immune responses. Although there are many macrophages in the lamina propria of the small intestine in coeliac disease, these have not hitherto been studied. We have used simultaneous double labelling of jejunal biopsy cryostat sections with monoclonal antibodies to demonstrate macrophage subsets and their relationship to HLA-DR expression in individual cells in 19 patients with coeliac disease (11 treated, Grades 1 to 3; eight untreated, Grades 3 and 4) and 11 controls.

Antigen presenting macrophages, as identified by RFD1 antibody were a minor subpopulation. In the controls, all such cells expressed HLA-DR whereas up to 70% of antigen presenting cells in coeliac patients had lost their expression of HLA-DR. HLA-DR expression is believed essential for functioning of these cells. Scavenger macrophages, as indicated by RFD2 antibody, were increased about three-fold in coeliac disease as compared with controls, although the proportion of scavenger cells which appeared to be in the activated state, as judged by histochemical markers and HLA-DR expression, was unchanged. Regulatory macrophages have previously been shown to exist in functional assays and are now believed to be identified by the RFD7 marker. Some RFD7 cells in coeliac disease are of a distinctive type, not hitherto described. They are crescentic in shape and surround aggregates of lymphocytes. All these changes were proportional to the degree of pathological damage.

It is clear that macrophages are involved in the immunological disturbances in the intestinal mucosa in coeliac disease. The presence of regulatory macrophages surrounding lymphoid aggregates might suggest that they were in some way controlling the cells within, perhaps being responsible for reducing the expression of HLA-DR and thus reducing antigen presentation and minimising T cell stimulation. The increase in scavenger cells may represent a response to the tissue damage.

**T20**

Inflammatory cell subpopulations in normal and coeliac small intestinal mucosa

**T21**

Small round viruses in acute diarrhoeal disease in children

**T22**

Toddler’s diarrhoea – intestinal hurry?
decreased towards control values. No drugs or basic dietary modification had been used. One child had relapsed one month before the test, after being well over the previous year, and her MCTT increased.

The results of this study show, contrary to what has been accepted, that children with IBT-toddler's diarrhoea have prolonged small bowel transit which decreases as the condition resolves.

T23
Study of postoperative gastrointestinal motility in man using radiotelemetry
D L MORRIS, A G CLARK, D F EVANS, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Abnormal motility has been shown in the stomach and duodenum after operation but has not been measured simultaneously in the small bowel and colon in man.

In 10 patients undergoing cholecystectomy intraluminal pressure was measured by three radiotelemetry capsules. One un­tethered capsule was swallowed 12 hours before operation to allow it to reach the caecum followed by two capsules tethered in the gastric antrum and proximal jejunum. After a period of recording when fasting migrating motor complexes (MCCs) and colonic motility were confirmed, patients underwent surgery. Motility was continuously monitored for up to 72 hours after the operation. In two patients recordings were of insufficient quality for analysis. Fasting jejunal activity returned quickly after operation (mean 100-4 min ±47SD) but with shorter interval (mean 36-6 min ±32SD) compared with normal (approximately 120 min). Normal fasting patterns denoted by a gastroduodenal MMC were not seen in any patient during the recording period, but a typical gastric activity was seen in three patients between 12-24 hours. Colonic motility returned variably from 1-50 hours in six patients, but was absent in two. We have confirmed that gastrointestinal motility is disrupted by anaesthesia and surgery and returned at a variable rate in the stomach and colon and although recovery was more rapid in the jejunum, it was abnormal in type.

T24
Clinical efficacy of peripheral intravenous nutritional support
C M ROYCE, M MULLEE, AND S J KARRAN (University Surgical Unit, Southampton General Hospital, Southampton) Total parenteral nutrition is of proven efficacy in the perioperative period but remains unpopular. Blackburn pioneered the use of isotonic amino acids for nutritional support but their value remains controversial.

Forty six consecutive patients who underwent oesophagectomy for carcinoma were randomly allocated on the day after surgery to receive one of three peripheral intravenous support regimens: (a) an isotonic amino acid solution (Perifusin) at a rate of 1 g/kg/day. (b) an isotonic amino acid solution as above plus 500 ml 20% intralipid/day, (c) 4th dextrose and 0-18% n/saline in equivalent volumes.

Groups (a) and (b) were designated as being 'fed' and group (c) formed the 'unfed' clinical control group. The regimen was continued until adequate oral fluid intake was reestablished. Patients in the three groups were well matched for age, nutritional status, stage and grade of tumour, operative procedure, surgeon, duration and blood loss.

Postoperative complications were reduced in 'fed' patients (a) and (b), compared with (unfed) group (c) (p=0-004). The reduction was due to a much lower incidence of nutritionally associated complications (NAC), mainly sepsis. Technical (T) and non-nutritionally associated complications (NNAC), - for example, myocardial infarction, were similar in all groups.

T25
Influence of human and murine giardiasis on intestinal permeability
F ANDRÉ, C ANDRÉ, J GUZMAN, AND S CAVAGNA (INTRODUCED BY R N ALLAN) (Groupe d’Immunopathologie Digestive INSERM, Centre Hospitalier LYON SUD, Pierre Bénié, France) Reports of an association of giardiasis with urticaria and bronchial asthma suggest that troubles of intestinal permeability may be provoked by this parasite. Using gas chromatography, we have measured five hour urine clear­ance of 5 g mannitol and 5 g lactulose ingested as markers of intestinal permeability, respectively to small and to large molecules. This study was undertaken in seven patients with untreated giardiasis, four of these patients after effective treatment with metronidazole, and in 90 controls.

Mean mannitol excretion was 14-11% and mean lactulose excretion was 0-26/ in controls. In patients with giardiasis, the results were 12-91% and 1-25% before treatment. The results were 14-70% and 0-63% after treatment.

During the spontaneous elimination of giardiasis by BALB/c mice, the number of intestinal mast cells, the histamine mucosal content and the intestinal permeability to mannitol and lactulose were measured at weekly intervals during eight weeks.

The experimental disease was associated with an increase of the number of mast cells and of mucosal histamine content, and with the same abnormalities of gut permeability as detected in humans. Absorption of lactulose was increased three-fold. Mice receiving 6 mg/kg histamine orally also developed gut hyperpermeability to lactulose: absorption of lactulose was also increased threefold.

These results suggest that the type one hypersensitivity reaction to giardia infection induces an increase of gut permeability to macromolecules. Therefore this infective episode may be the occasion of food sensitisation.

T26
Effect of bicarbonate on efficacy of oral rehydration therapy in a rat model of secretory diarrhoea
E J ELLIOTT, M J KELLY, A J D WATSON, E A WALKER-SMITH, AND M l G FARTHING (Department of Gastroenterology and Academic Department of Child Health, St Bartholomew’s Hospital, London) Controversy exists regarding the necessity for inclusion of bicarbonate (Bic) and other base precursors in oral rehydration solu­tions (ORS). Our previous work in rat proximal small intestine indicates that Bic enhances cholera toxin (CT)-induced water and sodium secretion. Recent clinical stud­ies suggest that the absence of Bic does not alter clinical efficacy of ORS. To investigate this further we have now prepared the entire rat small intestine (SI) with the widely used UK oral rehydration formulation ‘NaCl and glucose oral powder compound’ (Na 35, K 20, Cl 37, Bic 18, Glucose 200 mmol/l, British National Formu­lary) and an equivalent solution in which Bic was replaced by Cl. Per­fusions were done before and after induction of a secretory state by 2h pre-exposure to 75 µg CT. In the normal SI water absorption was significantly greater from the Bic-containing ORS (+108±8±28 µl mm g dry weight) than the Bic-free ORS (+72±8±22).
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p<0.01). In the secreting SI, however, net water absorption was two-fold greater with Bic-free ORS (+25±1±4) than Bic-containing ORS (+11±1±6; p<0.05).

Both solutions failed to produce net Na absorption in normal and secreting SI, Na secretion being significantly greater with Bic-free ORS (−16±8±4 vs −9±6±5; p<0.02) in the secreting SI.

These findings indicate that Bic does not contribute to the promotion of water absorption during secretory diarrhea. Failure to achieve net Na absorption from ORS in the SI suggests an important role for the colon during oral rehydration therapy.

T27

Effect of ileal and intravenous lipid infusions on feeding and satiety in humans

J MCL WELCH AND N W READ (Clinical Research Unit, Royal Hallamshire Hospital, Glossop Road, Sheffield) The effect of ileal infusion of a lipid emulsion, containing 50% corn oil and 3% albumen, on food intake and satiety was measured in paired experiments in six healthy volunteers. Subjects ate for shorter periods of time during ileal lipid infusions compared with infusions of albumen and saline (25±1 vs 32±3 min, p<0.025) and consumed less food (670±23 vs 884±89 g or 1016±79 vs 1591±228 Kcal, p<0.05). The quantity of liquid drunk and the rates of eating and drinking were not affected by the lipid infusion. In five further experiments, ileal infusion of lipid emulsion delayed gastric emptying compared with infusion of albumen and saline (1±2; 203±48 vs 68±12 min, p<0.02). Food intake was not affected by intravenous infusions of intralipid compared with saline in six volunteers suggesting that the above observations were not related to the effect of absorbed fat. Intestinal lipid may interact with ileal receptors to induce early satiety; this result is probably explained by early gastric distension caused by delayed gastric emptying, although the release of an ileal mechanism having a direct action on the satiety centre cannot be excluded.

T28

Abnormal c-myc oncogene product expression in coeliac small intestinal epithelium

J STEWART, G EVAN, K SikORA, AND P CicLI- TIRA (Ludwig Institute for Cancer Research, MRC Centre, Cambridge, and Gastroenterology Research Unit, Rayne Institute, St Thomas’s Hospital, London) Oncogenes are sections of DNA that are involved in normal cellular growth control. There is evidence that they may be associated with the rapid cellular transformation resulting in neoplastic change. Molecular cloning has allowed characterisation of the amino acid sequences of several oncogenes including c-myc. Production of a monoclonal antibody to a solid-phase synthesised peptide, permitted investigation of the distribution of the oncogene product in human tissue.

The pathogenesis of coeliac disease is not understood. We have investigated the distribution of the c-myc oncogene product in normal (n=5), treated (n=5) and untreated (n=5) coeliac small intestinal biopsies. The method used peroxidase staining of the c-myc gene product in paraffin embedded sections. Normal subjects and treated coeliac patients express very low levels of the oncogene product while untreated coeliac patients or those on a gluten free diet subjected to a gluten challenge exhibited raised levels in the enterocytes of the upper third of the villi.

T29

Late failures of the Angelchik prosthesis

R L OWLEVERSON AND J G TEMPLE (Queen Elizabeth Hospital, Edgbaston, Birmingham) Since its introduction in 1979 the Angelchik prosthesis has gained widespread popularity as a simple and safe procedure for the treatment of gastro-oesophageal reflux. We reported our early favourable results using this device, but recently increasing numbers of significant problems have been encountered. Between 1981 and September 1983 we inserted 17 prostheses in 25 patients, six of these (24%) have now had to be removed. In two of the six this was because of disruption of the securing tapes on the prosthesis. One of the patients had a second prosthesis inserted and this subsequently had to be removed as it migrated into the posterior mediastinum and caused dysphagia by angulating. Another prosthesis was removed again for a similar reason. Two further prostheses were removed for dysphagia thought to be due to fibrous capsule formation around the Angelchik and therefore around the gastro-oesophageal junction.

The technical problem of the tape disruption has been solved by the manufacturers. A failure rate of 3/25 (16%), however, is still unacceptably high. Detailed follow up of our remaining 19 patients indicates that 3/19 (15-8%) are developing sympotms related to swallowing and may well require removal of their prosthesis and subsequent alternative antireflux surgery carried out.

T30

Patterns of gastroesophageal reflux associated with oesophagitis

S SADIK, W CHEADLE, G VITALE, C CRANFORD, N W CARTER, AND A CUSCHIERI (Department of Surgery, Ninewells Hospital and Medical School, Dundee) Prolonged ambulatory pH monitoring in normal subjects and patients with varying degrees of reflux injury as assessed by endoscopy can provide information on the evolution of oesophageal disease. A comparative study was therefore carried out between the following groups: Group 1: asymptomatic normal volunteers (n=50); group 2: symptomatic patients with normal endoscopy (n=26); group 3: symptomatic patients with oesophagitis (n=46); group 4: symptomatic patients with ulcerative oesophagitis and/or strictures (n=31).

Comparison between groups 1 and 2 – that is, the development of symptoms – showed an increase in acid exposure exclusively in the erect posture due to increase in the number of short events. The transition from group 2 to 3 (development of oesophagitis) involved changes in the supine posture and decrease in oesophageal clearance. The transition from group 3 to 4 (development of ulcerative oesophagitis and/or stricture) was associated with increased acid exposure and a reduction in the oesophageal clearance of acid in both the erect and supine positions.

T31

Hydrostatic balloon dilatation of oesophageal strictures

B J M JONES, G F MASKELL, AND A R W HATFIELD (Department of Gastroenterology, The London Hospital, London) Hydrostatic balloons are now available for dilatation of oesophageal strictures other than achalasia. We report here our pre-
liminary experience with polyvinyl balloon catheters (W Cook) of 10, 15, and 22 mm diameter on full inflation.

Seventeen consecutive patients with benign (13), malignant (two) or postradiation stenosis (two) underwent 25 dilatations. The balloons were passed over an endoscopically placed guide wire in succession and positioned across the stenosis under radiological control. Each balloon was inflated with dilute contrast medium for three minutes and the expansion of the 'waist' in the balloon at the site of the stricture observed radiologically.

In nine procedures (36%) full dilatation to 22 mm was achieved and in the remaining 16 (64%) some degree of waisting persisted. To assess the significance of the residual 'waist' on the 22 mm balloon, Eder-Puestow olives were passed in nine patients and the effective stenosis diameter was found to vary from 11 to 15 mm. In these patients a greater degree of dilatation was then obtained with E-P olives or Celestin bougies.

The balloons were very easy to pass over the oropharynx with minimal discomfort but some patients experienced marked retrosternal pain on full inflation. In one patient with a post radiotherapy stricture a small localised perforation occurred after full dilatation which was successfully managed conservatively.

In conclusion balloon dilatation was simple and particularly suitable for elderly patients with cervical spine deformity but very narrow strictures were more difficult to dilate completely and additional conventional bouginage was often necessary.

T32
Does Valsalva's manoeuvre cause variceal bleeding?

S W Hosking and A G Johnson (University Surgical Unit, Royal Hallamshire Hospital, Sheffield) Large increases in variceal pressure recorded during Valsalva's manoeuvre may cause variceal bleeding but no studies have measured intravariceal pressure simultaneously. This prevents measurement of the pressure difference across the varix wall which is a more likely predictor of variceal rupture. We have measured intravariceal and intravarical pressure simultaneously during Valsalva's manoeuvre to determine this pressure difference. Thirteen patients with oesophageal varices were studied before sclerotherapy. A perfused manometer line was passed into the oesophagus followed by an Olympus GIF-Q10 endoscope to approximately 4 cm above the oesophagogastric junction. A perfused variceal injection was used to obtain intravarical pressure readings. At rest, corrected intravarical pressure (intravarical minus intravariceal pressure) varied between patients from 6-22 mm Hg. During voluntary Valsalva's manoeuvre, uncorrected intravarical pressure rose to between 16 and 74 mm Hg (p<0.001 Paired t-test).

After correcting for intravariceal pressure, the change in pressures were from -9 to +18 mm Hg (not significant), and showed no correlation with readings obtained at rest. Repeated Valsalva's manoeuvre within each patient showed a similar change on each occasion. These results suggest that Valsalva's manoeuvre causes only a small rise or even a fall in the pressure across the varix wall, and seems unlikely to initiate variceal haemorrhage.

T33
Follow up of laser palliation for malignant dysphagia

S G Brown, K Matthewson, C P Swain, and C G Clark (Department of Gastroenterology University College Hospital, London) We treated 18 patients aged 57 to 88 with endoscopic Nd YAG laser therapy to palliate dysphagia from advanced malignancy of the oesophagus and gastric cardia and were able to restore satisfactory swallowing in 14. Failure was caused by massive extrinsic tumour in three and a laser perforation in one. The other 14 were followed up. Thirteen have died. Three died without further dysphagia after eight, 11 and 42 weeks (the first of these was the only patient also to receive radiotherapy, which he tolerated poorly). Four had poorly defined difficulty with swallowing near to the time of death from disseminated disease after four, five, 14 and 14 weeks. Three had recurrent dysphagia attributable to exophytic tumour at four, five and 11 weeks. Two of these had excellent results from further laser therapy, one survived a further 19 weeks without dysphagia and the other is still swallowing well after a further 28 weeks. The third had a Celestin tube inserted but its introduction caused a tracheobronchial fistula from which she died after three weeks. The other four had recurrent stenosis due to extrinsic tumour at 10, 12, 14 and 16 weeks. Intubation was attempted in three with bad results; one perforated, one aspirated and one died 24 hours postoperatively.

T34
Ambulatory oesophageal pH monitoring in achalasia

H L Smart, P N Foster, D F Evans, B Slevin, and M Atkinson (University Hospital, Queen's Medical Centre, Nottingham) Radiotelemetric ambulatory oesophageal pH monitoring was performed in 12 patients with symptomatic achalasia, seven of whom had a dilated oesophagus with retained food residue. pH Monitoring revealed that classical episodes of gastro-oesophageal reflux occurred in only one patient. Overall an abnormally high percentage acid exposure time (AET), was found for pH<5 (44.4%) and pH<4 (20.3%) prior to treatment. In patients with food residue these values were significantly higher than those found in patients without retained food. Repeat studies one week after pneumatic dilatation showed a fall in AET in patients with initial food residue (pH<5 from 65.1% to 51.7%) but an increase was seen in those without initial food residue (pH<5 from 7.8% to 46.2%). Gastro-oesophageal reflux occurs infrequently in untreated achalasia and the abnormally high AET is presumably because of fermentation of retained food material. The fall in AET after pneumatic dilatation is explained by improvement in oesophageal emptying in those patients with initial food residues whereas the rise in AET in those without initial residue is probably attributable to gastro-oesophageal reflux after dilatation.

T35
Altered drug pharmacokinetics in smokers—an effect of smoking on gastric emptying

D A Johnson, E J S Boyd, and K G Wormsley (Ninewells Hospital, Dundee, Scotland) Gastric inhibition by antisecretory drugs is impaired by cigarette smoking. We undertook studies to determine whether this effect is attributable to an alteration of drug pharmacokinetics. Eight habitual smokers underwent two studies on separ-
rate days. The stomach was intubated, resting contents aspirated, and 300 ml of a meal containing Oxoid meat broth and PEG 4000 (2.5 g/1) was introduced into the stomach. Gastric contents were sampled after 10 minutes and aspirated completely after 20 minutes. Gastric secretory responses and the volume of gastric contents discharged into the duodenum were calculated by the method of Hunt. On one of the study days, in random order, subjects smoked at a rate they found comfortable. On the other day cigarettes were prohibited. Ten habitual smokers underwent two studies on separate days. On each day either ranitidine 150 mg (five subjects) or cimetidine 200 mg (five subjects) was taken orally with a meal. Blood levels of ranitidine or cimetidine were measured at 0, 15, 30, 45, 60, 90, 120, 150, 180, 240, and 360 minutes after dosing. Cigarettes were smoked on only one study day. Ten further smokers underwent similar studies in which they received either ranitidine 50 mg (n=5) or cimetidine 200 mg (n=5) intravenously.

When cigarettes were smoked the volume of gastric contents discharged into the duodenum during the meal increased by 23%. Drug absorption after oral dosing was more rapid, and peak plasma levels achieved sooner, when cigarettes were smoked. For any given time after peak plasma levels had been achieved, however, plasma drug levels were lower when cigarettes were smoked. Smoking did not alter the pharmacokinetics of intravenously administered drugs.

We conclude that cigarette smoking alters the pharmacokinetics of antisecretory drugs in a manner which may contribute to the impaired therapeutic response. The effect is attributable solely to an increase in the rate of gastric emptying.

T36
Natural history of silent duodenal ulcer
G Bianchi Porro, M Lazzaroni, M Petrillo, F Parente, and F Pace
(Gastrointestinal Unit, L Sacco Hospital, Milano, Italy)
Endoscopic follow up of duodenal ulcer patients during maintenance treatment with H2-blockers have raised the problem of asymptomatic recurrence of duodenal ulcer. In order to define the natural history and the clinical significance of the silent recurrence of ulcer, we followed up during nine months 62 patients with a silent recurrence of duodenal ulcer, detected in the course of a routine endoscopic examination of patients undergoing long-term ulcer treatment. Among these patients, 25 were receiving cimetidine (400 mg nocte), 21 placebo (2 tablets nocte), and 16 no therapy except for antacids when needed. Each patient continued the treatment unchanged during the nine month follow up period. Endoscopic reexaminations took place after three and nine months, and at symptoms occurrence, whereas clinical examinations were performed at bimonthly intervals. The cumulative rate of spontaneous ulcer healing after nine months was 39%: 48% in H2-blockers group, 37% in the group without any therapy, and 29% in placebo group, respectively (p>0.05). The cumulative frequency of symptoms occurrence was 50%: 40% in patients receiving cimetidine, 44% in those receiving no therapy, and 67% in those receiving placebo (p>0.05). The percentages of unhealed asymptomatic ulcer after nine months were 12% in the H2-blockers treated group, 19% in the no-treatment group, and 49% in the placebo treated group (p>0.05). One patient receiving no treatment bled from his ulcer during the follow up period.

T37
Immediate effects of vagotomy on parietal and oxyntic cell function
P D Scott and R F McCloy
(University Department of Surgery, Manchester Royal Infirmary, Oxford Road, Manchester)
The time course and pathophysiology of changes in gastric secretion by vagotomy remain unclear. Grassi suggested that gastric acidity falls to pH 5-5 immediately but gastric function tests in the early postoperative period reveal the pH is often less than 2. Gastric acidity and pepsin concentration were measured in samples of gastric juice aspirated hourly in 11 patients undergoing vagotomy (seven proximal gastric vagotomy, four truncal vagotomy and pyloroplasty) for duodenal ulcer disease. Standard pre- and postoperative basal/sham/pentagastrin tests were performed to assess the changes in basal and stimulated gastric acid outputs.

In nine of 11 patients there was a rise in pH above 5.5 within two hours of completion of vagotomy. The pH remained >4 for a mean duration of 20-8 hours (range 4-41). There was no correlation between this time period and postoperative reduction in BAO. The pH returned to preoperative levels in all patients within 14-54 hours (mean 31-4). Pepsin concentrations did not mirror this pattern and showed a variable response.

These findings suggest that the operation of vagotomy leads to a near total inhibition of parietal and oxyntic cell function which then recovers to expected levels by the third day.

T38
Human gastric enterochromaffin-like (ECL) cells – demonstration of histamine content and its cholnergic nerve supply
W M Hui, H C Liu, and S K Lam
(Departments of Medicine and Anatomy, University of Hong Kong, Queen Mary Hospital, Hong Kong)
The source of histamine in the human stomach has not been established. To examine for possible relationship between the nerve supply and the endocrine ECL cells of the stomach and whether the latter contain histamine, endoscopic biopsies of the gastric fundus of four healthy subjects and eight patients with duodenal ulcer were meticulously studied. Modified silver impregnation method was used to stain up simultaneously the ECL cells and nerve fibres, and cholinesterase activity of nerve fibres were examined histochemically. Modified o- phthalaldehyde fluorescence method was used to examine for possible histamine content of the ECL cells, which were then counter-stained for ECL cells by Grimelius silver method. The results were (i) o-phthalaldehyde staining was taken up by the mast cells and the ECL cells, which corresponded to the argyrophil staining cells. (ii) Nerve fibres possessing acetylcholinesterase activity ramified to the basement membrane of the ECL and parietal cells, which were in close proximity to each other. This intimate anatomical relationship and the demonstration for the first time that human ECL cells contain histamine strongly suggest that the human ECL cells play an important role in the control of acid secretion, possibly under vagal influence.

T39
Thromboxanes and gastric mucosal damage
C A Price, G Pipkin, A Currington, L Davies, L Darling, and M E Parsons
(Smith Kline & French Research Limited, The Frythe, Welwyn, Hertfordshire)
Thrombaxane (TX) synthetase inhibitors reduce experimental gastric damage in the rat. If they act by preventing the formation of potentially damaging TX then a TX anta-
gonist should also be effective. Dazoxiben (TX synthetase inhibitor, 30 and 60 mg/kg po) reduced ethanol induced damage in the conscious rat. At 60 mg/kg% area of mucosa damaged was reduced from 16 ± 2.2% (n=8) to 5.9 ± 2.0% (n=8, p<0.01). The TX antagonists SK&F 88046 (10 and 50 mg/kg po) and BM13177 (50 mg/kg po) also reduced this form of damage. SK&F 88046 (50 mg/kg) reduced % area of mucosa damaged from 9.8 ± 2.7% (n=7) to 0.12 ± 0.1% (n=6, p<0.01). The duration of action of SK&F 88046 against U46619 (TX mimetic) induced hypertension was short (40 min) in the rat, therefore in the rat ex vivo gastric chamber preparation SK&F 88046 was given as an iv bolus (20 mg/kg) followed by an infusion (40 mg/kg/h). This dose reduced blood and albumin loss into the gastric chamber after two hours exposure to acidified Na taurocholate (50 mM). Blood 113Cr red blood cells loss, was reduced from 11.9 ± 3.4 to 2.8 ± 0.6 ml x 10^-3 (p<0.05). SK&F 88046 antagonised the effect of U46619 on rat platelet rich plasma (IC50 4-2 μM) and on the rat fundus strip (log Kp 7.53) confirming that SK&F 88046 acted as a TX antagonist in the rat, as in other species. These results suggest that TX may be involved in the pathogenesis of ethanol and bile induced damage in the rat.

**F1 Identification of human progastrin**

H P Desmond, S Pauwels, R Dimalone, and G J Dockray (Department of Physiology, University of Liverpool, Liverpool, and Centre de Medecine, Nucleaire, University of Louvain, Brussels, Belgium)

The gene sequence encoding the human gastrin precursor, progastrin, has been elucidated, but little else is known of the biosynthesis of this hormone. We have raised antibodies to a synthetic analogue of the C-terminal hexapeptide of progastrin; unlike other gastrin antibodies, these are expected to react with the intact precursor as well as fragments of it. They should therefore help elucidate biosynthetic pathways. In human antral mucosal extracts fractionated on Sephadex G50 we found two peaks of immunoreactivity: a major one (84 ± 2% of total; n=10) corresponded to the C-terminal tryptic fragment of progastrin (Kα= 0.65), and a minor one was of higher apparent molecular weight (Kα= 0.20). In contrast, in three of eight gastrinomas, the latter material accounted for over 50% of total immunoreactivity (mean 39 ± 6%; n=8). Digestion of the high molecular weight form with trypsin liberated peptides identified by antibodies to the N-terminus of G17 and of G34, indicating a structure extending from the C-terminus of progastrin to beyond the N-terminus of G34.

We conclude that: (1) material with the properties of intact progastrin is found in antral mucosa and gastrinomas. (2) In some gastrinomas it is the predominant form of gastrin. (3) There are differences between gastrinomas and antral mucosa in the biosynthetic processing of progastrin.

**F2 Recombinant urogastrone-EGF can provide a proliferative signal after small resection in parenterally fed rats**


It is now known that animals maintained on total parental nutrition (TPN) do not show the dramatic proliferative response to partial small bowel resection seen in orally fed animals, suggesting that the presence of food in the lumen is an important signal. If this proliferative signal is hormonal it might be expected that hormone(s) themselves could initiate this process. The response of the gastrointestinal tract to urogastrone-EGF was investigated in rats maintained on TPN with or without 75% small bowel resection. Orally fed rats (±resection) were also studied. Two way analysis of variance showed that resection caused a significant increase (p<0.01) in proliferation below the anastomosis and in the ileum of TPN rats; however, the response of the ileum was much less than that observed in orally fed rats, which confirms the importance of ‘luminal nutrition’ in the response to resection. There was no evidence for a significant positive interaction (synergistic effect) between the effects of urogastrone-EGF and resection. Continuous infusion of 60 μg/rat/day of recombinant beta urogastrone significantly increased proliferation (measured by the accumulation of vincristine arrested metaphases) in the stomach (p<0.05), small intestine and colon (p<0.001) in resected and unresected rats maintained by TPN. Thus urogastrone-EGF has the novel property of being capable of stimulating a proliferative response in the resected intestine of parenterally fed rats.

**F3 Serotonin, a physiological role in gastrointestinal motility?**

G B Hopkinson, J Hindsdale, and B Jaffe (Introducyed by J B Elder) (Department of Surgery, Downstate Medical School, Brooklyn, New York, USA) Freyburger in 1951 showed a spasmodogenic action for 5HT in the canine jejunum, but its physiological significance was unknown. Five chronic conscious dogs fitted with gastric and jejunal strain gauges were infused intravenously with 5HT in doses between 0.25 μg/kg/min and 120 μg/kg/min over 20 minute periods during the quiescent phase (Ph I) of the interdigestive myoelectrical complex (IDMEC). Over 200 such infusions were carried out. Coeliac artery 5HT levels were monitored by radioimmunoassay. Below 1 μg/kg/min no contractile response occurred. Between 1-4 μg/kg/min three dogs showed a response. At 8 μg/kg/min all dogs showed responses to intravenous 5HT. The gastric contraction rate increased from 2.1±0.50 (contractions per minute (CPM)±SEM) before infusion, to 4.6±0.21 CPM during infusion of 5HT at 8 μg/kg/min (p<0.001) (n=20). The gastric contraction force increased from 16.1±6.20 mV/mins before infusion, to 14.5±1.4 mV/mins during infusion (p<0.001). The jejunal contraction rate increased from 1.2±0.57 CPM before infusion, to 16.4±0.50 CPM (p<0.001) (n=20), with an increase in contraction force from 6.1±3.0 mV/mins before infusion to 125.2±15.2 mV/mins. Arterial levels before infusion of 5HT were 658.3±187.6 ng/ml of whole blood and increased to 719.5±68.7 ng/ml during infusion. The contraction force during 5HT infusion was similar to that found during the spontaneous maximum contraction of the bowel. During infusion of 5HT at 8 μg/kg/min serotonin appears a major mediator of intestinal motility.

**F4 Glucocorticoid-induced Na and K channels in the apical membrane of rat distal colon**
The British Society of Gastroenterology

G I Sandle (Department of Medicine, University of Manchester School of Medicine, Hope Hospital, Salford) Na and K channel blockers (amiloride and tetraethylammonium chloride (TEA), respectively) have been used with microelectrodes to study stimulation of Na absorptive and K secretory processes in rat distal colon by dexamethasone (600 μg/100 BW/day for three days). In dexamethasone treated animals (n=15), transepithelial voltage (V_τ; −31±4 mV) and total conductance (G\textsubscript{T}; 8.5±0.5 mS/cm²) were higher than in controls (−6±1 mV, p<0.001 and 5.3±0.2 mS/cm², p<0.001 respectively, n=12); these changes reflected an increase in basolateral membrane voltage, and decreases in apical membrane voltage and the basolateral/apical conductance ratio. Mucosal amiloride (10^{-4} M) and then TEA (30 mM) had no effects in control animals. In dexamethasone treated animals, amiloride reduced V_τ to the control value, decreased G\textsubscript{T} from 8.5±0.5 to 6.9±0.3 mS/cm² (p<0.001), hyperpolarised the apical membrane by 13 mV (p<0.005), and increased the basolateral/apical conductance ratio by 63%, indicating inhibition of apical Na channels and electrically Na transport. Subsequent addition of TEA decreased G\textsubscript{T} from 6.9±0.3 to 6.4±0.4 mS/cm² (p<0.001), depolarised the apical membrane by 8 mV (p<0.025), and increased the basolateral/apical conductance ratio by 66%, indicating inhibition of apical K channels. Thus, stimulation of Na absorptive and K secretory processes in rat distal colon by dexamethasone involves an increase in the conductance of the apical membrane to both Na and K.

F5

Is gall bladder emptying really exponential?

P Howard, G M Murphy, and R H Dowling (Gastroenterology Unit, Division of Medicine, UMDS of Guy’s and St Thomas’ Hospitals, London) Previous ultrasound studies of gall bladder (GB) emptying have used standard Lundh meal or CCK stimuli and long intervals (>15 min) between imaging. The pattern of response to a normal, dual phase (liquid plus solid) meal, is unknown. Therefore, in 10 control subjects, we measured GB size with frequent ultrasound recordings, after a meal of baked beans on buttered toast with milk.

In nine of 10 subjects, the GB emptied before the meal, the mean reduction in GB vol (Δ vol) recorded during this ‘cephalic phase’ being 5.28±SEM 1.76 ml. After the meal, all 10 subjects showed the same triphasic pattern of response with: (i) an early phase of GB emptying from a mean pre-ingestion vol of 18.9±3.48 ml to 11.21±2.35 (p<0.05) at 17±1±5.4 min; (ii) a net refilling phase to 16.6±3.24 ml at 36±6.5 min; and (iii) a late emptying phase to a final nadir vol of 5.6±1.51 ml at 1.38±9.9 min. In four subjects, US imaging at more frequent intervals (1/min) showed that this overall triphasic response was punctuated by min to min fluctuations in vol with mean filling and emptying rates of 0.82 and 0.95 ml/min respectively.

We conclude that, surprisingly, the pattern of GB emptying after a dual phase meal is not a simple exponential but is interrupted by an episode of net refilling before the final nadir is reached, with superimposed minute by minute fluctuations in volume throughout.

F6

Intestinal tissue oxygen tension measurement using a surface electrode

M B Hallett, A Shandall, R H Lowndes, H L Young (University Department of Surgery, University of Wales College of Medicine, Heath Park, Cardiff) If a surface electrode truly measures tissue oxygen tension (TO\textsubscript{T}), this could be used to assess intestinal perfusion/viability. To determine this we have studied the relationship between TO\textsubscript{T} measured with the Clark electrode, blood flow (F) measured by Xe\textsuperscript{133} clearance and arterial O\textsubscript{2} tension (PaO\textsubscript{2}) measured by blood gas analysis, in a rabbit experimental model.

Using serial devascularisation in nine rabbits F & TO\textsubscript{T} were measured in mid-ileum and mid-sigmoid colon. In six rabbits inspired O\textsubscript{2} (FiO\textsubscript{2}) was varied between 0–100% with PaO\textsubscript{2} measured on rabbit ear arterial blood, and TO\textsubscript{T} on ileum and colon as above.

Using known physiological parameters of oxygen capacity, oxygen supply, oxygen consumption, oxygen diffusion and haemoglobin saturation a formula relating F, PaO\textsubscript{2} and TO\textsubscript{T} was derived. Curves based on this showed the expected sigmoid relationship between F and TO\textsubscript{T}, PaO\textsubscript{2} and TO\textsubscript{T}, which fitted the experimental data with a correlation of r=0.93, p<0.001 (TO\textsubscript{T} vs F), r=0.96, p<0.001 (PaO\textsubscript{2} vs TO\textsubscript{T}) on linearising the equation. This relationship would not be expected if the electrode was merely detecting capillary O\textsubscript{2}, or if ambient air was significantly influencing the measurement.

We conclude that the Clark electrode is a true measure of tissue oxygen tension and can be used clinically for this purpose.

F7

Dissociated effect of atropine on hypergastrinaemia induced by single dose and repeated omeprazole treatment

F Halter, F EiGEMnANN, and H R KoELz (Gastrointestinal Unit, University Hospital, Inselspital Bernie, Switzerland) Omeprazole has been shown to increase serum gastrin and antral G-cell density in the rat. Acute hypergastrinaemia following acid inhibition induced by histamine H\textsubscript{2}-antagonists can be blocked by high doses of atropine, both in fasting and fed rats. We studied whether hypergastrinaemia induced by single or repeated dose treatment with omeprazole can be prevented by additional atropine.

Gastric pH and serum gastrin were measured in 10 chronic gastric fistula rats before and four hours after sc omeprazole (O, 40 μmol/kg); omeprazole combined with atropine (O+A, 40 μmol/kg and 3 mg/kg, respectively); atropine (A, 3 mg/kg); or the omeprazole solvent (S, 40% PEG). Gastric pH of all animals treated with O or O+A became neutral within four hours. After O, fasting serum gastrin levels rose from 34±4 to 110±9 pmol/l (x±SEM, p<0.001), but were not influenced in the other groups. Four groups of six intact, fed animals received similar treatment for 10 days. O was given once daily, A twice daily. In contrast to single dose treatment, both O and O+A increased mean serum gastrin levels by approximately seven-fold as measured four and 12 hours after the last dose of O or O+A. Treatments A and S did not influence serum gastrin.

We conclude that atropine blocks the acute rise of serum gastrin after a single dose omeprazole administration. The more pronounced hypergastrinaemia following prolonged omeprazole treatment, however, is atropine resistant, suggesting a change in the regulatory mechanisms of G-cells. It appears thus unlikely that G-cell hyperplasia following prolonged omeprazole treatment represents a simple work hyperplasia directly related to acid inhibition.

F8

Prostaglandin E\textsubscript{2} stimulates chloride secretion in guinea-pig isolated gastric mucosa
C F Spragggs and K T Bunce (Department of Neuropharmacology, Glaxo Group Research Ltd, Ware, Herts) The effect of prostaglandins on gastric mucosal ion transport has been investigated in vitro mainly in amphibian mucosa and little information is available on the effect of prostaglandins in mammalian tissue. We have investigated the effects of prostaglandin E2 (PGE2) on sodium and chloride transport and short circuit current (SCC) in guinea-pig isolated gastric mucosa in which acid secretion had been inhibited by omeprazole (100 μM).

PGE2 (1 μM) produced increases in SCC of 73±5 μA cm⁻². The ionic basis of this response was determined by ³⁶Cl⁻ and ⁷⁴Na flux studies in mucosae pretreated with omeprazole (n=7). Under control conditions the net secretion of ³⁶Cl⁻ (2.90±0.69 μEq cm⁻²/30 min) was not significantly different from SCC (4.30±0.39 μEq cm⁻²/30 min, p>0.05), while the net absorption of ⁷⁴Na (−0.02±0.08 μEq cm⁻²/30 min) was significantly different (p<0.001). PGE2 (1 μM) stimulated a significant increase in both SCC (5.36±0.31 μEq cm⁻²/30 min, p<0.001) and ³⁶Cl⁻ secretion (5.53±0.63 μEq cm⁻²/30 min, p<0.001), but had no significant effect on net ⁷⁴Na absorption (−0.27±0.12 μEq cm⁻²/30 min, p>0.05).

These results show that PGE2 stimulates electrogenic chloride secretion in guinea-pig isolated gastric mucosa, and provide an ionic basis for the stimulation of a NaCl-rich secretion by E-prostaglandins in mammalian gastric mucosa in vivo.

F9

Adaptive cytoprotection: evidence against mediation by prostaglandins

C J Hawkey, R T Kemp, R P Walt, N K Baskar, J Davies, and B Filipowicz (Department of Therapeutics, University Hospital, Nottingham) Mild irritants – for example, 20% ethanol – increase gastric mucosal resistance to consequent necrotising stimuli – for example, 100% ethanol. We have investigated the proposition that this phenomenon (adaptive cytoprotection) occurs because mild irritants stimulate prostaglandin (PG) synthesis.

Male Wistar rats were dosed orally with vehicle or indomethacin 2.5 mg/kg or 10 mg/kg. One hour later 20% ethanol (1 ml) was introduced into the stomach followed 15 minutes later by 100% ethanol (1 ml) and mucosal necrosis subsequently quantitated macroscopically. Other rats were killed 15 minutes after 20% ethanol and ex vivo release of PGE2 from mucosal fragments measured by radioimmunoassay.

In control rats release of PGE2 was 28±3 pg/mg/minute (mean±SEM, n=5); 36±10% of the mucosa was necrosed by 100% ethanol (n=7). After pretreatment with 20% ethanol PGE2 release was 99±12% of control values but mucosal necrosis induced by 100% ethanol was reduced to 6±2% (p<0.05). After pretreatment with indomethacin and 20% ethanol PGE2 release was reduced by 62±15% (indomethacin 2.5 mg/kg, p<0.01) and 80±8% (indomethacin 10 mg/kg, p<0.001) but there was only 8±1% (p<0.01) and 16±4% (p<0.05) mucosal necrosis respectively.

These observations show that adaptive ‘cytoprotection’ can occur in the face of reduced prostaglandin synthesis and may involve other mechanisms.

F10

Arachidonic acid metabolism and leukocyte infiltration, as determined by myeloperoxidase activity in a model of IBD

N K Boughton-Smith, J L Wallace, and B J R Whittle (Department of Mediator Pharmacology, Wellcome Research Laboratories, Beckenham, Kent) A chronic model of IBD in the rat, which has the pathological features of Crohn's disease can be induced by colonic administration of trinitrobenzene sulphinic acid (TNB). We have investigated colonic ¹⁴C-arachidonic acid (AA) metabolism and, as a measure of leukocyte infiltration, myeloperoxidase (MPO) activity, during the development of colonic inflammation in this model.

The distal colons of rats were removed at various times (one hour to one week) after a single intracolonic application of TNB (20 mg in 0.25 ml of 30% EtOH). Segments of colon (200 mg) were homogenised, incubated (30 min, 37°C) with ¹⁴C-AA (0.25 μCi/ml) and the ¹⁴C-AA metabolites separated by TLC. Cell free supernatants of colon were also used for spectrophotometric (at 460 nm) determination of MPO activity.

The relative formation of eicosanoids from ¹⁴C-AA by control colon was PGE₂:\textgreater\textgreater\textgreater\textgreater\textgreater HETE\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\textgreater\text 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lular conductance than distal colon, which mainly reflects its permeability to Cl; (ii) proximal colon has a greater apical conductance than distal colon, which may reflect K channels, as there appear to be no Na or Cl channels in this membrane.

F12
Activation of intestinal epithelial protein kinases by calcium

G Warhurst, G S Smith, A Tonge, and L A Turner (Department of Medicine, University of Manchester School of Medicine, Hope Hospital, Salford) Intestinal secretagogues such as acetylcholine and 5-HT are believed to mediate their actions by raising cytosolic Ca concentrations. The cellular events which follow and which lead to ion secretion are largely unexplored but may involve the phosphorylation of key proteins by specific protein kinases. We therefore investigated Ca activated protein kinase activity in cytosolic and particulate fractions from rat enterocytes. Endogenous protein phosphorylations determined in cell homogenates incubated with 32P ATP revealed a Ca dependent phosphorylation of several proteins, the most apparent being of M,~50 000. Labelling of this protein was stimulated at 3 x 10^-6 M Ca and was maximal at 10^-6 M Ca. Inclusion of calmodulin (CDR) had no effect on the level of phosphorylation, although the CDR antagonist TFP inhibited labelling suggesting the involvement of CDR dependent protein kinase activity.

Using a specific histone protein as exogenous substrate a second Ca activated kinase could be demonstrated. This enzyme was located in the 100 000 g cytosolic fraction and was dependent on the presence of phosphatidylserine (PS) for full activity. PS produced a dose-dependent stimulation of activity (4 mg/ml, 142%; 18 mg/ml, 235% of control). In conclusion this study shows the presence in rat enterocytes of two distinct Ca activated protein kinase activities - both of which may serve to mediate the secretory events initiated by increases in intracellular Ca.

A G Morgan, W A F McAdam, C Pacsoo (Endoscopy Unit, Airedale General Hospital, Keighley, West Yorkshire) So far 48 patients with benign gastric ulceration have been enrolled in a double blind endoscopically controlled study, and randomly allocated to treatment with either enprostil, a synthetic dihydro-prostaglandin E2 (70 mg twice daily) or ranitidine. Endoscopic examination was repeated at monthly intervals for three months or until healing. Dyspeptic symptoms were recorded on a diary card and a return drug count and safety screening performed at each endoscopic visit.

The results of the treatment were similar for the two drug regimes. With enprostil 63% had healed ulcers at one month, 91% at two months and three months. The healing rates for ranitidine were 50%, 83%, and 96% respectively. Diary card analysis showed that both drugs rapidly relieved dyspeptic symptoms. No clinically important side effects were encountered. A years follow up after ulcer healing and without maintenance therapy is planned. So far there have been 20 recurrences out of the 32 patients who have completed the first six months of follow up.

Enprostil appears to be an effective and safe drug in the treatment of gastric ulceration.

F14
Enprostil (E) versus ranitidine (R) in duodenal ulcer (DU)

K D Bardhan, K Bose, R F C Hinchliffe, Lesley Whittaker, Pamela Morris, Helen Massey, and Moira Thomson (District General Hospital, Rotherham, and Syntax Research, Maidenhead, Berks) We have investigated enprostil (E), a new synthetic prostaglandin E, derivative with antisecretory and mucosal-protective effects, in DU healing. In a double blind double dummy study, 85 patients with DU were randomly allocated to receive either E 35 mcg (n=44) or R 150 mg (n=41) both taken twice daily. The patients were interviewed at two, four, and six weeks and endoscoped at four weeks and again at six weeks if unhealed earlier.

Patients in both treatment groups were well matched for age, sex, length of history, smoking, and ulcer size. Healing in the two groups was: at four weeks, E 46%, R 93% (p<0.01); at six weeks E 82%, R 97% (ns). Smoking retarded healing but ulcer size and length of history had no effect. Reduction of daytime and night-time pain was equally quick with both drugs.

The main adverse events noted were: abdominal pain (E 16%, R 0%), diarrhoea (E 5%, R 2%), nausea (E 7%, R 2%), dizziness (E 2%, R 5%), and depression (E 0%, R 5%); and three patients (E1, R2) were withdrawn because of continuing or recurrent abdominal pain. There was no major treatment related haematological or biochemical abnormality.

In conclusion, at this dose E heals DU less rapidly than R but is equally effective in relieving ulcer pain.

F15
Natural history of chronic antral gastritis in duodenal ulcer (DU) and its response to treatment with prostaglandin E1 (misoprostol)

W H Hui, J Ho, S K Lam, H Lui, M T Ng, C L Lai, and A Lok (Departments of Medicine & Pathology, University of Hong Kong, Queen Mary Hospital, Hong Kong) The natural history of chronic antral gastritis in relation to healing of DU and its response to treatment, if any, are unknown. We carried out a double blind controlled trial using an oral prostaglandin E1, misoprostol (Searle), in 213 patients with active DU randomised to receive placebo (n=69), misoprostol 200 mg (n=73), or misoprostol 300 mg (n=71) qid respectively. Healing of DU was assessed bi-weekly up to 12 weeks by endoscopy at which at least two antral and two fundal biopsies were taken. The activity and chronicity of gastritis as assessed historically by the infiltration of, respectively, polymorphs and chronic inflammatory cells were graded blind by the pathologist as nil, mild, moderate or severe. Before treatment, 80% of patients had moderate to severe antral gastritis and 1-5% had fundal gastritis. In the placebo group, healed DU was associated with significantly (p<0.01, life table analysis) higher rates of regression of antral gastritis (nil or mild as end point) than unhealed DU (30% vs 4% at week 8). Irrespective of whether DU was healed or unhealed, significantly (p<0.01) more patients on misoprostol (50% at week 8) showed regression of antral gastritis than the placebo group. The chronicity of antral gastritis showed similar changes.

In conclusion, healing of DU was associated with improvement of chronic antral gastritis, which, as shown for the first time, could be further enhanced by a therapeutic agent - prostaglandin E1.
F16 Will overnight response to cimetidine predict healing of duodenal ulcers?

M DEAKIN, J RAMAGE, ANGIE PAUL, JO SHOULER, S P GRAY, J BILLINGS, D G COLIN-JONFS, AND J G WILLIAMS (Department of Gastroenterology and Biochemistry, Royal Naval Hospital, Haslar, Department Gastroenterology, Queen Alexandra Hospital, Portsmouth, Devon) We have studied prospectively the evening and nocturnal pH profiles, nocturnal acid and pepsin outputs of 33 patients with endoscopically diagnosed acute duodenal ulcers. The study was carried out before treatment and while taking cimetidine 400 mg bd (0800 and 2300 hours). All patients were re-endoscoped after six weeks treatment with cimetidine: in 13/33 the ulcer had not healed, in 7/33 an erosive duodenis remained and in 13/33 complete healing had occurred.

All 13 patients whose ulcers had healed had a profound pharmacological response to cimetidine 400 mg with a mean overnight pH of 6-06±0-46 SEM compared with 1-92±0-14 before treatment and a 97% fall in nocturnal acid output, 22-46±3-6 to 0-75±0-35 mmol between 0030-0730 hours. While taking cimetidine few overnight specimens contained detectable peptic activity. Mean fall in pepsin output was 28-1±5-39 to 3-45±1-55 IU.

The 13 patients with unhealed ulcers had smaller pH changes overnight (1-47±0-05 to 3-74±0-62) (p<0-01), a smaller reduction in mean acid output, 57-29±18-07 to 13-28±5-12 mmol (p<0-01) and pepsin output 45-96±11-71 to 22-16±5-6 IU (p<0-01).

A poor response to cimetidine overnight will predict slow healing of duodenal ulceration. This may be because of inadequate inactivation of pepsin as well as poor inhibition of acid.

F17 Is persistent duodenal prostaglandin E2 deficiency the cause of relapse in DU?

S PUGH, SIAN WILLIAMS, M ISHAQUE, M R LEWIN, TINA BARTON, K BOE, K BARDHIAN, AND C G CLARK (Department of Surgery, University College London, and Department of Gastroenterology, Rotherham District General Hospital, Rotherham) It has been shown that the ability of the duodenal mucosa to synthesise PGE2 is deficient in association with DU. As PGE2 may be an important mediator of duodenal defences such a deficiency may be causally related to DU. We report a two centre study on the effects of treatment with H2 receptor antagonists and the healing of the DU on duodenal PGE2 synthesis. At endoscopy, biopsies were obtained from the duodenum in normals (22), untreated DU rim (18), patients with healed DU but still on H2 receptor antagonist treatment (22), patients with healed DU off treatment (6) and also patients being treated with H2 receptor antagonists for GU or oesophagitis (the patients act as treatment controls (20)). All biopsies were treated similarly by inducing synthesis of PGE2 by vortexing and measuring released PGE2 by RIA.

Results were (mean±SD in pg PGE2/mg wet wt), normals 110±32±2, untreated DU rim 60-3±22-5 (p<0-001 vs normal), healed DU on treatment 84-7±38-2 (p<0-025 vs normal), healed DU off treatment 75-7±26-1 (p<0-02 vs normal, NS vs healed DU on treatment) and patients on treatment for conditions other than duodenal disease 121-6±40-2 (NS vs normal, NS vs healed DU on treatment).

We conclude that the initial deficiency of PGE2 in association with DU is confirmed and that this deficiency persists despite treatment with H2 receptor antagonists. This persistent deficiency may be one of the causes of the rapid recurrence of DU in most patients off treatment.

F18 Prostaglandin E2 in the prevention of gastric stress bleeding

H A VAN ESSEN, M VAN BLANKENSTEIN, J H P WILSON, B VAN DEN BERG, AND H A BRUNING (Departments of Internal Medicine and Surgery, University Hospital, Rotterdam, The Netherlands) The effect of prostaglandin E2 (PGE2) in the prevention of acute gastric stress bleeding in intensive care patients was investigated in a prospective, double blind, placebo controlled study. Ninety patients with two or more risk factors (major surgery, multiple trauma, respiratory insufficiency, renal insufficiency, jaundice, hypotension, peritonitis, sepsis) were randomised for treatment with either PGE2 0-5 mg every four hours via a nasogastric tube, or placebo. Blood loss in 24 hour gastric aspirates was measured by a peroxidase test (orthotolidine) and by 31Cr-labelled autologous erythrocytes, a loss ≥15 ml/day being the criterion of bleeding.

Fifty seven patients could be evaluated after at least three days: 29 had received PGE2 and 28 placebo. Bleeding occurred in nine (31%) of PGE2 treated patients and in 13 (46%) placebo treated patients (NS). No correlation was found between the blood content of gastric aspirates as measured by the 31Cr-method and the peroxidase test.

It is concluded that (1) PGE2 0-5 mg administered intragastrically four hourly did not provide adequate protection against stress bleeding. (2) Peroxidase tests cannot be used to quantify blood loss in gastric aspirates. The results of previous trials on the prevention of stress bleeding using peroxidase tests are therefore questionable.

F19 Effect of aluminium on bicanarate secretion by isolated amphibian gastroduodenal mucosa

J R CRAMPTON, L C GIBBONS, AND W D W REES (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) Aluminium containing antacids cause symptomatic relief of dyspepsia despite the negligible buffering capacity of doses commonly used. Recent evidence suggests that aluminium antacids may possess cytoprotective properties although it is possible that mechanism of such action is not clear. The effect of neutral aluminium salts on bicarbonate secretion by bullfrog (Rana catesbeiana) fundic, antral, and duodenal stripped mucosa has therefore been examined. An isolated chamber preparation has been used enabling measurement of bicarbonate secretion by pH stat titration of the luminal solution with recording of transmucosal potential difference. Addition of neutral aluminium sulphate 3×10-3 M (equivalent to one tablet of aluminium hydroxide in 2 l) caused a marked increase in bicarbonate secretion by antrum (mean±SE: 214±63%, n=4, p<0-05, fundus (mean±SE: 144±48%, n=5, p<0-05) and duodenum (mean±SE: 133±44%, n=6, p<0-005). Transmucosal potential difference was not altered during these experiments. These results demonstrate that aluminium is a potent stimulant of mucosal bicarbonate secretion in concentrations which may be achieved in vivo. The mechanism of this stimulation deserves further evaluation since it may provide a clue to the therapeutic effect of aluminium containing antacids in peptic disorders.
Experimental studies of new mechanical methods of endoscopic haemostasis: stitching, banding, clamping, and ulcer removal

C P Swain, T N Mills, and T C Northfield (The Norman Tanner Gastroenterology Unit, St James’ Hospital and Department of Medical Physics, University College Hospital, London) Mechanical occlusion of bleeding vessels in the gastrointestinal tract at endoscopy might offer greater security of haemostasis than thermal methods. We have designed and tested new mechanical methods for occlusion of bleeding vessels at endoscopy including: (1) an improved endoscopic sewing machine (SM); (2) an ulcer clamp (C); (3) a method for delivering rubber bands (B) or self-retaining plastic ties over a suction polyp (PS); (4) banding or tying of a suction polyp over an acute ulcer followed by monopolar snare ulcer removal (UR). Forty five standard bleeding canine ulcers were randomised to endoscopic treatment with SM, B, C, UR or control. Bleeding was terminated by SM in 9/10, C 10/10, B 9/10, UR 10/10. Controls did not stop spontaneously. No secondary reblooding or perforation occurred in these survival experiments. Mechanical methods were compared with thermal methods; hot crush bipolar forceps (HS), heater probe (HP), monopolar probe (MP), Nd-YAG laser (YAG) and argon laser (A) in bleeding mesenteric vessels and isolated arteries of 1–4 mm, measuring bursting pressure of vessel occlusion. Mechanical occlusion achieved higher (p<0.01) bursting pressures (mean±SEM 120±230 mmHg) than thermal methods (320±120 mmHg) (SM C>HS+B+UR>HP+YAG with coaptation >MP+YAG>A).

We conclude that permanent mechanical occlusion of acute experimental ulcers by means of stitching, banding, clamping and ulcer removal is feasible and can occlude large vessels more securely than thermal methods.

Trial of the 7 FG bipolar probe in bleeding peptic ulcers

J D O’Brien and W R Burnham (Department of Gastroenterology, Oldchurch Hospital, Romford, Essex) Four hundred and sixty patients with upper gastrointestinal bleeding over a 27 month period were gastroscoped by two endoscopists. Two hundred and four patients examined within 24 hours who had peptic ulcers with active bleeding, visible vessel or adherent clot were allocated randomly to electrocoagulation with the probe (101 patients) or not (103 patients). Otherwise all patients were treated identically. Groups were stratified by ulcer site to give similar numbers in each. Management decisions and assessment of reblooding were made by a clinician unaware of the randomisation.

The treated patients were older than controls (mean age 68.7 years vs 64.6 years; p=0.054) had a lower initial mean haemoglobin (9.8 g vs 10.2 g) and lower mean transfusion requirement after endoscopy (4.6 units vs 7.3 units; p=0.13). Seventeen treated patients continued bleeding or rebled compared to 34 controls (x²=6.28, p<0.015); benefit was most marked in those actively bleeding; seven had surgery (10 controls) and nine died after reblooding (12 controls). One third of the mortality and nearly one quarter of the rebloed in the treated group were in the first seven patients treated suggesting that inexperienced application of the probe may be hazardous.

Risk of gastric cancer after benign ulcer surgery

G D Corcoran, J Ware, D W Day, R F A Logan, and S Gray (Departments of Surgery and Pathology, University of Liverpool, and Department of Community Health, Nottingham University, Nottingham) The gastric adenocarcinoma (GC) registrations between 1970–79 for the Mersey Region have been reviewed and a case controlled study from five inner city hospitals done to estimate the relative risk (RR) of late malignancy (OSC) after ulcer surgery.

Of the total number of GC, 1.8% were OSC cases (116/6613), GC mean age 68.6 years and OSC, 66.4 years. The mean interval between operation and diagnosis of OSC was 21.8 years while the three operative categories, numbers and age at operation were: gastric resection (GR) 80, 44.9 yr; gastrojejunitomy (GJ) 27, 42.2 yr; and vagotomy and drainage, nine, 42.4 yr. There were 1610 registrations including 38 OSCs from five hospitals. These cases were matched for age, sex, time of death and hospital with necropsy controls. The overall RR was 1.4 (95% conf limits 0.8–2.3) and the RR for GR (n=28) was 1.3 (0.7–2.2) and for GJ (n=10) was 2.0 (0.7–5.8).

It is concluded that OSC represents only a small number of all gastric cancers. Moreover, it is suggested that the larger RR for OSC previously reported may reflect the character of the control material rather than a real risk.

Pathologists problems in the recognition of early gastric cancer and gastric dysplasia

A B Price, G Williams, H Thompson, and BIBA Unwin (Departments of Pathology: Northwick Park Hospital, London, University Hospital of Wales, Cardiff, Birmingham General Hospital, and Department of Surgery, Leeds) This is preliminary pathological data from a multicentre investigation of early gastric cancer (EGC), and the natural history of gastric dysplasia. This report concerns interobserver variation of 41 cases of EGC, 22 with pre gastrectomy biopsies, and a second biopsy group with a consensus opinion of dysplasia from 13 non-operated patients (follow up three weeks – two years). Assessment was by three pathologists using a proforma of 20 attributes.

For 41 cases of EGC there was full agreement in 40 surgical specimens. There were six disagreements amongst the 22 pre gastrectomy biopsies from this group, with never more than one dissenting opinion. Only once was there discretion over the actual presence of dysplasia, five of the six disagreements involved grades of dysplasia.

Of the 13 non-operated cases with at least one biopsy classified dysplasia, the initial ‘blind’ assessment produced total agreement in only four. In six at least one opinion was against dysplasia regardless of grade. This reflects the pathologist’s problem with the lesser grades of dysplasia predominant in this group in contrast to the EGC group and borne out by analysis of the proforma attributes by Kappa statistics and positive predictive values. Clearly the interpretation of graded gastric dysplasia, like dysplasia in colitis, suffers interpretative difficulties, while follow up from this study will determine any clinical significance.

BSG early gastric cancer/dysplasia survey: the first 104 cases

F T de Dombal, B J Unwin, P Cotton, G R Giles, A G Morgan, A B Price, H Thompson,
AND G T WILLIAMS (University of Leeds, Leeds) At the BSG/SKF International Workshop on early gastric cancer (EGC) in 1982, it was decided to set up a register of patients diagnosed as having 'EGC' or 'gastric dysplasia' in Britain, and create a databank of information about these patients. This interim report outlines some initial findings of the survey.

By May 1985, some 59 BSG members from 22 hospitals had contributed 104 fully evaluated patients (a further 40 patients await review). After evaluation by the BSG panel (three independent pathologists) only 41 cases were confirmed as having EGC; 21 cases were classified as 'advanced gastric cancer', 25 patients as 'dysplasia' and 17 as other conditions. All but five EGC cases presented with pain, usually epigastric. The commonest mode of presentation (15 cases) was finding cancer in association with an existing gastric ulcer. Eleven patients were on long term H2 blocking drugs when their cancer was discovered. Only two patients had undergone previous gastrectomy. These interim results emphasise (i) differences between UK and Japanese presentation, a high proportion of UK cancers occurring in 'benign' gastric ulcers; (ii) dangers in prescribing H2 blockers for 'benign' gastric ulcer without regular biopsy.

F25
Collagenous colitis: a report of five cases
C H MASON AND D P JEWELL (Departments of Histopathology and Gastroenterology, John Radcliffe Hospital, Headington, Oxford) We have studied five cases of collagenous colitis occurring in four women and one man, varying from 62 to 79 years of age. Four patients had a history of watery diarrhoea. The fifth case had a 20 year history of intermittent diarrhoea with occasional bleeding suggestive of ulcerative colitis. Diagnosis was made on colorectal biopsy specimens by the presence of a subepithelial collagen band greater than 10μ in thickness.

Two patients had borderline collagen in the rectum (5–17μ) but had a well developed band (12–50μ) throughout the rest of the colon similar to that seen in the rectum of the other three. The collagen band showed marked variability in thickness. All cases showed a mild, non-specific inflammation. One case had multiple rectal biopsies over several years. Initially, these showed non-specific chronic inflammation but subsequently a collagen band appeared. Immunohistochemistry showed the collagen bands to be composed mainly of Type III collagen with some fibronectin. One case responded dramatically to steroid enemas and two showed partial response to oral sulphasalazine.

Collagenous colitis may exhibit minimal rectal involvement and the diagnosis could be missed on rectal biopsy. Clinical observation and histochemical staining are compatible with collagen developing in response to an inflammatory stimulus.

F26
Does super-efficient starch absorption promote diverticular disease?
J R THORNTON, A DRYDEN, J KELLEHER, AND M S LOSOWSKY (Department of Medicine, St James's University Hospital, Leeds) Populations eating a relatively low fibre diet have an increased prevalence of diverticular disease, but the factors determining individual susceptibility to this disease remain unclear. We, and others, have shown previously that dietary starch is incompletely absorbed and that unabsorbed starch is a quantitatively important source of colonic carbohydrate additional to that provided by fibre. The degree of starch malabsorption shows considerable variation between individuals.

We tested the hypothesis that super-efficient starch absorption, by reducing the provision of colonic carbohydrate, may promote diverticular disease. Eight patients with extensive, symptomatic diverticular disease were compared with eight age- and sex-matched healthy controls. On separate days, all subjects consumed, in random order, a standardised potato meal providing 60 g starch or 6.5 g lactulose. Breath H2 was measured every 15 minutes for up to 12 hours. The relative quantities of H2 generated enabled calculation of the amount of malabsorbed potato starch. The amount of unabsorbed potato starch provides a good approximation of unabsorbed starch from all food sources.

Percentage unabsorbed starch was low in all patients and was only about one quarter of that found in the controls (mean±SEM: 3.3±0.5% vs 12.4±1.8%, p<0.01). For the average Briton consuming 150 g starch and 21 g fibre daily, this difference represents nearly 14 g of unabsorbed starch, equivalent to almost two-thirds of the colonic carbohydrate provided by consumption of fibre. Mouth-to-caecum transit time of unabsorbed potato starch was similar (patients 321 min vs controls 272 min, NS).

Super-efficient starch absorption, by reducing the provision of colonic carbohydrate, may promote the development of diverticular disease.

F27
Effect of ampicillin on the colonic salvage of carbohydrate
S S C RAO, C A EDWARDS, C J AUSTEN, V A BEATTIE, N W READ, AND C D HOLDSWORTH (Clinical Research Unit, Royal Hallamshire Hospital, Sheffield) The colon normally salvages unabsorbed carbohydrate by bacterial conversion to volatile fatty acids, which are then rapidly absorbed together with water. Impairment of bacterial fermentation may therefore result in an osmotic diarrhoea in people ingesting unabsorbable carbohydrate. We have tested this hypothesis by studying the effect of 500 mg ampicillin tid on stool weight and frequency and breath hydrogen production in 13 normal volunteers before and after administration of 20 g lactulose. Studies were separated by two weeks and dietary intake was similar during each study. Administration of lactulose did not increase stool weight and frequency under control conditions (190±31-4 g/day vs 195±12.8±6 g, mean±SEM and 1.38±0.28 motions/day vs 1.46±0.13) but after administration of ampicillin stool weight (273±3±62.2 g vs 390±7±43 g, p<0.02) and stool frequency were significantly increased (1.38±0±26 vs 2.30±0.35, p<0.01). Ampicillin did not significantly increase basal stool weight and frequency under basal conditions. There was no significant change in the breath hydrogen response to lactulose after ampicillin, although in two subjects the response was nearly abolished. Mouth-to-caecum transit of the lactulose meal was prolonged during antibiotic ingestion (49±5.9 min vs 75±7.4 min, p<0.05) but there was no significant change in the whole gut transit time. These results suggest that antibiotic associated diarrhoea could result from impaired salvage of carbohydrate.

F28
Emergence of Clostridium difficile and...
disturbance of faecal flora after single dose intravenous antibiotic administration

R G TUDOR, N S AMBROSE, M JOHNSON, D YOUNGS, D W BURDON, AND M R B KEIGHLEY (Department of Surgery, The General Hospital, Birmingham) We have studied the effect on faecal flora and the emergence of *Clostridium difficile* (CD) over a two week period after a single dose of eight cephalosporins and seven penicillins. Each antibiotic was administered to six volunteers (total 90 volunteers) and a further group of six volunteers served as controls. Stool samples were obtained prior to antibiotic administration and at 1, 4, 7, and 14 days subsequently, and at similar time intervals in the controls. Total viable counts of individual bacterial and fungal species were obtained and the presence of *C. difficile* and its toxin specifically sought.

Alteration in faecal flora by antibiotics was estimated by expressing the number of individual bacterial species present in all five specimens as a percentage of the total number of species identified.

These results show that the cephalosporins produce a more marked disturbance in faecal flora and this is often associated with emergence of *C. difficile*.

F29 Use of monoclonal antibodies to ras oncogene product in the differentiation between benign and malignant diseases of the colon

N A HABIB, H NIMAN, A THOMPSON, R C N WILLIAMSON, AND C B WOOD (Department of Surgery, RPMS, London, Department of Surgery, Bristol Royal Infirmary, and Department of Molecular Biology, Scripps Res Center, La Jolla, California, USA) Proto-oncogenes are responsible for normal cell growth and their conversion to a cellular oncogene leads to abnormal cell proliferation.

The expression of c-ras oncogene on chromosome 12 has been demonstrated in carcinoma of the colon and rectum. Using the peroxidase-anti-peroxidase technique colonic tissue (obtained from mounted paraffin blocks) was stained with a monoclonal antibody against ras-oncogene product (Mo-RAP) to a concentration of 1:200. The patients studied were five normal subjects and 25 patients with various pathological conditions (five Crohn's disease, five ulcerative colitis, five diverticular disease, 10 colorectal carcinomas). A sharp contrast was found between the strong positive staining in the cytoplasms of all 10 carcinomas and the weak cryoplastic staining mainly at the crypt base in normal and inflamed large intestine. Therefore, staining of colorectal tumour tissue with Mo-RAP may open new avenues for diagnostic and therapeutic modalities. These findings suggest a much stronger expression of ras-oncogene in cancer tissue compared with normal or inflammatory tissue, and that Mo-RAP staining offers new diagnostic and therapeutic opportunities in colorectal malignancy.

F30 Histological grading of rectal cancer: a multivariate analysis

J R JASS AND W S ATKIN (St Mark's and St Bartholomew's Hospitals, London) The pathological grading of rectal carcinoma is a subjective exercise associated with considerable interobserver variation. The aim of this study was to identify and rank prognostic factors in order to refine current methods of grading.

Tissue sections through the primary tumours from a consecutive series of 447 patients were examined. All patients had survived radical surgery for rectal cancer for at least 28 days and had been followed up for 20 years. Histological factors graded subjectively were: architecture (regular, irregular, no glands), nuclear polarity (easily discerned, just, lost), pattern of growth (expanding, infiltrating), lymphocyte infiltration at growing edge (marked, moderate, little) and fibrosis (little, moderate, marked). Lymph node status was not known. Multivariate analysis using the Cox regression model was employed.

Factors most strongly related to survival were ranked: (1) lymphocyte infiltration, (2) pattern of growth, (3) architecture, (4) nuclear polarity, (5) fibrosis. A prognostic model was constructed by adding each factor in turn to the first. Prediction of survival was not improved beyond architecture. When lymph node status and extent of spread were added to the model, only lymphocyte infiltration was found to be significant (p<0.001). The overriding influence of lymphocyte infiltration upon survival has not been demonstrated previously.

F31 Frequency of colorectal cancer among the first-degree relatives of patients with cancer or polyps of the large bowel

M PONZ DE LEON, A ASCARI, A ANTONIOLI, F MANENTI, G MELOTTI, C PECZOLLER, I PICCAGLI, A GRISINI, D MAZZEO, AND A MISELLI (Istituto di Patologia Medica, Università di Modena, Italy) Despite the importance of environmental factors there is evidence that cancer of the large bowel may involve a genetic component. The institution of a registry for colorectal tumours in our health care district gave us the opportunity to test if close relatives of patients with colorectal cancer or polyps are more likely to develop large bowel cancer than members of the general population. For each registered patient a careful clinical history was taken and the genealogic tree, limited to the first-degree relatives, was drawn. Particular attention was given to relatives affected or deceased of neoplastic diseases. Each patient was matched to a control - that is, a patient of the same age (±5 years) and sex hospitalised but not for neoplastic or colonic diseases. At one year, a total of 139 cases of cancer and 157 of polyps were registered; there were 2202 first-degree relatives in the diseased group (1325 alive) and 2203 in the controls (1328 alive). Among the relatives of patients with tumours we found 71 cases of colorectal cancer as compared to 16 in the controls (Relative Risk = RR=4.55, $\chi^2=34.1$, p<0.001). As for the parents there were 23 cases vs 10 (RR=2.35, p<0.02); among the siblings 44 vs 4 (RR=12.2, p<0.001); as for sons vs 2 (ns). When considered separately, an increased frequency of cases of colorectal cancer among first-degree relatives was found either in the cancer or in the polyps group. It is concluded that large bowel cancer occurs four times more often in relatives of patients with colorectal cancer or polyps than in controls. Nearly 20% of the registered tumours may be defined as familial. Since a familial aggregation was observed both in the cancer and in the polyps groups, our findings provide further evidence to the 'polyp-cancer theory'.

F32 Use of monoclonal antibodies against ras oncogene products to inhibit the metabolism of human colorectal cancer cells in vitro

N A HABIB, C B WOOD, H L NIMAN, B FERMOR,
MO SYMES, AND R C N WILLIAMSON Department of Surgery, Royal Bristol Infirmary, Bristol, Department of Surgery, Royal Postgraduate Medical School, London, and Department of Molecular Biology, Scripps Institute, La Jolla, USA) Proto-oncogenes are responsible for normal cell growth. During malignant cell transformation they become activated oncogenes and produce growth factors. c-ras oncogene is specifically expressed in colorectal carcinomas. To test their potential therapeutic role, monoclonal antibodies against ras-oncogene products (Mo-RAP) were applied to disaggregated human colorectal cancer cells obtained from nine primary tumours. After 24 hours exposure in tissue culture for Mo-RAP, the tumour cells were cultured to a further 24 hours with 1 μCi/ml of radioactive selenomethionine (35Se). Protein synthesis was then measured in terms of incorporated radioactivity.

Mo-RAP caused marked inhibition of protein synthesis by colorectal cancer cells obtained from four out of the nine patients. The isotope uptake relative to untreated cells was significantly reduced in four tumours (p<0.05, <0.02, <0.001 and <0.005). In all these four patients a cytosin preparation of the tumour cells stained specifically with Mo-RAP. The widespread expression of oncogenes and their encoded proteins in human malignancies could thus provide possible therapeutic targets.

F33 Monoclonal antibody binding to primary and metastatic colorectal cancer

K C BALLANTYNE, L G DURRANT, N C ARMITAGE, R A ROBINS, R W BALDWIN, AND J D HARDCASTLE (Departments of Surgery and Cancer Research, University of Nottingham, Nottingham) The pattern of antigen distribution in primary colorectal tumours has been defined by monoclonal antibodies. The distribution and degree of antibody binding to metastatic, however, compared with primary colorectal cancer has not been fully evaluated. Using flow cytometry and immunohistochemistry we assessed the binding of the monoclonal antibodies 791T/36—antiosteosarcoma, C14/1/46—anticoliconic adenoma and C161/25—anticarcinoembryonic antigen, to 35 primary colorectal cancers, 13 lymph node metastases and nine hepatic/omentum metastases.

After disaggregation tumour cell binding was measured by flow cytometry using indirect immunofluorescence. Fluorescence values were corrected for non-specific binding using normal mouse immunoglobulin. Immunohistochemistry was carried out using the indirect peroxidase technique.

The median linear fluorescence (fluorescence units FIU) for each antibody was: 791T/36 162 FIU (primary), 180 FIU (node), 239 FIU (metastasis), C14/1/46 407 FIU (primary), 623FIU (node), 833 FIU (metastasis), C161/25 899 FIU (primary), 380 FIU (metastasis), 1312 FIU (metastasis). Immunohistochemistry demonstrated that the antigen distribution of primary colorectal cancer is retained in metastatic tumour deposits.

Confirmation that metastases retain similar pattern with increased antigen expression to primary colorectal cancer provides further evidence that targeted immunotherapy may effectively treat metastatic colorectal cancer.

F34 T lymphocyte subpopulations in the blood, primary tumour and normal colonic mucosa of patients with colorectal carcinoma

T W J LENNARD, A WARFDA, B K SHENTON, G PROUD, R M R TAYLOR (INTRODUCED BY D A JOHNSTON) (Departments of Surgery and Pathology, University of Newcastle upon Tyne, Newcastle upon Tyne) The degree of 'host response' within tumours has been related to prognosis. The immunoregulatory T lymphocyte subpopulations in 36 primary colorectal carcinomas have been characterised using cryostat immunohistochemistry and a panel of monoclonal antibodies to pan T (OKT3), helper (OKT4) and suppressor/cytotoxic (OKT8) lymphocytes. Normal colonic mucosa from the proximal resection line of 26 of the tumours was also analysed. The mean ratio of helper to suppressor/cytotoxic lymphocytes ±SD in the stroma of the tumours was 0.55±0.21, and in the lamina propria of normal mucosa 1.68±0.34 (p=0.001) (Student's paired t test). The mean peripheral blood ratio ±SD in 34 patients with colorectal carcinomas was 1.5±0.28. The finding of a significant increase in suppressor/cytotoxic lymphocytes within colorectal carcinomas compared to normal mucosa and peripheral blood may contribute to down regulation of the host immune response in situ. These findings were independent of histological grade or stage and the presence or absence of venous invasion by tumour.

F35 Cell cycle kinetics during experimental colonic carcinogenesis

T COOKE, J L MATTHEWS (INTRODUCED BY A PARKINS) (Charing Cross Hospital, Fulham Palace Road, London) Increases in crypt cell production rate, maximal in the descending colon, occurs during induced carcinogenesis. To determine its mechanism, cell cycle kinetics in colonic crypts were investigated.

At week 25, rats treated with azoxymethane or saline sc for 12 weeks were given vincristine 1 mg/kg ip, to arrest cells in metaphase, and killed at 15 minute intervals. Metaphases were counted in 100 descending colon crypts per animal expressed as a percentage of total crypt count and plotted against time. Entry into mitosis was calculated from the slope of the resulting regression line and cell cycle time derived as its reciprocal.

There was a significant hyperplastic response in treated rats compared with controls increasing from 36-69±2.71 to 48-84±4.64 cells crypt (p<0.001). The proliferation zone increased from 23 to 29 cells although the proportion of dividing cells (growth fraction) did not alter between controls (0.62) and carcinogen groups (0.59). Rate of entry into mitosis decreased significantly from control values of 6.48±0.87% cells per hour (p<0.001) and cell cycle time increased from 30.86 to 59-09 hours.

Absolute increases in the numbers of proliferating crypt cells, despite a slowing down of cell division, explains the previously observed elevation in crypt cell production rate (1), advancing our understanding of the mechanism of colonic carcinoma development.

F36 Specialist investigation of obscure gastrointestinal haemorrhage

R SALEM, J N THOMPSON, A P HEMINGWAY, H C REES, H J F HODGSON, C B WOOD, D J ALLISON, AND J SPENCER (Departments of Surgery, Radiology and Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) The cause of gastrointestinal haemorrhage is not identified by routine investigations in about 5% of cases. Over six years 131 patients with 'obscure' gastrointestinal bleeding have been investigated. The median age was 62 years (range 10–95) and 70 patients were
men. Only 25 presented as emergencies, while 87% were referred for specialist investigation. The mean presenting feature was melaena (55 cases), anaemia (35), rectal bleeding (34), haematemesis (six), and ileostomy bleeding (one). The median duration of symptoms was 50 weeks (range 1 day–36 years) with a median two previous hospital admissions (range 0–20). Twenty six had undergone previous surgery.

The lesions identified were colonic angiodysplasia (52 patients), small bowel vascular anomalies (16), Meckel's diverticula (nine), leiomyomas (seven), gastric vascular anomalies (four), chronic pancreatitis (three), colonic diverticular disease (three), and 16 single other causes. Sixty per cent of lesions were first shown on visceral angiography, 22% at surgery, 10% on endoscopy, 5% on barium examinations and 3% at ERCP. Seventy eight patients underwent surgery. No lesion was found in 21 cases (16%).

Specialist investigation, especially expert angiography, identified the cause of obscure gastrointestinal haemorrhage in the majority of cases. In a significant proportion, however, the cause was not found until exploratory laparotomy.

F37
Functional changes after mucosal proctectomy with colo-anal anastomosis (CSA) for chronic radiation rectal injury
J S Varma, A N Smith, and A Busuttil (University Department of Surgery/Urology and Department of Pathology, Western General Hospital, Edinburgh) Despite its success in dealing with the complications of chronic radiation rectal injury, marked urgency and frequency of defecation and anorectal incontinence occasionally follow CSA. To elucidate the cause, anorectal physiology was compared in eight patients and matched control subjects. Conventional manometric techniques were used to measure rectal compliance (RC, ml/cm H₂O), maximal tolerable volume (MTV, ml H₂O), resting (MRP) and squeeze (SP) anal pressures (cm H₂O), sphincter length (HPZ, cm) and the rectosphincteric reflex (RSR). Concentric needle EMG determined pelvic floor activity during contraction, straining and balloon rectal distension. Resected rectal specimens were examined using conventional techniques for histopathology.

There is significant reduction in RC, MTV, MRP and SL but not in SP after CSA (RC: control 8.7±1.1, mean±SEM, CSA 1.8±1, p<0.01; MTV: control 504±29, CSA 120±25, p<0.01; MRP: control 104±5, CSA 54±8, p<0.01; SL: control 3.5±0.25, CSA 2.4±0.2, p<0.02; Wilcoxon's signed rank sum test). Four CSA patients had an absent RSR, four expelled the balloon at the MTV and four showed increased pelvic floor EMG activity on strain and rectal distension (none of the controls). Myenteric plexus abnormalities, including paucity and vacuolation of ganglion cells and nerve fibre proliferation, was a prominent feature in all the excised specimens and may be responsible for many of these abnormalities.

F38
Outcome of surgery in colonic angiodysplasia
R R Salem, J N Thompson, H C Rees, A P Hemingway, D J Allison, J Spencer, and C B Wood (Departments of Surgery, Histopathology and Diagnostic Radiology, Royal Postgraduate Medical School, London) Bleeding from colonic angiodysplasia may be treated by endoscopic coagulation or by resection. Twenty nine patients who were diagnosed as having angiodysplasia by selective visceral angiography or colonoscopy underwent resection for persistent gastrointestinal bleeding.

Peroperative colonoscopy with transillumination was undertaken in 10 patients and in eight this was valuable in visualising the lesions and determining their extent. Histology on 28 of the 29 resected specimens (with barium injections in 17) confirmed the diagnosis in 20 (71%). There were three postoperative deaths. Of the remaining 26 patients, five bled subsequently (median follow up = 24 months) one from a definite source and two from less clearly defined sources. In two of these patients additional lesions were resected at the same operation while in seven other patients resection of the angiodysplasia was not undertaken because alternative lesions more likely to have bled were identified at laparotomy.

Endoscopic coagulation is being used increasingly to arrest haemorrhage in angiodysplasia, however resection may be required if this is unsuccessful. In 19% of patients, however, bleeding recurred despite successful resection of an area of proven angiodysplasia. An extensive search for concurrent pathology appears indicated to identify alternative sources of haemorrhage.

F39
Smoking and inflammatory bowel disease
M Y Tobin, R F A Logan, M J S Langman, R B McConnell, and I T Gilmore (Gastroenterology Unit, Royal Liverpool Hospital, Liverpool, Departments of Therapeutics and Community Health, Queen's Medical Centre, University of Nottingham) While the intriguing association of ulcerative colitis (UC) with non-smoking is now established, the association of smoking and Crohn's disease (CD) has yet to be confirmed and it is uncertain whether these associations are not secondary to developing inflammatory bowel disease (IBD). We have, therefore, investigated smoking habits in 280 patients (157 UC, 123 CD) and 280 general practice controls matched for age, sex and locality, with over 95% of subjects returning a postal questionnaire.

Compared with the controls CD patients were more likely to report being current smokers (48% relative risk (RR) 1.4) and UC patients less likely (14% RR 0.17 p<0.001). Crohn's disease patients were also more likely to have ever smoked (76% RR 3.2 p<0.001) and UC patients less likely (50% RR 0.53 p<0.025). Before the onset of disease CD patients were again more likely to be smokers than their controls (63% RR 4.1 p<0.001) and UC patients less likely (17% RR 0.24 p<0.001). Compared to never smokers ex-smokers had small but non-significant increased risks of both UC (RR 1.4) and CD (RR 1.8). Smokers with IBD are almost three times as likely to have CD as UC.

Both associations are strong, consistent and antedate disease onset and use of identical methods minimises the possibility of systematic biases. By confirming the contrasting associations of smoking habit in UC and CD this study strengthens the claim for an aetiological role of cigarette smoking in IBD.

F40
Indirect evidence against the viral hypothesis in Crohn's disease in the Lyons area
C Andre, L Descos, and S Daniere (Introduced by R N Allain) (Groupe d'Immunopathologie Digestive INSERM, Centre Hospitalier, Lyon Sud, Pierre Bénite,
Many discrepancies exist with regard to the direct demonstration of the presence of an infectious agent in Crohn's disease. A general agreement does exist with regard to two indirect elements, (1) the high prevalence of lymphocytotoxic antibodies suggest that a viral agent may be involved in the pathogenesis, (2) Crohn's disease ultratitrfates produce lymphoma in athymic mice.

Crohn's disease is infrequent in France and particularly in the Lyons area. Thus the same studies were repeated on patients from this region. Lymphocytotoxic antibodies were screened by an objective technique measuring the lymphocyte viability of a panel of eight donors by the determination of the residual ATP content (average killing of 20% or more of target cells from at least four donors).

Serum lymphocytotoxic antibodies were detected in three out of 56 healthy controls (5%), in two out of 56 patients with Crohn's disease (3-5%), in 16 out of 57 patients with ulcerative colitis (28%) and in 11 out of 13 patients with infectious mononucleosis (85%).

Twenty patients with Crohn's disease and 23 patients with ulcerative colitis were studied both when the disease was active and quiescent. No evident relationship could be established between the presence of lymphocytotoxic antibodies and clinical activity.

Mucosal and mesenteric lymph node homogenates from 10 patients with Crohn's disease were injected into 100 nude mice. Mice were killed after seven to 14 months. None developed a lymphoma.

If an infective agent is responsible for Crohn's disease it does not seem to be present in the Lyons area or possibly it differs in its characteristics from those agents demonstrated in other countries.

Deaths. Twenty nine died postoperatively mostly (20) from sepsis. Sepsis was the main cause of death in a further 13 patients. Cancer of the gastrointestinal tract was the primary cause of death in 22 patients. Other less common problems included pulmonary embolism (eight), steroid related deaths (seven), amyloidosis (four), others (six) and early in the series electrolyte imbalance (10).

We conclude that the use of peroperative antibiotic prophylaxis and the identification and treatment of sepsis at other times should improve mortality rates. Changes in peroperative management should reduce the incidence of thromboembolic disease. Finally, screening for colorectal cancer should be considered in patients with longstanding extensive colitis.

F42 Adhesive E coli in ulcerative colitis

D A Burke and A R Axon (Gastroenterology Unit, The General Infirmary, Leeds) E coli from patients with ulcerative colitis have been studied for adhesive properties using a buccal epithelial cell (BEC) adhesion assay. This technique has several advantages over HeLa cells as it allows quantitation of adhesive properties and assessment of host factors.

Suspensions of BEC were incubated with E coli isolates in the presence of D-mannose for 30 minutes. An 'adhesion index' was obtained for each assay by counting the number of BEC (out of 100) with greater than 50 adherent organisms. E coli isolates from controls (n=18) adhered significantly more than those from controls (n=12). Colitic isolates; median adhesion index=43.5 (18-68); control isolates; median=2.0 (0-15) p<0.0001. Using a single adhesive strain there was no significant difference between the adhesion to BEC's obtained from colitics (n=12 median 67 (45-84)) and those from controls (n=12 median 69 (59-78)). Similarly for non-adhesive E coli.

This study shows different populations of E coli in the two groups. The BEC adhesion assay clearly separates colitic E coli from controls by their adhesive properties raising the possibility of a pathogenic role for adhesive organisms in ulcerative colitis.

F43 Abnormal presence of lactosylceramide detected in Crohn's disease by thin layer chromatography

The British Society of Gastroenterology

C Stevens, W Oberholzer, J Walker-Smith, and A Phillips (Queen Elizabeth Hospital for Children, London) We are currently investigating the involvement of phospholipids and related compounds in Crohn's disease. Lipids were extracted from mucosal biopsy homogenates with chloroform, methanol and water. Two dimensional thin layer chromatography was used to separate the phospholipid fraction. Small and large bowel samples (from adults and children) were studied from 10 patients with Crohn's disease, 11 patients with active ulcerative colitis (UC), and 11 patients with normal colonic histology. Samples from involved sites in nine patients with Crohn's disease strongly displayed two abnormal compounds of chromatography. These were faintly present in eight of the 11 patients with UC and the remaining patients with Crohn's disease, but did not appear on any other chromatography. Oricolin and diphenylamine tests showed the compounds to be glycolipids. They were also isolated from neutrophil-enriched peripheral leukocytes of healthy adults and co-migrated with purified lactosylceramide from human neutrophils (donated by Dr B A Macher, California). We therefore have a biochemical marker which appears to discriminate between Crohn's disease and UC. The degree of mucosal neutrophil infiltration was similar in the samples from Crohn's disease and UC and thus cannot fully explain the strong presence of lactosylceramide in Crohn's disease. Additional mucosal sources of lactosylceramide are being sought, as is its presence in other inflammatory diseases.

F44 Rapid bowel preparation for outpatient flexible sigmoidoscopy

S H Silverman and M R B Keighley (Department of Surgery, General Hospital, Birmingham) Fibreoptic flexible sigmoidoscopy (FFS) can easily be done at the initial outpatient attendance provided that efficient bowel preparation is possible. In a prospective randomised study the efficiency of two preparations, phosphate enema (Fletchers phospate PHARMAX) and Micralax microemina (SK&F) were compared in unstarved and unpurged outpatients at a Rectal Clinic.

Faecal loading was assessed during rigid sigmoidoscopy and patients then received randomly either a phosphate enema (n=32) or Micralax microemina (n=24). The patient having relieved himself, FFS
was performed and faecal loading reassessed. Faecal loading was graded as I = no faeces, II = minor residue, III = gross residue.

Before preparation faecal loading was equivalent in the two groups. Phosphate enema produced a highly significant reduction in faecal loading ($\chi^2=9.43$, $p<0.001$) but Micralax did not ($\chi^2=0.9$, $p=NS$). After preparation faecal loading was significantly lower in the phosphate group than the Micralax group ($\chi^2=11.25$, $p<0.001$). Phosphate enema is superior to Micralax in preparing unpurged unstarved patients for FFS; furthermore, purging prior to FFS is unnecessary as a single phosphate enema gave adequate preparation in 29/32 (91%) of cases.

F45
Azidosalicylate for the treatment of active ulcerative colitis (UC)

A Ireland, W S Selby, G D Barr, C H Mason, AND D P Jewell (Gastroenterology Unit, Radcliffe Infirmary, Oxford) Sodium azidosalicylate (ADS) consists of a dimer of 5-aminosalicylic acid (5-ASA), the active ingredient of sulphalazine. Azidosalicylate has been assessed, double blind, in both enema and oral form in patients with mildly active distal UC. All patients were assessed clinically, sigmoidoscopically and histologically. For the enema trial, 60 patients were randomised to receive either ADS enema 1 g nightly or a dummy enema for two weeks. Nineteen of 29 on ADS improved, nine remained unchanged and one deteriorated. Twelve of 28 on dummy improved, 14 remained unchanged and two deteriorated. These differences were not significant. Sigmoidoscopic responses showed a similar pattern. Response was unrelated to previous sulphalazine therapy or length of history. For the oral trial, 40 patients were randomised to receive either ADS capsules 2 g/day or dummy capsules for two weeks. Sulphasalazine was stopped on entry. Thirteen of 20 on ADS improved, six remained unchanged and one deteriorated. On dummy, eight of 20 improved, three remained unchanged, and nine deteriorated. These differences were statistically significant ($p<0.002$). Sigmoidoscopic responses were also better in the ADS group ($p<0.05$). Responses were unrelated to length of history or previous sulphasalazine. The drug was well tolerated in both trials, and adverse reactions were minimal. Azidosalicylate in oral form is therefore effective in mildly active distal UC, and is a useful alternative to sulphalazine.

F46
High performance liquid chromatography (HPLC) of plasma PABA – a sensitive assay for pancreatic exocrine dysfunction

I M Chesner, J Berg, N Lawrence, AND P Asquith (The Metabolic Unit and Department of Clinical Chemistry, East Birmingham Hospital, Birmingham) The NBT-PABA test has a recognised role in the investigation of pancreatic dysfunction. Conventionally PABA excretion is measured in the urine by chemical methods. The assay is subject to interference by a wide range of drugs – for example, aspirin and paracetamol, and the method depends upon normal hepatic and renal function, plus a complete six hour urine collection. Using an HPLC assay for the detection of PABA in plasma we have studied nine patients with proven pancreatic steatorrhea, seven patients with chronic pancreatic disease without steatorrhea, and 11 healthy controls. The test was carried out in the standard way using 1g NBT-PABA, 25 g casein and 5 ml C14 PABA taken orally. Serial blood specimens were taken at one, two, three and four hours. Separation between the three groups was evident at two, three and four hours and was maximal at three hours. The three hour mean (SD) for healthy controls was 47.9 (±10.4) that for the pancreatic disease group without steatorrhea 17.6 (±5.4) (p<0.01). In the group with proven pancreatic steatorrhea eight of the nine had an undetectable three hour level, the other a level of 9.3 μmol/l (p<0.001).

We conclude that an HPLC assay of PABA in plasma is a rapid and accurate method of assessing pancreatic exocrine function. A single three hour plasma level will discriminate between normals, pancreatic damage and pancreatic malabsorption.

F47
Use of fresh frozen plasma in the treatment of acute pancreatitis

T Leese, K P West, AND A W Hall (The Department of Surgery and Pathology, University of Leicester, Leicester) Administration of fresh frozen plasma (FFP) may reduce mortality in acute pancreatitis, possibly by replenishing the plasma antiprotease system. An animal study has been undertaken to assess further the value of FFP in acute pancreatitis. Acute haemorrhagic pancreatitis was induced in male AS rats 250-300 g by transduodenal infusion of 0.2% enterokinase and 3-5% sodium taurocholate into the pancreatic duct system. Animals underwent right internal jugular vein cannulation and, on recovery from anaesthetic, 30 animals were randomised to each of three intravenous fluid regimes. Group A received 8 ml of normal saline and 16 ml of dextrose saline per 24 hour. Group B received 8 ml of 'Haemacel' and 16 ml of dextrose saline and group C received 8 ml of FFP and 16 ml of dextrose saline. Infusions were repeated each 24 hour for 72 hours.

There were nine survivors (30%) at 72 hours in group A, 13 (43%) in group B and 22 (73%) in group C. Using a χ2 test the improved survival in the FFP group reached significance when compared with the crystalloid controls (p<0.001) and the colloid controls (p<0.05). A randomised prospective trial is now underway comparing FFP (2 units per day for three days) to plasma protein fraction (400 ml per day for three days) as part of the intravenous fluid administered to patients admitted with acute pancreatitis.

F48
Ultrasound assessment of bile duct obstruction: level, cause, and tumour resectability

R N Gibson, E Yeung, H A Bradpiece, J N Thompson, D H Carr, A P Hemingway, I S Benjamin, D J Allison, AND L H Blumgart (Departments of Radiology and Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London) In a prospective study of 65 patients with bile duct obstruction the role of ultrasound was evaluated in relation to other radiological modalities. Computed tomography (CT) was carried out in 51 patients, direct cholangiography in 57, and angiography in 32. Of ultrasound determined the correct level of obstruction in 61 patients and in predicting cause was correct in 56, incorrect in three and indeterminate in five. The corresponding results for CT were 45, 32, 3 and 16.

Thirty seven of the 58 patients with malignant obstruction had hilar tumours. Of this group irresectability was established radiologically in 27 and operatively in a further two. Ultrasound alone predicted irresectability in 21 and in two of these it was the only modality to do so. One patient judged by ultrasound to be
probably irresectable was in fact resectable. Computerised tomography was able to predict irresectability in only 11 out of 25 cases. In 21 patients with non-hilar malignant obstruction ultrasound assessment of resectability disagreed with the combined prediction of the other modalities in only five cases and in three of these the ultrasound prediction was correct on operative findings.

We conclude that good quality ultrasound is the most useful and frequently the only necessary imaging modality for patients with bile duct obstruction.

F49
Acid stable lipase in the treatment of pancreatic steatorrhoea

S M Griffin, D Alderson, and J R Farndon (Introduced by M B Clague) (Department of Surgery, New Medical School, Framlington Place, Newcastle upon Tyne) Pancreatic exocrine insufficiency in cystic fibrosis and chronic pancreatitis results in steatorrhoea with concomitant poor nutrition and social embarrassment. Long term conventional treatment has been unsatisfactory because up to 90% of the lipase content of such therapy is inactivated by gastric acid. This results in a need for large volumes of medication to provide adequate supplementation. The aim of this study was to investigate the efficacy of a new acid resistant agent—fungal lipase in the treatment of pancreatic exocrine deficiency steatorrhoea.

Eleven dogs with pancreatic insufficiency were studied while taking a fixed dietary intake of fat. All animals were randomly allocated to fungal lipase, pancreatic and placebo for two week courses of treatment regimens. Ten grams (60 000 U lipase) of pancreatic was compared with 400 mg (24 000 U lipase) of fungal lipase given with each meal against a placebo. Mean faecal fat concentrations over a three day period were performed. Data were analysed using the Wilcoxon's rank sum test for paired data. There was no significant difference between pancreatic and lipase treated animals. Both groups had significantly reduced steatorrhoea when compared with placebo (p<0.01). This study shows that a markedly reduced volume of treatment in the form of fungal lipase controls steatorrhoea as effectively as pancreatic, and represents a potentially valuable new therapy for pancreatic exocrine insufficiency.

F50
Is cholecystectomy needed after endoscopic removal of common bile duct stones in the elderly?

D F Martin and D E Tweedle (University Hospital of South Manchester, Manchester) Between July 1981 and December 1983, 35 patients aged between 50 and 94 years (mean 79) underwent successful endoscopic clearance of common bile duct (CBD) stones. They presented with a combination of obstructive jaundice (25 patients), acute cholangitis (10), acute pancreatitis (two) and biliary colic (11). Ten patients had a history of myocardial infarction or stroke and three others had been treated for bronchial carcinoma. Twenty five patients remain alive and symptom free 19 to 46 months (mean 28 months) after treatment. Seven patients have died, none as a result of gall bladder disease. One patient, aged 50, underwent elective cholecystectomy but had been symptom free for four months since endoscopy. Two patients have required cholecystectomy for acute cholecystitis five and six months after common duct clearance. In both the gall bladder had filled at ERCP. Exploration of the CBD was not necessary. These results suggest that endoscopic treatment alone for CBD stones is indicated in elderly high risk patients with gall bladder, subsequent cholecystectomy proving necessary in less than 10%. Lack of filling of the gall bladder at ERCP does not appear to be a useful indicator of the future need for cholecystectomy.

F51
Does drainage increase the risk of subhepatic collection following cholecystectomy?—a prospective study

J R T Monson, H Irving, A W Tanner, J Macrie, and T G Brennan (St James's University Hospital, Leeds, West Yorkshire) Intraperitoneal drainage after cholecystectomy is traditional but unsupported by scientific data. In an uncontrolled study in 1983, Elboim demonstrated with ultrasound a significant incidence of subhepatic collections following cholecystectomy, with the figure much higher in drained patients, suggesting a causative link. We have evaluated the influence of intraperitoneal drains on the incidence of these collections in a randomised prospective trial. Ninety three patients undergoing cholecystectomy were randomised at the end of the operation into a drainage, (1" suction drain for 48 hours (n=44)), or non-drainage group (n=49). Patients with perforated gall bladders or undergoing exploration of the common bile duct were excluded. All patients had abdominal ultrasound carried out 72 hours postoperatively. The number of patients with acute cholecystitis was similar in the drainage and non-drainage group (11% vs 12%). Ultrasound detected six collections in the drainage group and one collection in the non-drainage group (p<0.05 χ). The average volume of the collections was 300 ml. None was clinically significant. These results suggest that drains may actually increase the risk of developing a subhepatic collection after cholecystectomy. Further prospective studies are required.

F52
Cholecystokinin provocation test in suspected acalculous biliary pain—the first half years of clinical use

T W J Lennard, J R Farndon, and R M R Taylor (Introduced by J D A Johnson) (Department of Surgery, University of Newcastle, Newcastle upon Tyne) A double blind placebo controlled infusion of cholecystokinin (CCK) has been used to attempt to reproduce the presenting symptom in 123 patients with unexplained right upper quadrant abdominal pain. Sixty two patients (53 women, nine men, mean age 44 years) developed pain with CCK and not with saline infusions (CCK positive). Fifty nine patients (46 women and 13 men, mean age 43 years) developed no pain during either infusion (CCK negative) and two patients developed pain during both infusions. Fifty four patients who were CCK positive v.e have undergone cholecystectomy to date, and of these 51 (94%) have been relieved of their pain and have had no response to postoperative CCK/ placebo infusions (mean follow-up 11-9 months, range two months to 3-5 years). Gall bladder histology was abnormal in 48 cases (chronic cholecystitis and/or cholesterolosis) and a small gall stone was found in two cases. Cholecystokinin negative patients have been followed up and nine have spontaneously improved. Fifteen remain undiagnosed and in 35 an alternative cause for their pain has been found. The cholecystokinin provocation test will identify those patients who are likely to have a good response to cholecystectomy.