The British Society of Gastroenterology

The 49th Meeting of the British Society of Gastroenterology was held at the University of Sheffield on 14–16 September, 1988, under the Presidency of Dr J J Misiewicz. Below are printed the abstracts of the 285 oral and poster communications selected for presentation at the meeting.

The liver

Investigation of hepatic disease by echo planar imaging

R M CHARNLEY, M K STEHLING, D F EVANS, R COXON, A M HOWSEMAN, R J ODRIDGE, I D HARDCASTLE, P MANSFIELD (Departments of Physics and Surgery, Nottingham University, Nottingham) Conventional magnetic resonance imaging of the liver is hampered by the motion related problems of blurring and image artefact which are caused by respiration. In addition, the long image acquisition time means imaging one liver may take up to 45 minutes.

The Echo planar imaging (EPI) variant MBEST (Modulus Blipped Echo-Planar Single Shot Technique) is a rapid magnetic resonance imaging technique which produces a complete image in 62 ms, allows up to 200 frames to be taken per minute and is not subject to distortion by respiration. The whole depth of the liver can be imaged in transverse slices during one breath hold.

We have carried out EPI of the liver on three patients with focal liver lesions and on one healthy volunteer. Focal lesions (hepatic metastases and one cyst) were imaged without blurring or image artefact and blood flow in the hepatic veins could also be visualised by producing a cine loop.

Echo planar imaging has the potential to revolutionise magnetic resonance imaging of the liver in that a complete scan of the liver can be carried out in less than a minute. The intrinsic T2 weighting of the MBEST technique ensures good soft tissue contrast and is very sensitive to pathological tissue changes so enabling imaging of focal lesions.

Plasma leucine enkephalin is increased in liver disease

J R THORNTON, M S LOSOWSKY (Department of Medicine, St James’s Hospital, Leeds) The liver may play a role in elimination of blood borne, small, opioid peptides. In favour of this hypothesis, the pentapeptide methio-

dine enkephalin, but not the much larger peptide β-endorphin, is increased in hepatic disease. Administration of an opioid antagonist to patients with cirrhosis produces a withdrawal reaction, and relieves pruritus and fatigue, indicating that increased opioid activity contributes to some of the manifestations of hepatic failure.

To determine whether another small opioid peptide, pentapeptide leucine enkephalin, is increased in liver disease, venous blood samples were collected from six groups, each of 15 subjects: (i) acute liver disease, (ii) cirrhosis with ascites, (iii) cirrhosis without ascites, (iv) severe chronic renal failure, (v) disease controls, (vi) healthy controls. Leucine enkephalin was measured by a highly specific radioimmunoassay. It was raised significantly (p<0.001) in group (i) (median 1490 pmol/l, range 830–2420) and group (ii) (960, 470–2900) compared with the other four groups (iii) 415, 180–620; (iv) 560, 180–1020; (v) 325, 180–740; (vi) 305, 180–560. In acute liver disease, plasma leucine enkephalin correlated with the prothrombin time (r=0.691, p<0.01) and alanine aminotransferase (r=0.78, p<0.05) measured in the same sample.

Plasma leucine enkephalin is increased in acute liver disease in proportion to its severity and in cirrhosis with ascites.

Alpha-1-antitrypsin granules in the liver – a discrete entity?

A M BRIND, M F BASSENDINE, M K BENNETT, O F W JAMES (University of Newcastle upon Tyne) It has been hypothesised that AAT accumulation, demonstrated as perportal AAT granules, leads to chronic liver disease. Review of our liver clinic records from 1978–1988 revealed 29 patients whose biopsies contained granules by both PAS diastase resistant and specific immuno-

peroxidase staining. Age range 19–85 years, 14 over 65 years, 15 men and 14 women.

Clinical presentation: symptoms suggestive of liver disease and abnormal LFTs 19, portal hypertension seven, lung transplant work up two, chance necropsy finding one. Diagnostic work up revealed alcohol as the likely aetiology in 10, primary biliary cirrhosis (PBC) in four. Serum AAT concentrations were low in 8/24, phenotyping (available in 23) revealed: PiZZ, five (0-03%); PiMZ, one (80-5%); PiMZ, 12 (3-0%); PiSZ, one (17-0%); and PiMS, three (9%) (population frequency).

Histology: cirrhosis 16, PBC four, CAH three, CPH two, central vein fibrosis one, fibrosis and steatosis one, normal two (lung transplant one, necropsy one) 14/21 patients followed for two years survived. There was no discernable relationship between phenotype, type or severity of liver disease and age at presentation.

Serum AAT deficiency is not seen in the majority of patients with perportal AAT granules. A rare Z related liver disease occurs but in routine practice the finding of AAT granules may not carry any important diagnostic or prognostic implications.

Sympathetic activity and atrial natriuretic peptide (ANP) in cirrhosis

A J MAGGIECHRIST, C HAWKSBY, J BROWN, J L REID (University Department of Materia Medica, Stobhill General Hospital, Glasgow, and Department of Clinical Pharmacology, The Royal Infirmary, Edinburgh) This study addresses two questions relating to the pathogenesis of ascites. First, does the sympathetic overactivity that we and others have demonstrated in cirrhosis with established ascites also occur in cirrhosis without ascites? Second, does a deficiency of atrial natriuretic peptide (ANP) contribute to the sodium retention of ascites?

We measured plasma noradrenaline (NA), plasma renin activity (PRA) and ANP in 23 cirrhotics with ascites, 17 cirrhotics without ascites and 34 matched control subjects. Values quoted are median with the range and have been compared by one way ANOVA on log values; p values are compared with controls. NA was significantly higher both in cirrhosis with (4-7, 1-4 to 17-4 mmol/l, p<0-01) and without (3-8, 0-9 to 10-4, p<0-05) ascites than in controls.
Plasma levels and brain receptors of gamma amino butyric acid in human hepatic encephalopathy

H AMLARDINI, K BARTLETT, R WILLIAMS, C O RECORD (Liver Units, Royal Victoria Infirmary, Newcastle and Kings College Hospital, London) In recent years there has been much interest in the role of the gamma amino butyric acid (GABA) system in hepatic encephalopathy. GABA is the principal neuroinhibitory transmitter in the central nervous system and an excess of gabaergic transmission could account for the development of coma. As GABA is degraded in the brain within one minute of death previous studies in hepatic encephalopathy have relied heavily on animal models where an increase in brain GABA receptors has been demonstrated. In the present study we have determined GABA receptors in the brain of patients dying of acute and chronic hepatic encephalopathy using a radioreceptor assay. We have also determined GABA concentrations in the blood of patients sequentially during the course of the disease.

Two GABA receptors (KD1 and KD2) were demonstrated in frontal cortex in eight patients and compared with eight controls dying of ischaemic heart disease but without significant alterations in either the affinity or number was seen (KD1 14-3 (SE) 0-8 v 12-7 (0-7) nmol/l; KD2 148 (18) v 113 (10) nmol/l; BMA1 1-6 (0-2) v 1-2 (0-1) pmol/ml; BMA2 1-9 (0-3) v 1-8 (0-1) pmol/mg). Plasma GABA concentrations were significantly increased in 57 patients with liver disease and hepatic encephalopathy (3-3 (0-3) v 0-7 (0-1) pmol/l; 2 p<0-001) the highest values being seen in those deeply unconscious. Thus the role of GABA in this condition remains controversial the present studies providing support both for and against the hypothesis.

Natural history of chronic non-A, non-B hepatitis: immunosuppressive therapy may accelerate disease progression

M SCHOEMAN, M BILOUS, J GRIESSON, C LIDDLE, R G BATEY, G C FARRELL (Liver Research Unit, Departments of Medicine and Anatomical Pathology, Westmead Hospital, Westmead, NSW 2145, Australia) Chronic non-A, non-B hepatitis (NANB) is an increasingly common condition and management of this disorder remains problematical. We studied 43 patients (25 men, 18 women; median age 32 years) with chronic NANB hepatitis over an eight year period and followed for a mean of 27-7 months to determine: (1) severity of disease, and (2) impact of immunosuppressive therapy on progression of disease. NANB hepatitis was diagnosed by exclusion of all other causes of chronic liver disease. Risk factors for infection included iv drug abuse (63%), transfusion of blood products (30%), tattoos (5%), and nosocomial spread (3%). 63% had anti-HBc and/or anti-HBs while 11% had low titre ANA (1:40). Fifty six per cent of patients had constitutional symptoms, usually tiredness, and the remainder were asymptomatic. Physical signs of chronic liver disease were present in 42% and none exhibited hepatic decompensation. Liver biopsies were obtained in 33 patients; chronic persistent hepatitis was present in four chronic active hepatitis (CAH) in 21 and CAH and cirrhosis in eight. Neither presence of symptoms nor serum ALT correlated with histology. Among eight patients treated with prednisolone or prednisolone/azathioprine, only one had sustained three year normalisation of ALT (not rebiopsied). Seven others had minor falls in ALT but in six rebiopsied patients (six to 96 months) progression of fibrosis was evident with cirrhosis present in four. In contrast, progress biopsies (eight to 30 months) in four untreated patients with histologically similar disease showed progression in only one.

Histological assessment is required in all patients with suspected chronic NANB hepatitis as ALT and symptoms are unreliable in following progress. In biopsied patients CAH±cirrhosis was present in the majority. Immunosuppressive therapy is not only unhelpful, but may accelerate disease progression.

Natural history and mortality in primary sclerosing cholangitis

R HERMANN, J S DOOLEY, S SHERLOCK, N M MCINTYRE (Royal Free Hospital School of Medicine, Pond Street, London) Recent reports suggest that primary sclerosing cholangitis (PSC) progresses slowly particularly in asymptomatic patients, and that the overall 10 yr survival from diagnosis is 75-80% (Gastroenterology 1987; 92: 1869; Scand J Gastroenterol 1987; 22: 665). We reviewed the course of 70 patients (46 men, 24 women) with PSC diagnosed by accepted criteria. Major presenting symptoms were jaundice (39%), pruritus (34%) and lethargy (26%); 17 patients (24%) formed an asymptomatic group. Cholangiography showed combined extrahepatic and intrahepatic disease (EH) in 44 patients (63%) and intrahepatic changes (IH) alone in 21 patients (30%). Asymptomatic patients were more likely to have IH disease alone (59%). The mean follow up was 8.3 yr (range 0.5-25 yr). The condition deteriorated in 28 (53%) of the symptomatic group: 24 (45%) developed decompensated liver disease (mean 5.7 yr), and three cholangiocarcinoma (mean 10.3 yr). Ten (59%) of the asymptomatic group showed clinical progression (mean 3.1 yr); seven developed jaundice, five pruritus, four hepatic decompensation, and one died. The overall estimated 10 yr survival (Kaplan-Meier) was 55%. Twenty one patients (40%) in the symptomatic group died; the mean time to death after diagnosis was 7.2 yr (range 0.5-20 yr). 20 of 49 (41%) patients with EH disease died, compared with two of 21 (10%) of those with IH disease alone (p<0.01). In conclusion, PSC progresses more rapidly than recently reported whether or not patients are initially asymptomatic. Combined intra- and extrahepatic duct disease was associated with a worse prognosis.

Controlled trial of prophylactic sclerotherapy for oesophageal varices in England: Interim analysis of 103 patients

D R TRIGER, H L SMART, S W HOSKING, A G JOHNSON (Departments of Medicine and Surgery, Royal Hallamshire Hospital, Sheffield) One hundred and three consecutive patients with cirrhosis and oesophageal varices which had not bled were invited to enter a prophylactic sclerotherapy trial. Seven declined and the remaining 96 underwent wedge hepatic vein catheterisation. Those with WHVP gradient <12 mmHg were not randomised (group 1), the others.
were allocated to prophylactic sclerotherapy (group II), or no treatment (group III). Forty patients (41.3%) had alcoholic liver disease (ALD). Patients who bled were treated by injection sclerotherapy irrespective of randomisation. During a median follow up of 44 months (1–88), 38 have died and three underwent transplantation for liver failure. Thirty three patients suffered 78 variceal bleeds, which led to death in nine. Bleeds occurred in all groups (group I 8/31, group II 11/32, group III 14/32), but only four were related to injection. Variceal size was not an accurate predictor of bleeding (small 8/39, medium 20/46, large 5/11). In non-alcoholic liver disease survival in groups II and III was identical, with slightly better survival rate in group I. In ALD survival in groups I and II was significantly longer than in group III (p<0.05). We conclude that in non-alcoholic cirrhosis prophylactic sclerotherapy does not prolong survival. The difference in survival between ALD and non-ALD suggests that factors other than sclerotherapy may be responsible.

A prospective randomised controlled clinical trial comparing somatostatin and injection sclerotherapy in the control of acute variceal haemorrhage: preliminary results

S A JENKINS, J N BAXTER, S ELLENBOGEN, R SHIELDS (University Department of Surgery, Royal Liverpool Hospital, Liverpool) Recent studies have suggested that somatostatin (SRIF) may be of value in the control of bleeding oesophageal varices. In view of the efficacy of injection sclerotherapy in controlling variceal bleeding, however, it has been suggested that this treatment should be the ‘gold’ standard against which new therapies are evaluated. Therefore, the aim of this study was to compare the efficacy of SRIF with emergency injection sclerotherapy in the control of acute variceal haemorrhage.

Forty three consecutive patients admitted with endoscopically proven, severe, bleeding oesophageal varices were randomised to either emergency injection sclerotherapy or SRIF (bolus dose of 250 μg followed by a continuous infusion of 250 μg/h for five days). The aetiology of the portal hyperten-
sion was similar in the two groups as was the distribution of the patients among the categories of the Child’s classification.

Twenty two patients received SRIF and 21 injection sclerotherapy. The initial variceal haemorrhage was controlled in all 22 patients receiving SRIF but three rebled during the five day trial period. Overall control of bleeding was achieved in 19 of the 21 patients randomised to injection sclerotherapy. There was no significant difference (p=0.52 Fisher’s Exact Test) between the two forms of treatment.

The initial results of this trial suggest that SRIF is as effective as injection sclerotherapy in controlling acute variceal haemorrhage.

M2 autoantigens in primary biliary cirrhosis (PBC)

D J MUTIMER, S P M FUSSEY, S J YEAMAN, P KELLY, O F W JAMES, M F BASSENDINE (University of Newcastle upon Tyne) Primary biliary cirrhosis is characterised by AMA directed against trypsin sensitive antigens (M2) of the inner mitochondrial membrane. We have shown that two M2 autoantigens are the E2 component and protein X of pyruvate dehydrogenase complex (PDC) (Lancet 1988, i: 1067). Pyruvate dehydrogenase complex is one of three related 2-oxo acid dehydrogenase complexes within mitochondria, the others are 2-oxoglutarate dehydrogenase (OGDC) and branched-chain 2-oxo acid dehydrogenase (BOCADC) complexes.

Purified E2 components of PDC, OGDC, and BOCADC were prepared and used in immunoblotting against sera from the following: 129 PBC patients (abnormal LFTs, AMA +ve ≥1:40 by immunofluorescence, 37 histological Stage I, 42 Stage II–III, 50 Stage IV; follow up 1–19 years, median 5 years); 50 AMA –ve patients with other chronic liver diseases; 12 healthy women.

Primary biliary cirrhosis patients: 118 (92%) +ve immunoblot against E2 (+X) of PDC, 87 (67%) +ve against E2 of OGDC, 70 (54%) +ve against E2 of BOCADC, 59 (47%) +ve for all four proteins. Three-quarters +ve for all four proteins were Stage I. Sixty two control sera –ve for all four proteins. In PBC, no correlation between pattern of immunoblotting and histological stage or disease progression (p=NS).

The E2s of OGDC and BOCADC are also M2 autoantigens in PBC. Ninety seven per cent of PBC patients reacted with one or more E2 (M2 antigen) but these reactions showed no histological or clinical correlates.

Symptom development and prognosis in asymptomatic primary biliary cirrhosis (PBC)

H MITCHEISON, P KELLY, J NEUBERGER, M BASSENDINE, R WILLIAMS, O JAMES (University of Newcastle upon Tyne and King’s College Hospital, London) The prognosis of patients with PBC but without symptoms of liver disease at the time of diagnosis is uncertain. We present data on 95 patients with PBC confirmed histologically, immunologically, and biochemically (14 with normal LFTs but diagnostic histology) from two centres. Seventy patients from centre A (regional referral units), 25 from centre B (international tertiary referral unit). Mean age at presentation: centre A 59–6 years, centre B 53–5
years, overall 58 years. Follow up three to 16 years: centre A 69 months, centre B 70 months, overall 69 months.

(i) Symptoms: 19/70 centre A, 172/5 centre B developed symptoms of liver disease (p<0.001); mean time to symptom appearance 43 months, centre A, 35 months, centre B (p=NS). (ii) Deaths: centre A 1570/8; 19/19 who had developed symptoms (all liver deaths), 7/57 remaining asymptomatic (all non-liver deaths). Centre B 10/25; 9/17 who had developed symptoms (all liver deaths) 1/8 asymptomatic (non-liver). Total 25/95 died: 17/36 who had developed symptoms v 8/59 remaining asymptomatic (p<0.001). Comparison of these patients developing symptoms with 103 patients presenting with symptoms from centre A and 165 from centre B (FU 3–18 years) suggests no difference in survival once symptoms appear.

(i) Differences in mortality of initially asymptomatic patients and in proportion developing symptoms may be due to different referral patterns. (ii) Mortality is strongly related to symptomatic development: Patients developing symptoms have similar prognosis to ‘classical’ symptomatic patients.

Soluble interleukin 2 receptors in serum and bile of patients following liver transplantation

D H ADAMS, L WANG, S G HUBSCHER, E ELIAS, J M NEUBERGER (Liver Unit, Queen Elizabeth Hospital, Edgbaston, Birmingham) After liver transplantation, 80% of patients develop acute rejection and 15% progress to chronic irreversible rejection. Rejection is most reliably diagnosed histologically; a sensitive, less invasive test would aid management of graft dysfunction. As lymphocytes are involved in the inflammatory response of rejection we used an enzyme linked immunosorbent assay to measure interleukin 2 receptor (IL2R) a stable, soluble product of activated lymphocytes, in bile and serum after liver transplantation. Serum concentrations of IL2R were raised in acute rejection (n=20; median 3433 U/l; (range 1427–4667 U/l)) compared with liver dysfunction due to other causes (n=10; 2370 U/l; (1267–3213 U/l)); p<0.0025 and stable grafts (n=12; 1410 U/l (45–2495 U/l)); p<0.0001. In chronic rejection higher levels were seen in patients with early severe progressive disease (n=7; 3500 U/l; (2200–3853 U/l)) than in end stage chronic rejection (n=5; 140 U/l; (44–2200 U/l)); p<0.001. Biliary levels were also raised in acute rejection (n=14; 106 U/l; (0–1264 U/l)) compared with other causes of graft dysfunction (n=10; 24 U/l; (0–291 U/l)); p<0.024 and stable grafts (n=5; 0–27 U/l)); p<0.0025. Serial studies showed that IL2R rose progressively in bile and serum before rejection and fell after treatment. These data suggest (1) IL2R may be a useful marker of rejection after liver transplantation, (2) biliary levels may be more specific than serum, (3) lymphocyte activation is a feature of early chronic rejection but is less important in end stage disease suggesting that treatment with immunosuppression at this stage is inappropriate.

Will biodegradable microspheres enhance regional delivery of a cytotoxic to hepatic tumour?

D CHANG, S A JENKINS, D M NOTT, J S GRIME, P MALBLY, L HÅKANSSON, T COOKE (Departments of Surgery and Nuclear Medicine, Royal Liverpool Hospital and Department of Oncology, University Hospital, Linköping, Sweden) The aim of this study was to investigate the mechanisms whereby degradable starch microspheres (DSM) enhance hepatic tumour uptake of cytotoxins given concomitantly.

Overt hepatic tumour was induced in Lister rats by intraportal injection of HSN fibrosarcoma cells, its vascularity characterised and the optimum dose of DSM to minimise the passage of a labelled marker, 99mTc methylene diphosphonate (MDP), representing a cytotoxic drug, established. Methylene diphosphonate alone and in combination with DSM was injected regionally to determine the distribution of the marker to tumour and normal liver tissue immediately after injection, and 90 minutes later.

The tumour was hypovascular and the distribution expressed in % injected dose/cm³ for 99mTc-MDP injected alone (n=8) was 1-04 (0-10) in tumour compared with 0-77 (0-04) in normal liver. When given with DSM the distribution of marker immediately after injection (n=6) was significantly greater (p<0.001, Mann-Whitney) in tumour 16-52 (1-63) compared to normal liver tissue 7-11 (0-71). Ninety minutes later when DSM degradation was complete (n=8) the distribution of marker to tumour was further increased 10-73 (1-06) compared to normal liver tissue 0-67 (0-07). These results show that DSM immediately increases the retention of a marker in tumour probably because of its redistribution from normal tissue blocked by DSM. After degradation of the DSM, the T:N ratio of marker increases possibly because of portal venous washout from normal liver tissue.

Small intestine

Modulation of intestinal tone by visceral reflexes in man

J M ROULLON, F AZPIROZ, J R MALAGELADA (Digestive System Research Unit, Hospital General Vall d’Hebron, Barcelona, Spain) Intestinal tonic muscular activity (intestinal tone) has never been quantified in man because of the lack of appropriate methodology. We have developed an original technique to investigate the modulation of intestinal tone by intestino-intestinal reflexes. In six healthy volunteers intestinal tone responses were quantified as variations in the air volume within a flaccid bag (12 cm long) maintained at a constant pressure by an electronic barostat. The bag was located in the proximal jejunum and balloon distentions (one min duration at 10 min intervals) were randomly performed 8 cm oral (A) and 8 cm (R1) and 20 cm (R2) caudal to the bag. Perception was scored by a graded (0–6) questionnaire. Distentions were done in 8 ml stepwise increments until the participants reported discomfort (score >5). Stimuli below the threshold for discomfort (3-5 (0-3) perception score for A, 3-5 (0-2) for R1 and 3-7 (0-2) for R2; mean (SE) elicited significant intestinal reflex relaxation; interestingly the responses were similar for antegrade and retrograde reflexes (11 (3) ml Δ intestinal vol for A, 11 (1) ml for R1 and 12 (3) ml for R2; p<0.05 for all). We conclude that antegrade as well as retrograde distention triggered reflexes modulate the tonic contractile activity of the human jejunum.

Does somatostatin analogue (SMS 201-995) reduce high output stoma effluent? A controlled trial

J L SHAFFER, T O'HANRAHAN, S RUNTRE, K SHIPLEY, M H IRVING (Hope Hospital, Salford and Sandoz Products Ltd, Feltham, Middlesex) Uncontrolled observations have suggested a role for somatostatin analogue (SMS 201-995) in reducing stoma effluent in patients with the short bowel syndrome. We have carried out a randomised placebo controlled crossover trial in six patients with a persistently high stoma effluent (1-3–6 l/day). After a two day control period, the patients received 50, 100, and then 150 μg...
of SMS 201-995 or matching placebo on three successive days. After a 14 day washout period the patients repeated the study with the alternative medication. Somatostatin analogue markedly reduced stomal volume, median 2-39 l/day (range 0-62-4-48) active; 4-03 l/day (1-28-5-98) placebo (p<0-001) (Wilcoxon); sodium output, median 153 mmol/day (range 27-271) active; 311 (94-594) placebo (p<0-001). Potassium output, median 39 mmol/day (8-3-58) active; 54 (23-154) placebo; (p<0-01). There was a corresponding increase in urine volume, 2-09 l/day (0-75-6-62) active; 1-16 (0-47-5-13) placebo (p<0-002) and body weight 57-6 kg (46-5-65-7) active 56-3 (45-4-61-9) placebo (NS). There was no improvement in nitrogen, magnesium and copper balance. Two patients have been on SMS 201-995 therapy for >2 years without developing any long term adverse effects or showing an evidence of pharmacological tolerance.

Somatostatin analogue significantly reduces high stoma effluent and may be of value predominantly in improving water and electrolyte balance.

Are alcohol-induced disturbances in small bowel motility due to a preferential loss of smooth-muscle apparatus?

VICTOR R PREEDY, TIMOTHY I PETERS (Division of Clinical Cell Biology, MRC Clinical Research Centre, Wadworth Road, Harrow, Middlesex) A distinguishing feature of chronic alcohol abuse is altered small bowel motility. A reduction in the amount of contractile apparatus may be a contributing factor. This hypothesis was tested in rats chronically fed a liquid diet containing ethanol as 36% of total calories. Controls were pair fed the same diet in which ethanol was substituted by isocoric glucose. Studies were done in young (80-90 g body weight) and mature (280-290 g body weight) animals. After six weeks total contractile protein content in the small bowel of young rats was reduced from 72 (7) mg to 49 (5) mg (mean (SE), n=6, p<0-01). In mature rats total contractile protein content fell from 95 (7) mg to 69 (3) mg (p<0-01). In young and mature rats, small bowel stomal protein contents were not significantly altered (p>0-05). Significant reductions in protein synthesis measured with [3-3H]-phenylalanine were obtained for absolute rates of contractile protein synthesis. In young rats values were 60 (6) mg/day and 42 (6) mg/day in control and ethanol fed rats, respectively (p<0-05). In mature rats corresponding values were 93 (14) mg/day and 49 (4) mg/day, respectively (p<0-05). In contrast the fractional rates of contractile protein synthesis were relatively unaltered by ethanol treatment suggesting at least a partial adaptation to the ethanol feeding. Chronic ethanol administration reduces intestinal myofibrillar protein content and this may be pathogenic mechanism of alcohol induced motility disturbances.

Studies of gastrointestinal drug absorption

S A RILEY, F A SUTCLIFFE, M ROWLAND, L A TURBENGER (Departments of Medicine and Pharmacy, University of Manchester, Hope Hospital, Salford and Coupland Building 3, Oxford Road, Manchester) Hydrophilic drugs are variably absorbed from the gastrointestinal tract. We have therefore studied physiological factors which may influence absorption.

Twelve subjects participated in 46 experiments. After oral ingestion of multi-component solutions of atenolol, hydrochlorothiazide, frusemide and salicylic acid drug absorption was assessed by 24 hour urinary excretion. In six subjects, studies were designed to manipulate luminal water shifts using: glucose (glu), isotonic electrolytes (iso), or hypertonic electrolytes (hyper). Solution composition had a marked effect on the excretion of atenolol (glu>iso: p<0-02, iso>hyper: p<0-005), and hydrochlorothiazide (glu>iso: p<0-07, iso>hyper: p<0-02) but no effect on frusemide or salicylic acid. Between subject comparison revealed individuals who were consistently 'good absorbers' of all study drugs irrespective of solution composition.

In a further six subjects variations in gastric emptying and oroaeceleal transit were studied. Surprisingly, neither emptying (CoV 54%) nor transit (CoV 51%) correlated with drug excretion (except hydrochlorothiazide excretion and gastric emptying, r=0-47, p<0-01). Codeine pretreatment doubled transit (p<0-05) but left drug excretion unchanged.

Although gastrointestinal transit appears unimportant in the absorption of hydrophilic drugs, luminal water shifts (solvent drag) may be an important determinant.

Immunopathologic aspects of small intestinal mucosa in Gambian children with chronic diarrhoea – malnutrition syndrome

P B SULLIVAN, G NEALE, M N MARSH (Dunn Nutrition Unit, University of Cambridge and University Department of Medicine, Hope Hospital, Manchester) The pathogenesis of chronic tropical diarrhoea with severe malnutrition probably depends on multiple environmental factors, although small intestinal damage is likely to be its final common pathway. To characterise this syndrome, the immunopathologic features of jejunal biopsies from 52 Gambian children (ages 6-33 months) with chronic diarrhoea, protein energy malnutrition and anergy to standard recall antigens, were quantified by computerised image analysis and compared with further jejunal biopsies (from 28 patients) after three weeks' intensive nutritional rehabilitation. A broad spectrum of pathologic changes was observed, ranging from 'normal' to flat, coeliac like mucosae. The majority of specimens revealed crypt hypertrophy (<95% confidence limits for control mucosae), increased crypt cell mitotic activity and lymphocytic infiltration. Surface epithelium from villus-bearing mucosae contained increased numbers of small, non-mitotic lymphocytes, but as surface epithelial volumes progressively diminished epithelial lymphocyte populations fell in parallel. Lamina propria was expanded by increased numbers of mast cells, eosinophils and occasional basophils; neutrophils were rarely encountered. After hospitalisation, responsiveness of peripheral lymphocytes to PHA and candidin increased, whereas the intestinal mucosal abnormalities failed to improve or worsened. The intestinal lesion appears to be a reaction to environmental challenge which is modulated by nutritional status rather than a response to protein energy malnutrition per se.

Characterisation of experimental rotavirus (RV) diarrhoea in rat

A F M SALIM, J A WALKER-SMITH, M J G FARTHING (Departments of Gastroenterology and Child Health, St Bartholomew's Hospital, London) Rotavirus is the most common cause of acute gastroenteritis in children worldwide. We have established a rat model for RV diarrhoea and characterised it with respect to clinical impact, virus excretion and water and electrolyte transport. Eight to 10 day old neonatal rats (12-20 g) were inoculated orally with rat RV. At 24-36 h all animals developed diarrhoea. By 96 h clinical recovery had occurred. Weight gain was significantly less than control animals during the first 72 h, but by 96 h 'catch-up' growth had occurred. Rotavirus was excreted during the first 72 h of infection, being maximal at 48 h. Rotavirus recovered from infected rat faeces caused...
infection in non-infected neonatal rats. Water and electrolyte transport was studied in control and infected rats by in situ steady state perfusion of the entire small intestine. A plasma electrolyte solution (Na 140, K 4, Cl 104, HCO₃ 40 mmol/l; 300 mOsm/kg) produced net absorption of water in controls (+67-9±8-5 μl/min/g; n=7), whereas in infected animals there was a net secretory state for water between 18–48 h being maximal at 24 h (–21-5±7-1; n=6). By 72 h RV-infected intestine was recovering (water absorption +19-9±4-9; n=7), although still subnormal. This rat model has close parallels with human RV infection since it causes reversible secretory diarrhoea and impaired weight gain. This model may be useful for studying the pathogenesis of RV diarrhoea and examining new methods of treatment.

In vitro mucus glycoprotein synthesis and secretion in normal and coeliac jejunal mucosa

J E CRABTREE, R V HEATLEY, M S LOSOWSKY (Department of Medicine, St James's University Hospital, Leeds) Mucus is an important factor in intestinal defences. Evidence from animal models suggests that inflammatory mediators can influence mucus secretion and that T lymphocytes can induce goblet cell hyperplasia. Immunological abnormalities have been identified in coeliac mucosa which might be expected to influence intestinal mucus production.

To investigate mucus synthesis and secretion in coeliac disease, 24-hour in vitro cultures of jejunal biopsies from 19 patients with histologically normal mucosa and 22 patients with coeliac disease (13 treated and nine untreated) were undertaken. The incorporation of 3H glucosamine into tissue and secreted trichloroacetic acid precipitable glycoproteins was measured as an assessment of mucus production (DPM×10⁶/mg biopsy protein).

Total incorporation of glucosamine into tissue and secreted mucus glycoproteins was significantly greater (p<0.01) in patients with untreated coeliac disease (mean (SE) 414-5 (41-7)) than in patients with histologically normal jejunal tissue (248 (13)) or treated coeliac patients (264 (15-3)). The ratios of tissue to secreted glycoproteins in normal, treated, and untreated coeliac mucosa were 3:15:1, 2:63:1, and 1:56:1 respectively.

These results show that intestinal mucus production is enhanced in patients with untreated coeliac disease. This phenomenon may be relevant to the increased intestinal permeability observed in coeliac disease and also in the pathogenesis of the condition.

Coeliac proctitis? — a prospective morphometric study

D E LOFT, M N MARSH, P T CROWE (Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) An association between coeliac disease (CD) and proctitis has been suggested but there have been no prospective studies of rectal histology in CD. We report a prospective morphometric analysis of rectal mucosa in CD.

Forty five patients (n=10 untreated CD (UCD); 14 treated CD (TCD); 21 disease controls (C)) referred consecutively for jejunal biopsy also underwent rectal biopsy. Patients with colitis beyond rectosigmoid were excluded. 1 μm toluidine blue stained epon sections were measured by computerised image analysis in terms of: mucosal compartment volumes; enumeration of lamina propria cell types; and surface and crypt intraepithelial lymphocytes.

No difference in lamina propria, surface or crypt epithelial volume; lamina propria neutrophils or basophils; nor surface or crypt intraepithelial lymphocytes. The following were increased in CD: Mast cells (M (SE) UCD=63.8 (6) p<0.02, TCD=66.1 (11) p<0.05, C=38.8 (6)), Plasma cells (UCD=468 (30) p<0.002, TCD=273 (33) p=NS, C=257 (38)). The following showed a non-significant trend: T lymphocytes (UCD=62 (7), TCD=52 (9), C=46 (4)), Eosinophils (UCD=23 (12), TCD=8-3 (4), C=6 (3)).

In this prospective study, UCD was associated with a mild chronic inflammatory infiltrate which was not apparent in TCD. There was no oedema, glandular distortion, surface or crypt epithelial atrophy, and no increase in intraepithelial lymphocytes. Mast cells were increased in both UCD and TCD.

The treatment of NSAID induced small intestinal inflammation

I BJARNASON, N HOPKINSON, G ZANELLI, T SMITH, P SMETHURST, M J GUMPEL, A J LEVI (MRC Clinical Research Centre, Watford Road, Harrow, Middlesex) Long term ingestion of NSAIDs causes small intestinal inflammation in 70% of patients. Clinically the most important consequence of the inflammation is chronic blood loss (Lancet 1987; ii: 711) which may contribute to the iron deficiency which is so common in these patients. We assessed whether sulphasalazine and other second line drugs for rheumatoid arthritis (RA) affected the inflammation and the blood loss. Patients with RA requiring a second line agent underwent simultaneous study with 111Indium leucocytes and 111Cr red cells before and after three to seven months treatment with sulphasalazine (N14) or gold, penicillamine or chloroquine (N20), while maintaining an unchanged intake of NSAID's. Faecal 111Indium excretion (n<1)% D), which quantitates the inflammation, fell significantly in the sulphasalazine group (2.5 (0.6)% to 1.5 (0.3)% mean (SE), p<0.01) and this was matched by reduced intestinal blood loss (9-6 (3.2) ml/m⁴ D to 5.1 (1.9) ml/m⁴ D p<0.05). No such changes were found with the other second line agents: 3In excretion 2.0 (0.5)% , 2.7 (0.7)% and 111Cr red cells 8.8 (2.6) ml/m⁴ D, 7.9 (3.0) ml/m⁴ D respectively (p<0.1). Studies (N12) with 51Fe labelled red cells over six weeks and after six weeks sulphasalazine treatment indicate a delayed onset of action.

Sulphasalazine reduces small intestine inflammation and blood loss caused by NSAID's and may be indicated in rheumatoid patients who are prone to iron deficiency.

Does a somatostatin analogue (Octreotide) reduce the need for parenteral fluids in patients with a short bowel?

J M D NIGHTINGALE, E R WALKER, W R BURNHAM, M J G FARTHING, J E LENNARD-JONES (St Mark's Hospital, City Road, London and Oldchurch Hospital, Romford, Essex) Four patients with a residual small intestine length of 50–100 cm, each with a very high stool/faecal output and all needing home parenteral nutrition were studied to see if Octreotide would reduce their fluid requirements. Each patient was taking some oral nutrition and needed 4 or 5 l intravenous fluid daily. The test consisted of two control and two test days during which dietary intake remained constant and measurements were made of fluid, electrolyte, and caloric balance. Octreotide was given by a slow intravenous injection through the central feeding line.

In every patient the fluid output from the bowel exceeded the oral intake (intake 1-4–4.7 kg, output 3-5–6.4 kg). Octreotide at a dose of 50 μg bd reduced the mean output in every patient by 1–2 kg. Mean caloric absorption for each patient before and after therapy was 0.6, 29, 34% and 0, 20, 41.26%.
respectively. The results were of possible clinical benefit in two patients though treatment at home was continued in only one. This patient underwent repeat testing after three months with almost identical results.

In two patients a dose increase of Octreotide to 100 µg tds intravenously gave no additional benefit.

Octreotide reduces fluid output in patients with a short bowel and secretory diarrhoea but the improvement is great enough to justify longterm treatment in only some of these patients.

BASIC SCIENCE

Effect of campylobacter pylori on acid production by isolated guinea pig parietal cells

J Defize, J Goldie, R H Hunt (Intestinal Disease Research Unit, McMaster University, Hamilton, Canada) Campylobacter pylori (CP) is strongly associated with active chronic gastritis and peptic ulcer, but its role in pathogenesis is unknown. In vivo studies have indicated a reduction in gastric acid secretion in patients, infected with CP. The mechanism of acid hyposecretion is unclear. We have therefore studied the effect of CP on isolated guinea pig parietal cells. Guinea pig parietal cells were isolated by collagenase digestion of the gastric mucosa, and Percoll density centrifugation. Acid production was assessed using the [14C] amino pyrine uptake technique.

Campylobacter pylori caused a reduction of basal acid secretion (80%). Histamine stimulated acid production was reduced to 50% of maximal stimulation by addition of CP after 15 min. Only a partial return of responsiveness to histamine was observed when cells were washed after 15 min incubation with CP, indicating recovery of some cells. EM also showed some CP attached to parietal cells.

Campylobacter pylori reduces basal and histamine stimulated acid production. The effect is only partially reversible, and we conclude that the reduction in acid secretion is not solely the result of cytotoxicity or mechanical damage caused by CP.

Assessment of the fibrinolytic activity of gastric juice

S Patchett, H Enright, L O'Connell, N H Afdhali, D P O'Donoghue (St Vincent's Hospital and University College, Dublin, Ireland) Upper GI haemorrhage remains a serious cause of morbidity and mortality in patients with peptic ulcer disease despite modern therapy. Factors affecting the maintenance of a formed fibrin clot bathed in gastric juice are felt to be important in the high incidence of rebleeding.

In a series of in vitro experiments the Euglobulin clot lysis time, a sensitive and widely used method of assessing fibrinolysis was used to show the effect of gastric juice on a formed fibrin clot.

Gastric juice from 15 normal control patients and from 15 patients with peptic ulcer disease (all with pH less than 2) was found to enhance fibrinolysis by approximately 40% in both groups. The addition of 0-1 m HCL alone, however, caused no change in the ECLT. Alkalisation of gastric juice to pH 4 was found to abolish this effect in all cases. Heating of the gastric juice to 80°C for 30 minutes caused similar inhibition of fibrinolysis in the absence of any change in pH.

In further studies tranexamic acid, a specific plasmaminogen inhibitor, also abolished the fibrinolytic activity of gastric juice. Pepstatin, a specific pepsin inhibitor, only partially reversed the fibrinolytic activity. In contrast, however, succinate, an agent also with antipeptic activity, almost completely inhibited fibrinolysis. This effect was shown again to be independent of any change in pH.

This work confirms the presence of fibrinolytic activity in gastric juice and suggests that factors other than acid and pepsin may be primarily responsible for including clot lysis in the upper GI tract.

Evidence of acid secretion by the human gall bladder mucosa in vitro

J N Plevris, P C Hayes, I A D Boucher (University Department of Medicine, Royal Infirmary, Edinburgh) It is recognised that gall bladder bile is more acidic than hepatic bile and this has been attributed to HCO3 reabsorption by the gall bladder. The aim of this study was to investigate in vitro the acid base changes that occur across the gall bladder mucosa. Fresh gall bladder mucosa was obtained at cholecystectomy and placed in an Ussing Chamber and perfused with Ringer Krebs glucose bicarbonate solution. The viability of the gall bladder was assessed by measuring the potential differences across the gall bladder mucosa. In 10 gall bladder specimens aliquots from the mucosal solutions were taken at two minutes and 70 minutes and pH, pCO2, and HCO3 concentrations measured. A consistent and significant decrease was observed from two minutes to 70 minutes in pH (pH5= 0.112 (0.027), p<0.005) as well as HCO3 concentration (AHCO3= -1.65 mM (0.60), p<0.02) while pCO2 increased (ApgCO2=0.224 mmHg (0.90), p<0.05).

In contrast when the gall bladder mucosa was killed with formaldehyde, the pH was significantly increased (ΔpH= +0.336 (0.044), p<0.01, n=4) the pCO2 significantly decreased (ΔpCO2= -1.335 (0.166), p<0.01, n=4) with no significant change in HCO3 concentration.

The human gall bladder mucosa is capable of secreting acid and this may be an important mechanism for preventing gall stones forming in bile.

Epidermal growth factor receptor down-regulation during hepatocyte proliferation in vivo and in vitro

D A Vessev, A C Selden, H J F Hodgson (Department of Medicine, Royal Postgraduate Medical School, London) Epidermal growth factor (EGF), and insulin and glucagon, modulate hepatocyte proliferation, but the predominant stimulus to liver regeneration is uncertain. In vivo after partial hepatectomy there is a striking down regulation of hepatocyte EGF receptors. We therefore studied changes in EGF binding to hepatocyte membranes, when EGF or insulin and glucagon induced proliferation in vitro, and compared these with changes induced by 70% hepatectomy in rats. 125I-EGF binding to cultured adult rat hepatocytes was measured after stimulation with EGF (10 ng/ml), or insulin (350 ng/ml) and glucagon (400 ng/ml), and compared with binding to membranes from animals sacrificed after partial hepatectomy. We confirmed EGF receptor down regulation in membranes after 70% resection, with binding decreasing within four hours to a maximum (43%) at 24 h. In vitro EGF induced a similar magnitude of receptor down regulation within 24 h. In contrast insulin and glucagon, despite inducing similar increases in DNA synthesis, did not alter EGF binding. Insulin and glucagon in vitro thus fail to reproduce the changes in EGF binding seen during regeneration in vivo, and this study therefore supports EGF as a major mediator of hepatic regeneration. Differences in time course of receptor down regulation in vivo probably reflect delays before in vivo EGF binding.
Expression of the caeruloplasmin gene in adult and neonatal rat liver

L Barrow, M S Tanner (Department of Child Health, University of Leicester, Leicester)

Like the human newborn, the neonatal Wistar rat was found to show features of copper metabolism which resemble Wilson’s disease. Values significantly different from group III are denoted by *p<0.001, and from group I are denoted by ‡p<0.01 and ‡‡p<0.001.

Caeruloplasmin mRNA (Cp mRNA) has therefore been studied in the neonatal and adult rats, to determine whether low serum caeruloplasmin levels result from a pre-translational defect in caeruloplasmin synthesis. Total and polyadenylated RNA was isolated from samples of liver from Groups I–III. The caeruloplasmin mRNA was detected by Northern blotting and hybridisation with a 32P-labelled caeruloplasmin cDNA probe. A single species of mRNA, of approximately 4400 nucleotides, was detected in both adult and neonatal rats, with lower levels of Cp mRNA in the neonates. Thus reduced serum caeruloplasmin is associated with reduced caeruloplasmin gene expression or decreased Cp mRNA stability.

This technique is allowing study of caeruloplasmin gene induction by copper overload, and in situ hybridisation with a cDNA probe may be used to compare biopsy material from Wilson’s disease with the human newborn.

Role of interferons in immunologically mediated enteropathy

A MCI Mowat, M V Felstein, D M V Parrott (Department of Bacteriology and Immunology, Western Infirmary, Glasgow, Scotland) Several small bowel disorders, including coeliac disease are associated with an infiltrate of activated T lymphocytes. The exact role of these cells in producing mucosal pathology is, however, not clear. Graft-versus-host reaction (GVHR) in animals causes an immune mediated enteropathy which reproduces many of the features of the clinical diseases. Previous studies in mice have provided indirect evidence that soluble mediators derived from local immune cells are responsible for intestinal damage in GVHR and we have now examined directly the role of interferons in intestinal GVHR.

Administration of the interferon inducer, polyinosinic-polyribidylic acid (poly I:C) accelerated weight loss in neonatal mice with GVHR and mice given poly I:C had significantly more severe villus atrophy and crypt hyperplasia during GVHR. Poly I:C itself caused marked enhancement of natural killer cells and in some experiments produced significant crypt hyperplasia in the absence of GVHR. Monoclonal anti-γ interferon antibody inhibited the systemic features of GVHR in adult mice and eliminated the villus atrophy, crypt hyperplasia and increased numbers of intraepithelial lymphocytes normally found in GVHR. These results are direct evidence that interferons play a critical role in immune mediated enteropathy.

Basolateral membrane enzymes in coeliac disease

J A Smith, J Amoah, R G Long (Medical Research Centre, City Hospital, Nottingham) In coeliac disease (CD) brush border enzymes are known to be reduced. There are little data on the enzymes of the basolateral membrane (BLM) in this disease.

The BLM enzymes, Na⁺,K⁺ATPase and adenylate cyclase were measured in homogenates of human duodenal and jejunal biopsies. Na⁺,K⁺ATPase activity was expressed as μmoles Pi/min/mg protein (SE) and adenylate cyclase activity was expressed as pmoles cAMP/min/mg protein (SE).

The Na⁺,K⁺ATPase activity in normal jejunal (0-0524 (0-0234), n=20) was significantly greater than in normal duodenum (0-0250 (0-0081), n=38). This difference was not observed in patients with villous atrophy. Duodenal (0-0249 (0-0144), n=12) and jejunal (0-0226 (0-0202), n=5) activities in villous atrophy were similar. There was no significant difference between normal and coeliac duodenal Na⁺,K⁺ATPase activity.

Adenylate cyclase concentrations were not significantly different between normal and coeliac duodenum or jejunal. Normal duodenum and jejunal fluoride stimulated activities were 47-67 (3-65) (n=28) and 41-88 (9-30) (n=8) respectively. Corresponding coeliac values were 54-69 (7-60) (n=8) and 47-28 (18-13) (n=4). Jejunal Na⁺,K⁺ATPase activity appears to be adversely affected in coeliac disease (CD) whereas adenylate cyclase activity is not, even though both are situated on the BLM.

An inhibitor of interleukin-1 in Crohn’s disease

C D Dalley, J A Avery, N A Punchard, J Cason, R A Wolsentzcroft, R P H Thompson (Gastrointestinal Laboratory and Department of Immunology, The Rayne Institute, St Thomas’ Hospital, London) Increased interleukin-1 (IL-1) production by peripheral mononuclear cells has previously been shown in a proportion of patients with Crohn’s Disease (CD). In this study a circulating inhibitory activity for IL-1 has been shown in CD. Inhibitory activity in sera of 24 CD and 21 healthy subjects (HS) was determined using the mouse thymocyte co-mitogenic assay for lymphocyte activating factor: sera were tested at graded doses in thymocyte cultures containing a laboratory standard preparation of IL-1 at a fixed sub-optimum concentration. Inhibitory activity was expressed as a stimulation ratio of the thymocyte response (thymidine incorporation) in cultures containing the test sera compared to those without.

Sera from CD showed a dose-related inhibition with a maximum (median response, 0-74; range, 0-38–1-68) at the highest concentration used (1/50). In contrast, sera from HS showed a dose related enhancement of response (1-35; 0-75–3-13) at the same dose and the difference between these values was statistically significant (Mann Whitney U test, p<0-0002). Inhibition of IL-1 activity was not due to toxicity of the sera for the IL-1-responsive target cells. The relationship between spontaneous or inducible production of IL-1 by leucocytes and the circulating levels of its inhibitor(s) in CD deserves more precise definition.

Increased synthesis of the inflammatory mediators, PAF-acether and leucotriene B₄ in models of colitis
Fluorimetric determination of hypochlorite scavenging by Samino salicylic acid (5ASA)

J G WILLIAMS, M B HALLETT (INTRODUCED BY PROF L E HUGHES) (Department of Surgery, University of Wales College of Medicine, Heath Park, Cardiff, Wales) Recent evidence implicates scavenging of toxic oxygen metabolites as the mode of action of 5ASA in inflammatory bowel disease. We have previously shown that 5ASA inhibits the reaction of luminol with hypochlorite, generated by neutrophils or in cell-free systems. In this study we further investigated the reaction of hypochlorite with 5ASA by measuring its fluorescence.

Fluorescent measurements were done using a Spex Fluorolog III. Human neutrophils were prepared by sedimentation and density gradient separation of fresh blood. 5ASA, excited at 340 nm, produced maximum fluorescence at 500 nm. Fluorescence was abolished by addition of equimolar concentrations of sodium hypochlorite or a cell free hypochlorite generating system, hypoxanthine and xanthine oxidase in the presence of peroxidase. Neutrophils stimulated with f-met-leu-phe plus cytchalasin B also reduced 5ASA fluorescence. The time course was coincident with oxidase activity as measured by oxygen consumption. The reaction with 5ASA was abolished by 1 mM sodium azide, a peroxidase inhibitor, consistent with a role for hypochlorite.

These results show that hypochlorite reacts rapidly with 5ASA to produce a non-fluorescent product (as yet unidentified). This provides evidence for the mechanism of hypochlorite scavenging by 5ASA and suggests the possibility of monitoring this reaction of 5ASA in vivo.

Pseudo/Gastroduodenal Posters

Dysmotility-type non-ulcer dyspepsia is negatively associated with Campylobacter-like organisms (GCLO)

A CHUA, N P KENNEDY, D HAMILTON, J J KEATING, P W N KEELING (Departments of Clinical Medicine and Nuclear Medicine, Trinity College Dublin and St James’s Hospital, Dublin) Non-ulcer dyspepsia (NUD) patients can be categorised into those with symptoms suggesting oesophageal reflux, gastric dysmotility, peptic ulceration, or idiopathic dyspepsia. Although GCLO are associated with peptic ulcer disease (PUD) and gastritis, their effect on antral motility and their role in NUD remains unclear. This study was done to determine if antral GCLO colonisation is associated with delayed gastric emptying (DGE).

Gastric antral biopsies were obtained from 109 dyspeptic patients (44 men, 65 women, age range 18–75 years) with an endoscopically normal mucosa. Patients with heartburn were excluded. GCLO colonisation was detected by a rapid urease test. Patients were classified according to the presence (n=35) or absence (n=74) of symptoms suggesting DGE. In 20 patients, DGE was confirmed by dynamic scintigraphy (DS), using In111 for liquid phase and Tc99m for solid phase. The control group consisted of 84 patients with endoscopically confirmed active PUD.

Antral GCLO was detected in 63 (58%) patients with NUD and 78 (93%) with PUD. Only 11 (31%) of NUD patients with dysmotility-type symptoms had antral GCLO, in contrast to 52 (70%) of those with ulcer-like symptoms. Furthermore, 15 of 20 NUD patients with confirmed DGE did not have GCLO. This implies that GCLO-related gastritis is not associated with DGE and emphasises the need to categorise NUD patients into different groups that may respond to different therapies.

Campylobacter pylori (CP) in abattoir workers

D VAIRA, C D’ANASTASIO, J HOLTON, J DOWSETT, M LONDEI, F BERTONE, M MALDINI, A POLL, P R SALMON, L GANDOFI (Departments of Gastroenterology and Microbiology, The Middlesex Hospital, London, and Departments of Gastroenterology, VI Geriatric Section, Histopathology and Chemical Pathology, M Malpighi, Bologna Sunley Research Centre, London) Although a strong association has been shown between CP and gastritis little is known about the source and the spread of this organism. To increase our understanding of the transmission of CP we looked for antibodies to CP in 97 abattoir workers. The workers were divided in five groups: (1) clerks (n=11), (2) slaughterers (n=41), (3) porters (n=20), (4) gut men (n=18), (5) rabbit slaughterers (n=7). The sera of all were tested for IgG against CP, C jejuni (CJ) and Klebsiella (K) by the ELISA technique. We found a significant difference in antibody levels between the first group (clerks) and all the other four groups (P<0.001) when tested against CP and CJ. No statistical differences were found when the sera were tested against K. Further, 25 of the non-clerical workers (groups 2–5), with high titre of antibodies to CP, underwent voluntary upper gastrointestinal endoscopy. Campylobacter pylori associated gastritis was found and microscopy in antral biopsies of all 25, CP was cultured in 21/25 and CP-TEST was positive in 23/25.

These results suggest that workers in direct contact with freshly cut animal parts have significantly higher levels of antibodies to CP than workers not in direct contact. Moreover, endoscopic biopsies showed CP associated gastritis in 100% of a random sample from direct animal part exposure subjects with high CP IgG titres. These results may suggest for the first time that CP can be acquired from an animal source and that ELISA technique may help to define the colonised population.
The British Society of Gastroenterology

J WEL, G D BELL, G HARRISON, J TROWELL, P GANT, P JONES (Departments of Medicine, Medical Physics, Pathology, and Microbiology, The Ipswich Hospital, Heath Road Wing, Ipswich, Suffolk) Successful eradication of C pylori appears to reduce duodenal ulcer relapse. In agreement with other groups we have found recrudescence of C pylori one month after treatment with conventional dose De-Nol (seven successes of 35) or De-Nol plus Amoxil (15 successes of 39).

The aim of the present study was to determine if short term/high dose De-Nol would be more effective than the standard regime. A total of 37 patients were treated with either De-Nol tabs (n=17) or De-Nol liquid (n=20) both at 240 mg qds for two weeks.

C pylori was confirmed on antral biopsy before entry to the study and subsequent follow up was with the 13C-urea breath test. The 17 patients treated with De-Nol tablets all had positive 13C-urea breath tests before treatment, 82% were negative at the end of treatment but within a month all had relapsed and were again positive. The 20 patients treated with De-Nol liquid had a single 13C-urea breath test one month after treatment. Only one of the 20 was negative.

C pylori was eradicated from one of 37 patients receiving high dose De-Nol. These results are significantly inferior to conventional dose De-Nol regimes (p<0.02).

Mucosal T-cell subsets in normal gastric antrum and C pylori-associated chronic gastritis

B J RATHBONE, J WYATT, L K TREJDOSEWICZ, R V HEATLEY, M S LOSOWSKY (Departments of Medicine and Pathology, St James's University Hospital, Leeds) Chronic gastritis is a common condition of uncertain aetiology. We have studied 29 patients (10 with normal histology, 19 with C pylori associated chronic gastritis) being endoscoped for epigastric pain. Two antral biopsies were taken for routine histology (H&E and modified Giemsa staining) and for cryostat sections for double label immunofluorescence with monoclonal antibodies to T-cell subsets. The T-cell subsets of normal gastric antrum comprised 68-8% (14-5) CD8+ (suppressor/cytotoxic) T-cells in the epithelium, and 52-9% (19-8) CD8+ T-cells in the lamina propria. In chronic gastritis, there were reduced percentages of CD8+ cells (53-8% (15-6%) intra-epithelial; 43-7% (15-9%) in lamina propria) due to infiltration by CD4+ (helper/inducer) cells. The increase of intraepithelial CD4+ cells was significant (p<0.05). In the lamina propria, a raised percentage of CD4+ T-cells expressed the CD7 marker of T-blastoegenesis (37% v 26%: p<0.05) and there was a decrease of CD8+ T-cells which co-expressed CD5 (46% v 63%: p<0.05). Similar trends were also observed in the epithelial compartment. The alterations in T-subset distribution and phenotype considerably exceed those observed in intestinal mucosae in coeliac disease and ulcerative colitis, thereby suggesting a profound perturbation of the local mucosal immune system in response to C pylori colonisation of the gastric mucosa.

Duodenal secretion of campylobacter pylori-specific antibodies in patients with gastritis and duodenitis

J E CRABTREE, B J RATHBONE, T M SHALLCROSS, J J WYATT, R V HEATLEY, M S LOSOWSKY (Departments of Medicine and Pathology, St James's University Hospital, Leeds) Gastric secretion of C pylori specific antibodies by cultured biopsies in vitro is strongly associated with gastric C pylori colonisation and non-autoimmune gastritis. To investigate regional variations in the mucosal humoral response to C pylori, the duodenal secretion of C pylori antibodies has been examined.

Duodenal endoscopic biopsies were taken from 25 patients for histology and culture in vitro. C pylori-antibodies secreted during three-day cultures were measured by ELISA using a soluble antigen from one strain of C pylori.

In 12 patients with antral gastritis but normal duodenal histology (group A) significantly (p<0.05) raised levels of C pylori specific IgG and IgA antibodies were secreted relative to control subjects (B) with normal antral and duodenal histology (n=8). In five patients with both antral gastritis and active duodenitis (C) the levels of secreted C pylori specific IgA antibodies were significantly higher (p<0.01) than group A or B. Mean optical density values for C pylori specific IgA antibodies being 169 (59) (A), 16-1 (7) (B), and 802 (201) (C). Secretion of C pylori specific IgG antibodies in group C was comparable to group A, but significantly greater than that of control subjects (p<0.05).

These results demonstrate that C pylori specific antibodies are secreted by the duodenal mucosa of colonised subjects, and this may have particular relevance for those colonised with duodenitis.

Does sickle cell disease cause peptic ulceration?

J S DE CAESTECKER, I BATES (INTRODUCED BY R C HEADING) (Department of Medicine, School of Medical Sciences, UST, Kumasi, Ghana, W Africa) Duodenal ulceration is reported to be more common amongst young men with homozygous sickle cell disease (Hb SS). We performed haemoglobin electrophoresis on 70 healthy university students and 207 consecutive patients undergoing oesophagogastroduodenoscopy in a West African centre. In the endoscopy group, 70 had peptic ulcer (PU) disease (duodenal ulcer 42, gastric ulcer two, duodenal stenosis five, severe duodenitis seven, and duodenal scarring 14). Of the remainder, 92% had a normal endoscopy. A total of 108 oesophagitis and 12 miscellaneous conditions. There were no significant differences between the three groups in the prevalence of haemoglobin phenotypes (x<sup>2</sup>=2.15, p>0.45: PU (70): AA52, AS8, AC7, SS0, SC2, CC1; other endoscopy (137): AA105, AS17, AC14, SS1, SC0, CC0: students (70): AA51, AS11, AC7, SS0, SC1, CC1). The M:F ratio for PU was 2:7:1 (p<0.05 v other endoscopies). Mean age for PU was 42.8±14.6 years. Significantly more patients with PU were current or exsmokers (p<0.005) compared to other endoscopic groups, but there was no difference in alcohol consumption or domicile (urban or rural) between the two endoscopy groups. Sickle cell disease does not play a major role in the aetiology of peptic ulcer disease in West Africa.

A comparative study of dyspepsia in coal-miners and the general population

J D HARRISON, D J MORRIS (Department of Surgery, Queen's Medical Centre, Nottingham) Miners are known to have a higher incidence of gastric cancer. We are screening for gastric cancer using a dyspepsia questionnaire, and have therefore investigated the prevalence of dyspepsia in a group of 670 retired miners aged 50–75 years, comparing them with a randomly selected group of 743 age matched men identified from general practitioner records. All subjects were sent a selfadministered upper Gastro-intestinal symptom questionnaire. One hundred and seventy two (77%) miners replied, compared with 195 (76.7%) in the control group. One hundred and seventy two (37.8%) of the miners questionnaires were positive for at least one of the symptoms whilst 195 (30.2%) of the general population were symptomatic (x<sup>2</sup>=5.88, p=0.05). Significantly more miners complained of anorexia (24.3% v 8.9%, t=3.49, p=0.0006), weight loss (22.6% v 3.6%).
Duodenal pH is neutral in established duodenal ulceration

D D Kerrigan, L A Houghton, S R Brown, M E Taylor, N W Read, A G Johnson (Department of Surgery/Sub-Department Human GI Physiology, K Floor, Royal Hallamshire Hospital, Sheffield) We have recorded fasting (75±3 min) and post-prandial (224±18 min) intraluminal pH at three sites (antrum, duodenal bulb and duodenal loop) in 21 male subjects: seven healthy volunteers, eight healed DU, and six untreated active DU. Accurate positioning of the pH probe was ensured by attaching the pH electrodes to a multimeter catheter recording transmucosal potential difference (PD) continuously at two sites 4 cm apart. By maintaining the distal PD port just within the duodenum, bulb pH (measured 2 cm distally) could be recorded. Additional pH electrodes were located 6 cm beyond the duodenal PD port and 2 cm proximal to the gastric port. During fasting, the % of time pH fell to <4 in both the duodenal bulb and loop was greater in healed than in active DU (bulb pH: 12-6% (0-45-7) v 1-5% (0-7-2), median (range); p=0-03). Duodenal acidification was similar in active DU and controls (p=1-0). Meal ingestion did not significantly alter the % time that duodenal pH was reduced. Bulb pH was <4 for 16% of the postprandial period in healed DU, compared with 4-5% (normals) and 1-7% (active DU). A similar pattern was noted in the duodenal loop (healed v active: 1-4% v 0-2%; p=0-05). No significant differences were seen in antral pH throughout fasting and fed periods. Active DU is associated with normal bulb pH; once healing has occurred bulb pH is significantly reduced. This finding may explain the typical cycle of spontaneous healing, yet frequent relapse in DU disease.

Combined ranitidine and pirenzepine in the treatment of duodenal ulcer

G Bianchi Porro, M Lazzaroni, A Prada, A Ferrara, E Colombo, P R Dal Monte, F Sabbatini, G Jaquinto, V Benvenisto, B Pimbimbo (GI Unit, L Sacco Hospital, Milan, Gastroenterology Service, Bellaria Hospital, Bologna, and Chair of Gastroenterology, University of Naples, Italy) H₂-receptor antagonists administered together with pirenzepine suppress acid output more than either agent alone. The purpose of this study was to determine whether pirenzepine and ranitidine given together are superior to ranitidine alone in inducing healing of duodenal ulcers. One hundred and sixty six patients from seven centres were randomised to receive either ranitidine 300 mg (R), ranitidine 300 mg plus pirenzepine 50 mg (R+P50), or ranitidine 30 mg plus pirenzepine 100 mg (R+P100), all at night, for two periods of 4 weeks. One patient on R, two patients on R+P50, and two patients on R+P100 did not complete the treatment. The healing rates for all treatments did not differ significantly within each centre. After two weeks, amongst the patients who completed treatment, healing was 42% on R, 43% on R+P50, 35% on R+P100. At four weeks these proportions had risen to 74, 94, and 76%, with significant (p<0-03) differences in favour of the R+P50 group compared with the other two groups. Analysis by intent-to-treat yielded similar results. Patients in the three groups experienced a similar degree of relief of daytime and nighttime pain. Significantly (p<0-05) more patients (29%) on R+P100 complained of side effects than patients on R (11%), however, doubling the dose of pirenzepine with low dose pirenzepine in patients with duodenal ulcer results in significantly better healing than the H₂-antagonist alone. The failure to achieve a significantly higher healing rate with the combination including the higher dose of pirenzepine may have been due to side effects that reduced compliance.

Rebound nocturnal hypersecretion after four weeks H₂ antagonist therapy

G M Fullarton, G Mclauchlan, A Macdonald, G P Crean, K E L McColl (University Departments of Medicine and Surgery, Western Infirmary, Glasgow and Gastrointestinal Centre, Southern General Hospital, Glasgow) Daytime intragastric pH, fasting and Oxo meal stimulated gastrin response and nocturnal acid output were studied in eight male duodenal ulcer patients before, during, and two days after completing a four week course of nizatidine 300 mg nocte (2000 h). Median daytime intragastric pH pretreatment was 1-8 (range 1-0-3-2) and remained similar on the final day of treatment at 1-3 (1-2-3) and two days after completing therapy at 1-7 (1-1-1-8). The fasting serum gastrin was similar during therapy and post-therapy compared with pretreatment values. The median integrated gastrin response (pg/ml/min) pre-treatment was 4875 (range 4225-7375) and was not significantly altered on treatment being 5950 (range 3900-10000) (p=0-1) or two days after treatment being 5200 (3000-9300) (p=0-07). On the final day of treatment median nocturnal acid output (mmol) was 11-6 (range 0-4-26-7) compared with the pretreatment value of 39-4 (9-8-91-2), representing a median inhibition of 78% (p<0-01). Two days post-treatment median nocturnal acid output was 74-1 (11-181) compared with the pretreatment value of 39-4 (9-8-91-2) representing median rebound hypersecretion of 77% (p<0-05). This was the result of an increase in the (H⁺) concentration and volume of secretion. This rebound nocturnal hypersecretion may be relevant to the high ulcer relapse rates after discontinuation of H₂ receptor antagonist therapy.

Antibiotics potentiates colloidal bismuth subcitrate (CBS) effect in peptic ulcer disease

C O'Morain, G Coghlan, D McKenna, D Gilligan, R Tobin, R Ward, C Keane, E C Research Department of Gastroenterology, Meath/Adelaide Hospitals, Trinity College, Dublin, Ireland) Eradication of Campylobacter pylori (CP) results in a lower relapse rate of DU over a period of one year. Colloidal bismuth subcitrate, an effective ulcer healing reduces CP infection by 20 to 50%. The aim of this study was to see if adjunctive antibiotic therapy with CBS improves healing rates of DU, the associated gastritis and eradication of CP. One hundred and ten patients with endoscopically proven DU were randomised to receive CBS 120 mg qid for six weeks. n=56, CBS 120 mg qid for six weeks+suxamoxycillin, (A) 250 mg tds for the first week (n=24) or CBS 120 mg qid for six weeks+metronidazole 200 mg tds for the first week (n=26). At endoscopy before and after treatment two antral biopsies were taken. One was placed in formalin stained with haematoxylin and eosin and Warthin Starry silver stain and assessed to document the presence of gastritis and CP. The other biopsy was assessed microbiologically by
gram stain and culture for the presence of CP. There was no significant difference in duodenal ulcer healing rates for the three groups. Eighty-eight of 110 (82%) patients were CP positive and 97 of the 110 (89%) had antral gastritis before treatment. After treatment 33% of the CBS treated group became CP negative compared with 53% in the CBS+M group and 62% in the CBS+M treated groups. Gastritis was healed in 42% of patients in the CBS treated group compared with 64% in the CBS+M group and 56% in the CBS+M treated groups. There was a significant improvement in CP eradication and gastritis (p<0.05) in the antibiotic+CBS treated groups compared with CBS alone. This study suggests that antibiotic therapy is a useful adjunct treatment in duodenal ulcer disease.

The effect of colloidal bismuth subcitrate on symptoms and gastric histology in non-ulcer dyspepsia - a double-blind placebo-controlled study

J Y Kang, H H Tay, A Wee, R Guan, M V Math, J Yap (Division of Gastroenterology, Department of Medicine and Department of Pathology, National University Hospital, Singapore) The aim of this study was to determine the effect of colloidal bismuth subcitrate (CBS, De-Nol) on symptoms and gastric histology in patients with non-ulcer dyspepsia. Patients with food related upper abdominal pain not caused by ulcer disease were randomised to receive one tablet of CBS or matching placebo four times daily for eight weeks. Fifty one patients completed the trial: 28 patients in the bismuth group and 23 in the placebo group. Overall, there was no difference between the two groups in terms of symptom relief, reduction of gastritis or eradication of gastric spiral organisms. Amongst patients with histological gastritis, however (n=23), those who took CBS used fewer antacid tablets (number of tablets used being 3.1 v 19.3 for the first fortnight, p<0.02) when compared with the Wilcoxon's rank-sum test: 1.8 v 22.4 for the second, 0.2 v 0.02; 0.7 v 19.2 for the third, p<0.025; and 0.3 v 10.5 for the fourth, NS); they were more likely to become asymptomatic (8 of 11 v 3 of 12 p<0.05); their gastritis was more likely to resolve (5 of 10 v 0 of 12, p<0.025) and their gastric spiral organisms were more likely to be eradicated (8 of 9 v 0 of 12, p<0.001) when compared with patients taking placebo. In contrast, patients who did not have gastritis in their index biopsies (n=28) fared similarly whether they received CBS or placebo, the mean antacid usage in the two groups being 14.2 v 6.4, 8.4 v 6.3, 9.7 v 0.7, and 7.2 v 0.3 for the four fortnights (NS for any period).

Our results indicate that the administration of CBS benefited non-ulcer dyspepsia patients with gastritis but had no effect on those without. We suggest that histological gastritis is one of several causes of non-ulcer dyspepsia.

Double blind comparative study of omeprazole (40 mg od) vs cimetidine (400 mg qds) in the treatment of erosive reflux oesophagitis

T C B Dehn, H A Shepherd, D Collin-Jones, M G Kettlewell (John Radcliffe Hospital, Oxford, The Royal Hampshire County Hospital, Winchester, and Queen Alexandra Hospital, Portsmouth) The use of cimetidine (cin) is established in the management of oesophagitis: no study has compared the efficacy of this drug with that of omeprazole (om) in the treatment of non-refractory oesophagitis. Sixty seven symptomatic patients with endoscopically and histologically verified reflux oesophagitis were randomly allocated eight weeks of continuous treatment with either cin 400 mg qds (n=31) or om 40 mg od (n=36). Clinical assessment was made pre-entry by scoring symptomatic, endoscopic and histological severity. Symptoms were repeated twice weekly thereafter: endoscopy and histology at four and eight weeks. Healing was defined as complete epithelialisation of all oesophageal lesions.

At four and eight weeks, healing had occurred in 57% (om) v 29% (cin) (p=0.0028) and 74% (om) v 28% (cin) (p=0.0001) respectively. At two weeks complete relief of heartburn was achieved by om in 75% and cin in 42% of patients (p=0.007) and at eight weeks in 92% and 59% (p=0.005) respectively. At entry there was no significant difference in severity of histological scoring between groups. At four weeks a significantly greater proportion of patients on om were healed histologically with 16/26 (61%) v 9/29 (31%) healed on om and cin respectively (p=0.0028). Omeprazole is superior to full dose cimetidine in the treatment of reflux oesophagitis.

Effects of intravenous omeprazole on serum pepsinogens, serum gastrin and gastric pH

I Biemond, J B M Jansen, L C Baak, C B H W Lamers (Department of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands) Oral omeprazole treatment for one week has been shown to significantly increase serum pepsinogen (PG) A levels. This study was undertaken to determine whether intravenous administration of repeated doses of omeprazole for only 24 hours affects serum concentrations of PGA and PGC or the PGA/PGC ratio.

The results were related to serum gastrin and intragastric pH. Eight fasting men, median age 22 (19-62) yrs, received an iv bolus injection of 80 mg omeprazole followed by injection of 40 mg of the drug every six hours for a total period of 24 hours. Serum concentrations of PGA, PGC, and gastrin were measured before and at 3, 6, 12, 18, and 24 hours by radioimmunoassay. Intragastric pH was recorded continuously by an ambulatory pH monitor (PROXIMA Light). Statistical analysis was done by Wilcoxon's test.

PGA increased (p<0.05) from a basal value of 47 (6) μV/l at 12 h, 130 (39) μV/l at 18 h, and 134 (48) μV/l at 24 h. PGC was 19 (5) μV/l basally and showed non-significant increases to 29 (11), 57 (31), and 35 (12) μV/l, at 12, 18, and 24 h, respectively. The PGA/PGC ratio did not change. Serum gastrin increased (p<0.05) from 35 (7) to 94 (31), 59 (14), and 85 (27) ng/l, at 12, 18, and 24 h. Intragastric pH was 1 (0.1), significantly rising to 3 (8) (0.8), 2 (6), 3 (0.9), 4.5 (0.9), and 5.8 (0.5) at 3, 6, 12, 18, and 24 h, respectively.

Intravenous administration of repeated doses of omeprazole increases serum PGA as early as 12 hours after the first dose. The increase in serum PGA coincides with a significant rise in serum gastrin, but is preceded by a significant increase of intragastric pH for nine hours. Thus, the effect of antisecretory drugs on serum PGA may occur much earlier than previously shown.

Omeprazole provides faster ulcer healing and symptom relief than cimetidine in the treatment of gastric ulcer

C M Bate, G V H Bradby, S P Wilkinson, M C BateSon, W S Hislop, J P Crowe, C P Willoughby, E M Peers, P D Richardson, J Opus-Gotu Trial Investigators (UK and Eire) (Gastroenterology Department of Hospitals in Wigan, Sandwell, Gloucester, Bishop Auckland, Paisley, Dublin and Orsett and Astra Pharmaceuticals, Kings Langley) This first large study in the British Isles of omeprazole in gastric ulcer aimed to compare endoscopically assessed ulcer healing, symptomatic relief and tolerability of omeprazole (20 mg om) with...
cimetidine (400 mg bd). One hundred and ninety seven patients aged 18–80 years with symptomatic gastric ulcers (94% ≥5 mm diameter) were randomised to receive double blind treatment with omeprazole (105) or cimetidine (92) for four, or if unhealed after four weeks, for eight weeks. The groups were comparable at randomisation. Patients found later to have pre-existing carcinoma were excluded from analyses (three omeprazole and five cimetidine).

On an intention-to-treat analysis, after four weeks 74/102 (73%) of omeprazole patients and 48/87 (55%) of cimetidine patients had healed ulcers (p<0.05; 95% confidence interval (CI) for the therapeutic gain of 18% being +4% to +31%). After eight weeks the cumulative numbers of patients with healed ulcers were 86 (84%) for omeprazole and 64 (74%) for cimetidine (ns; CI 1% to +22%).

After four weeks treatment 81% of omeprazole patients and 60% of cimetidine patients were symptom free (p<0.01), and the omeprazole patients took fewer antacids than the cimetidine patients. Both drugs were well tolerated and the two groups of patients had a similar pattern of adverse events. Omeprazole once daily provides faster healing of the lesion, and swifter relief of the symptoms of gastric ulcer than cimetidine twice daily.

Gastric ulcer recurrence after six weeks' treatment with omeprazole and cimetidine—six months double blind comparative follow-up study

K LAURITSEN ON BEHALF OF A DANISH MULTICENTRE STUDY GROUP (INTRODUCED BY J RASK-MADSEN) (Department of Medical Gastroenterology, Odense University Hospital, Odense, Denmark) To compare ulcer recurrence after six weeks’ double blind treatment with omeprazole (30 mg daily) and cimetidine (1 g daily) in patients with gastric ulcers those with healed ulcers were seen after two, four, and six months, or more often if warranted. Endoscopy was done if the patient had experienced ulcer pain on at least four days during the same week and after six months, regardless of the presence or absence of symptoms.

Eleven centres contributed 218 patients of whom 110 had received omeprazole and 108 cimetidine. Ulcers recurred in 35% of the patients from the omeprazole group (95% confidence limits (CL): 26–44%) and in 41% (95% CL: 31–50%) of those from the cimetidine group (p>0.05; log-rank test) and were asymptomatic in 15% and 5% of cases, respectively. The recurrence rate was 45% among smokers (95% CI: 36–53%) compared with 25% among non-smokers (95% CL: 15–35%; p<0.05). Similarly, ulcers recurred more rapidly (p<0.05) in patients with a healed prepyloric ulcer (49%, 95% CL: 40–57%) than in patients with a healed ulcer in the body of the stomach (23%; 95% CL: 14–33%).

In conclusion, the ulcer recurrence rates are similar after six weeks’ treatment with omeprazole and cimetidine in patients with gastric ulcer disease. Smoking and a prepyloric ulcer location indicate an increased risk of early relapse.

Why refractory duodenal ulcers do not heal

M J ROGERS, J HOLMFIELD, J PRIMROSE, T GLEDHILL, D JOHNSTON (University Department of Surgery, The General Infirmary, Leeds) After three months therapy with H2 receptor antagonists (H2RA’s), 7% of duodenal ulcers remain unhealed; why these ‘refractory’ ulcers (RFDU) do not heal is not clear but H2RA’s may not suppress nocturnal acid in patients with RFDU.

Thirty eight consecutive patients referred for operation for duodenal ulcer (24 non-RFDU, 14 RFDU) had 24 hour ambulatory intragastric pH recorded on placebo and on 300 mg ranitidine nocte (RAN). Median 24 h, night time (0000–0800) and daytime (0800–0000) pH and 24 h, night time and daytime [H+] (area under [H+] v time curve) were calculated for each recording.

Twenty four hour, night time and daytime pH (on placebo and RAN) of patients with non-RFDU did not differ significantly from patients with RFDU. Ranitidine nocte reduced 24 hour [H+] a median (quartile) 41% (28–61) in patients with RFDU and 61% (36–67) in those with non-RFDU (NS); night time [H+] 87% (56–98) in patients with RFDU and 95% (83–99) in those with non-RFDU; daytime [H+] 32% (5–58) in patients with RFDU and 25% (1–46) in those with non-RFDU (NS). Ranitidine nocte suppressed acid as potently in patients with RFDU as in patients with non-RFDU; but reduced nocturnal [H+] less than 50% in three of 14 patients with RFDU but in 0 of 24 patients with non-RFDU (NS).

Ranitidine nocte adequately suppresses nocturnal acid in most patients with RFDU; we suggest these patients are erratic tablet takers. In a few patients with RFDU, RAN affords inadequate inhibition of acid; acid suppression sufficient to heal ulcers in these patients may be achieved with higher doses of ranitidine, other drugs or surgery.

Functional dyspepsia (FD): a meta-analysis of randomised placebo controlled clinical trials (PRCCT)

G DORBILLA, F VALLAPERTA, M COMBERLATO (Division of Gastroenterology, General Regional Hospital 39100 – Bolzano, Italy) The aim of this study was to produce a meta-analysis of the results of short-term PRCCT on the drug treatment of FD with antisecretory (as) and gastrokinetics (GK). Trials were retrieved from computerised data bases, by scanning of published reviews and Current Contents. Of a total of 74 retrieved trials, 23 proved eligible for meta-analysis on the basis of six essential selection criteria defined a priori. Results of treatment were expressed in terms of ‘therapeutic success’ (TS) (‘symptom-free patients’, ‘patients with significant improvement in symptoms’, ‘patients with excellent results’). Differences in TS rates between the various drugs and placebo were calculated in each trial as the algebraic difference together with the respective 95% confidence interval (95% CI); the pooling of results of all eligible trials was done using Cochran’s weighted method. With AS the mean difference in TS rates v placebo was +20% (95% CI: 14–24%). The therapeutic gain for the single AS was 25% (95% CI: 14–36%) for pirenzepine and 18% (95% CI: 12–24%) for H2-antagonists. Meta-analysis of trials with GK also showed superior efficacy of these agents compared to placebo, with a mean difference in TS rates of +46% (95% CI: 40–52%). Single the mean differences in TS rates v placebo were +43% (95% CI: 27–59%) for metoclopramide, +56% (95% CI: 46–74%) for domperidone, and +39% (95% CI: 30–48%) for cispapride, respectively.

Famotidine (F) in single morning (SM) v single nocturnal (SN) dose (D) in the treatment of duodenal ulcer (DU)

G DORBILLA, G DE PRETIS, G FONTANA, P MAIOLO, G MARENCO, G MENARDO, F P ROSSINI, A FERRARI, A SAGGIOLO, P PALLINI (GI Units of Bolzano, Bologna, Pietra Ligure, Torino, Mestre, Italy) In 1986 some of us reported an open study on 41 DU patients suggesting that the healing effect of SMD of cimetidine and ranitidine was comparable with that of the respective SND.

Aim of this multicentre study was to verify these results by a randomised double blind trial with F 40 mg in SND v SND. One hundred and eighteen of 127 DU patients, informed and consenting, completed the four to eight week trial. By week
four the healing rate at endoscopy was 77.2% (44/57) in patients on SMD compared with 78.6% (48/66) of patients on SND (95% IC for the difference: -15.18, p=0.84). By week eight these percentages were 85.7% (48/56) and 91% (55/60), respectively (95% IC for the difference: 7.41, p=0.03).

This study confirms the results of the previous open study and shows that the single morning dose of F (and probably of the H2-blockers) is equally as effective as the single nocturnal dose in healing DU. Such a result suggests that the inhibition of nocturnal acidity has a significant but not essential pathogenetic role in ulcer healing.

Sucralfate (S) v H2-antagonists (H2-A) in DU non-responders (non-R) to initial treatment with sucralfate

F CHILOVI, L PIAZZI, G DOBRIlla (Division of Gastroenterology, General Regional Hospital 39100 – Bolzano, Italy) The aim of this study was to compare the efficacy of either S or H2-A in non-R to an initial four week treatment with S 1 g qid.

Forty eight DU patients non-R to S were randomly allocated over the period 1981-1987 either to S 1 g qid (24) of H2-A (24: cimetidine (C) 1 g/day five; ranitidine (R) 150 mg bid eight; R 300 mg/nocte, four; famotidine (F) 40 mg/nocte, seven). Treatment groups were comparable for the following variables: age, sex, ulcer duration, and size, smoking habits, alcohol consumption, BAO, MAO, PAO, and serum gastrin levels. Endoscopy was repeated in all patients after eight weeks of treatment. Healing was defined as the complete disappearance of the ulcer lesion at endoscopy. Healing rates were 45.8% (11/24) in patients on S and 95.8% (23/24) in those on H2-A (x2=14.5; p 0.001). The 95% confidence interval of the difference (50% units) was 28.5-75.5. Five non-R, who initially had ulcer pain in each treatment group, were pain free after four weeks treatment both on S and H2-A. No dropouts, no protocol violators and no relevant side effects were registered during the study.

This trial appears to suggest that in non-R to a mucosa protective agent the use of H2-A is a good therapeutic option, just as mucosa protective agents have been found effective in non-R to H2-A.

Effect of enprostil on bicarbonate secretion in amphibian and human stomach

C J SHORROCK, L GIBBONS, W D W REES (Department of Gastroenterology, Hope Hospital, Eccles Old Road, Salford) Prostaglandins have been shown to protect gastroduodenal mucosa from damage by a variety of noxious agents. Enhancement of the protective ‘mucus-bicarbonate’ barrier may be an important mechanism of prostaglandin action on gastric mucosa and therefore we have examined the influence of enprostil, a synthetic dihydroprostaglandin E2, on gastric bicarbonate secretion in vitro and by the intact human stomach.

Addition of enprostil (10-6M) to the luminal side of isolated amphibian gastric mucosa, mounted in an Ussing chamber, produced a 28% increase in bicarbonate secretion (0.25 (0.08) to 0.32 (0.07) mmol/cm2/h, n=6, p<0.05; mean (SE)).

Using a perfusion technique the effect of enprostil (35 μg) on human gastric bicarbonate secretion was studied. Bicarbonate secretion was calculated from pH and pCO2 of gastric aspirates while acid secretion was suppressed by intravenous ranitidine. After a basal hour, enprostil (35 μg) was added to the perfusate and bicarbonate secretion measured for a further hour. This therapeutic dose of enprostil produced a 78% increase in bicarbonate secretion (489 (95) to 853 (136) mmol/h, n=6, p<0.01; mean (SE)).

In conclusion, enprostil stimulates gastric bicarbonate secretion in vitro and in man and this may be one of the mechanisms whereby this agent protects the mucosa from damaging agents.

Abolition by omeprazole of aspirin-induced gastric mucosal injury in humans

T K DANESHMEND, A G STEIN, N K BHASKAR, C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) The best strategy for prophylaxis of non-steroidal anti-inflammatory drug (NSAID) associated ulcer disease is unclear. H2 receptor antagonists reduce gastric mucosal injury partially. We attempted to abolish acute aspirin induced gastric mucosal injury with omeprazole.

Sixteen volunteers aged 19-36 (eight men) took omeprazole or placebo for seven days, with aspirin 900 mg bd on the last two days before assessment of intragastric bleeding. Aspirin increased bleeding from 1.4 (95% confidence limits 0.8-2.4) μl10 mins to 16.1 (9.5-27.5) μl10 mins. Both doses of omeprazole reduced this significantly (p<0.01). Bleeding after omeprazole 20 mg mane plus aspirin was 3.4 (1.4-5.2) μl10 mins, however, significantly higher than after placebo (no aspirin, no omeprazole, p<0.01), whereas after omeprazole 40 mg bd plus aspirin (2.4 (1.3-4.4) μl10 mins) it was not. The effect of omeprazole on intragastric acidity was dose dependent (pH 2.26 (interquartile range 2.11-2.58), aspirin alone: 3.6 (2.66-6.52), omeprazole 20 mg: 6.65 (5.59-6.88), omeprazole 40 mg bd (p<0.01) and the reduction in bleeding correlated with intragastric pH (p<0.01).

Omeprazole 20 mg, like H2 receptor antagonists, reduces acute aspirin induced microbleeding to levels which are still higher than with placebo. With omeprazole 40 mg bd, pH approaches anacidity and bleeding is not significantly different from placebo, suggesting that gastric injury can be abolished. This has therapeutic potential for elderly patients taking NSAIDs.

A new model of human gastric mucosal injury – protection by prostaglandin E2 and carbolip

C J HAWKEY, N K BHASKAR, P W DETTMAR, T K DANESHMEND (Department of Therapeutics, University Hospital, Nottingham and Reckitt and Coleman, Dansom Lane, Kingston upon Hull) Carbolip, a new mucoprotective polycyrate, prevents gastric mucosal injury by alcohol in rats. We developed an analogous human model, in which 80% ethanol is sprayed directly onto dependent gastric body mucosa and serial changes were evaluated by continuous endoscopic inspection in unsedated volunteers.

Ethanol caused mucosal reddening, superficial white slough and intramuscular haemorrhage during five minutes after application; these changes were scored on 10 point scales, five minutes later. Prostaglandin (PG)E2, 500 μg, given 20 minutes before 20 ml of 80% ethanol, reduced intramuscular haemorrhage scores from 4-5 (median, interquartile range 3.5-5.5) to 2.5 (1.5-2.5) but did not reduce white slough (5 (3-5.5) v 5 (3-5.5)) or erythema. Carbolip 0-67%, 80 ml, 20 minutes before 40 ml of 80% ethanol, also reduced haemorrhage scores from 6 (1.5-8.0) to 2.5 (0.5), compared with water control (n=10, p<0.05). Scores for white slough 4-5 (3-7.5) v 3-5 (1-4.5) and erythema, 4 (2-5.5) v 3-5 (1-4.5) were similar after carbolip and water.

In this model, protection of the human gastric mucosa against alcohol by carbolip is similar to that by PGF2α, with prevention of mucosal haemorrhage but not superficial desquamation. Carbolip may thus provide a clinically useful protection of human gastric mucosa.
Asymptomatic versus symptomatic gastric ulcers in patients with rheumatoid arthritis receiving non-steroidal anti-inflammatory drugs (NSAID)

R UPADHYAY, A HOWATSON, A W MCKINLAY, C GEMMELL, R D STURROCK, R I RUSSELL (Gastroenterology Unit, Department of Pathology, Department of Bacteriology and Centre for Rheumatic Diseases, Royal Infirmry, Glasgow) There is a high prevalence of gastric (antral) ulceration in patients with rheumatoid arthritis receiving NSAID, who often present with dyspeptic symptoms, but, may be asymptomatic. We have tried to identify the factors associated with asymptomatic and symptomatic gastric ulceration. Thirty four patients with gastric ulcer were included of whom 17 (50%) were asymptomatic. There was no significant difference in the mean age (asymptomatic 57.1 years, symptomatic 56.8 years), sex distribution (asymptomatic F 14, M 3; symptomatic F 16, M 1), or the mean duration of rheumatoid disease (asymptomatic 12.1 years; symptomatic 10.4 years) between the two groups. Eight patients with dyspepsia as compared with three in the asymptomatic group were smokers (0.5 < p < 0.1). Twenty one of 34 patients (61.7%) were C pylori positive (asymptomatic 12; asymptomatic 19). Neither the number, site and size of the ulcers or their association with gastric erosions and submucosal haemorrhages differed significantly between the two groups and there was no association with ingestion of any particular NSAID.

Thus, asymptomatic gastric ulcers are common in patients with rheumatoid arthritis receiving NSAID. We have been unable to identify any specific factors that distinguish asymptomatic gastric ulcers from those presenting with dyspeptic symptoms. Smoking may be weakly associated with dyspeptic symptoms. The C pylori prevalence is similar to that of gastric ulcers in the general population, although a higher prevalence is seen in younger age group.

Naproxene v etodolac: a controlled endoscopic study in patients with rheumatoid arthritis

G BIANCHI PORRO, M PETRILLO, S ARDIZZONE, I CARUSO (Gastrointestinal Unit, Rheumatological Unit, L Sacco Hospital, Milano, Italy) Aim of this clinical, endoscopic study has been to evaluate the therapeutic efficacy and the gastric tolerability of etodolac, a new anti-inflammatory, non-steroidal drug, v naproxene. The study has been carried out on 48 patients (42 women – six men, age 23–75 years) suffering from rheumatoid arthritis, 44 of whom have completed the trial. After an initial esophagogastroduodenoscopy to exclude the presence of gastric mucosal lesions, patients were randomly allocated to a double blind treatment, either with etodolac 200 mg bid or with naproxene 500 mg bid for a period of four weeks; followed by endoscopic control at the end of this treatment period. The endoscopic evaluation of the gastroduodenal mucosal lesions has been carried out according to the Lanza 0–4 scale. Both drugs proved efficacious in relieving clinical symptoms, without any statistically significant difference. Gastric mucosal lesions were observed in 15% of etodolac-treated patients (all of grade 2) and in 46% of patients treated with naproxene (70% of grade 2–3, 30% of grade 4; p=0.005). Painful dyspepsia has been observed in 15% of patients treated with etodolac v 38% of patients on naproxene therapy. This study shows that etodolac is at least as active as naproxene in relieving rheumatic symptoms, but its administration results in a significantly lesser degree of gastric damage.

Non steroidal anti-inflammatory drugs: retrospective study of bleeding and perforated peptic ulcers

F H SMEDELEY, M TAUBE, R LEACH, C WASTELL (Academic Surgical Unit, St Stephen's Hospital, Chelsea, London) The ingestion of non-steroidal anti-inflammatory drugs (NSAID) in 272 patients with bleeding and perforated peptic ulcer was compared with 272 age/sex matched controls. Twenty three of 116 (20%) patients with bleeding peptic ulcers were receiving NSAID and seven of 116 (6%) controls (p=0.003). Sixteen of 132 (12%) patients with perforated ulcer were taking NSAID compared with six of 132 (5%) controls (p=0.045) and 10 of 35 (28.5%) above the age of 65 compared with two of 35 (6%) controls (p=0.026). Twelve of 93 (13%) patients admitted with bleeding duodenal ulcers had received NSAID compared with five of 90 (6%) controls (p=0.126) and six of 18 (33%) over 65, compared with one of 18 (5.5%) controls (p=0.0038). Eleven of 26 (42%) patients with bleeding gastric ulcer had received NSAID compared with two of 26 (8%) in the matched controls (p=0.01). Eight of 24 (33%) patients with perforated gastric ulcer had received NSAID compared with two of 24 (8%) controls (p=0.019) and four of eight (62.5%) over the age of 65 compared with one of eight (12.5%) controls (p=0.0035). Thirty eight per cent of patients with bleeding and perforated gastric ulcers had received NSAID compared with 13% of bleeding and perforated duodenal ulcers (p=0.002). Forty two per cent of the bleeding gastric ulcers had received NSAID compared with 13% of the bleeding duodenal ulcers (p=0.003). A significantly higher proportion of patients with gastric ulcers had received NSAID than duodenal ulcers.

Peptic ulcer (PU) deaths: how many occur at home or after non-steroidal anti-inflammatory drug (NSAID) prescribing?

KEYA QUADER, RICHARD F A LOGAN (Department of Community Medicine and Epidemiology, Queen's Medical Centre, University of Nottingham, Nottingham) Recent studies have suggested that much of the increase in elderly PU mortality could be due to over a third of deaths occurring suddenly at home and to increases in non-steroidal anti inflammatory drug (NSAID) prescribing. We have identified all death certificates issued in South Derbyshire (population 520 000) in 1985 mentioning PU (ICD8 531-33) or unspecified gastro-intestinal bleeding and reviewed the general practitioner (GP) records and relevant hospital records. When PU was given as the underlying (part 1) cause the GP records of the next two deaths registered of the same age and sex have also been obtained. Of 69 deaths mentioning PU or unspecified bleeding this was given as the underlying cause in 48; 79% had occurred in hospital and only 14% at home, figures comparable with the 76% and 16% respectively reported for England and Wales (OPCS Mortality Statistics 1985). Thirty (63%) had had an autopsy and on review death was directly caused by a PU in at least 30. In 20 (42%) of part 1 deaths the GP records mentioned a NSAID prescription in the previous 12 months compared with 6 (29%) of part II deaths and 17 (20%) of control deaths giving a relative risk estimate of dying from PU after a NSAID prescription of 2.9 (95% cl 1.4-6.3). A NSAID had been prescribed in 43% of deaths where review had confirmed a PU complication. Using these figures, the proportion of PU mortality attributable to NSAID prescribing is about 25%.

Intragastric fibrinolysis and tryptic activity in bleeding peptic ulcer disease
It has been known for over 30 years that rebleding is the most important risk factor for mortality from bleeding peptic ulcers. Little is known of the factors responsible for rebleding, but disorders of fibrinolysis may be involved. Trypsin is a powerful proteolytic enzyme and preliminary studies have suggested that it is more commonly found in gastric juice of patients with bleeding than non-bleeding ulcers. We obtained gastric juice samples from seven patients with non-bleeding ulcers (DU five, GU two) and six with bleeding ulcers (DU four, GU two) over 24 hour periods through nasogastric intubation. Fibrinolytic activity was assessed using fibrin plates, and trypptic activity measured using a colourimetric technique. pH was also recorded.

Fibrinolytic activity was found in three of seven controls and all patients with bleeding ulcers (p=0.049). It was found in only 18/168 samples from controls, and 71/144 samples from patients with bleeding (χ² = 56, p<0.005). Fibrinolytic activity correlates well with trypptic activity (r=0.84) and is significantly commoner at pH>4 (χ²=28, p<0.005).

Episodes of gastroduodenal reflux of trypsin and increased intragastric fibrinolytic activity are significantly commoner in patients with bleeding peptic ulcers than uncomplicated ulcers.

An audit of gastro-intestinal unit admissions in a district general hospital: lower mortality in upper gastro-intestinal haemorrhage

J D Sanderson, R F H Taylor, S Pugh, F R Vicary (Department of Gastroenterology, Whittington Hospital, London) In 1986, 575 patients were admitted to a joint medical-surgical GI unit, 292 (50-7%) with upper GI haemorrhage. Liver disease (6-2%) and inflammatory bowel disease (4-5%) were the next most frequent diagnoses. Thirty two patients died (5-6%).

For upper GI haemorrhage, the mortality was 14 of 292 (4-8%). Thirty nine per cent of patients were over 65 years, and the majority of patients who died fell into this group. Peptic ulcer disease accounted for 42.4% of GI haemorrhage, gastritis 13-7%, oesophageal varices 4-8%. The operative rate was 16%.

The mortality rate found for upper GI haemorrhage is considerably lower than the average figures recorded in most series in the last 30 years. This lower rate may result from the use of a specialised GI unit, comprising both high dependency ward and endoscopy suite. All patients with upper GI haemorrhage are admitted to the Unit under the care of one of two gastroenterologists. All patients are seen by the duty surgical team. Strict protocols for management have been devised. Strict criteria for transfusion and surgery are also used.

Mortality of perforated peptic ulcer

T T Irvin (Department of Surgery, Royal Devon and Exeter Hospital (Wonford), Exeter) There has been a decline in the incidence of perforated peptic ulcer since the introduction of the histamine antagonist drugs but the epidemiology of this complication is changing, and it is increasingly encountered in elderly subjects.

In a consecutive series of perforated peptic ulcer (229 pyloroduodenal; 55 gastric) the average age of the patients was 70 years (range 19-98), and there was a 26% hospital mortality. Patients aged >70 years (176) had a significantly higher mortality (34%) compared with patients aged <70 (14%) (p=0.001). Multiple clinical variables were significantly more common in the elderly including women (63%), NSAID or steroid therapy (56%), absence of previous dyspepsia (69%), and surgical risk factors such as delayed presentation (33%) and preoperative shock (27%). Definitive operations (vagotomy or gastrectomy) had an increased mortality in the elderly (p=0.018). The use of risk scores based upon the presence of shock, delayed presentation or concurrent medical illness could have predicted 87% of postoperative deaths in elderly subjects, and it is suggested that risk stratification and greater caution in the use of definitive operations for perforated ulcer may result in a reduction in the high mortality in elderly subjects.

Is highly selective vagotomy (HSV) obsolete?

I M C MacIntyre, A Millar, W P Small (Surgical Review Office, Western General Hospital, Edinburgh) The ability of HSV to control duodenal ulcer disease has been questioned by recent reports from the units which pioneered the procedure. These suggested (1) a 30% recurrent ulcer (RU) rate at 14-18 years, the majority of the ulcers being 'malevolent' (bleeding or requiring operation or continual H2 blockers) and (2) that ulcers resistant to H2 blockers have a 30% RU rate at five years. In a prospective study of 291 patients followed up between five and 15 years, the RU rate was 16-8%. Of these 38-7% required no or occasional treatment only. Recurrent ulcer was no more likely in ulcers resistant to H2 blockers (RU rate 16-2%) than in those which had previously responded (RU rate 16-9%). When symptoms were analysed 21-4% of patients with RU experienced episodes of epigastric pain while overall 8-9% of patients had this symptom. The results for other dyspeptic symptoms were similar; 10-8% of patients took H2 receptor antagonists regularly or frequently. We conclude that the presence of a recurrent ulcer does not necessarily correlate with a bad result in symptomatic terms; that failure to respond to H2 blockers should not be regarded as a contra-indication to surgical treatment. The results at five to 15 years suggest that HSV remains a useful treatment for duodenal ulcer disease.

Advantages of anterior lesser curvature seromyotomy with posterior truncal vagotomy for chronic duodenal ulcer

T V Taylor, P E Thomas, J P Lythgoe, J B MacFarland (Manchester Royal Infirmary, Royal Preston Hospital, and Royal Liverpool Hospital) Anterior lesser curvature myotomy combined with posterior truncal vagotomy (AMPT) is a novel operation for chronic duodenal ulcer that has been previously reported in uncontrolled studies to have less adverse sequelae than current operations for duodenal ulcer. This operation can be done more expeditiously than highly selective vagotomy and it interrupts the vagal innervation of the stomach but preserves the pylorus. A randomised controlled trial was carried out to compare the results of AMPT with vagotomy and pyloroplasty (V and P) in the treatment of chronic duodenal ulcer in 146 patients. Inhibition of gastric acid secretion to insulin and pentagastrin stimuli was similar after both procedures. Over a two to six year period of follow up no deaths have occurred. Dumping, diarrhoea, epigastric distress, and duodenogastric reflux were more common after V and P. Gastric emptying rate was unchanged after AMPT but was more rapid after the V and P. Five recurrent duodenal ulcers occurred after AMPT with two after the V and P but this difference did not reach statistical significance (p=0.05). In this first randomised controlled trial of a new operation for duodenal ulcer, the results compare favourably with the V and P in that morbidity has been less and the tendency for an increased incidence of recurrent ulcer remains less than that which has been observed after highly selective vagotomy.
Foregut screening in familial adenomatous polyposis (FAP)

A D SPIGELMAN, R K S PHILLIPS, C B WILLIAMS, H J R BUSSEY (St Mark's Hospital and St Bartholomew's Hospital, London) Duodenal adenomas may account for foregut malignancy in FAP. Their reported incidence ranges from 20% to 100%.

We report a prospective upper gastrointestinal endoscopic screening programme in 35 patients with FAP (men 23, women 12; age range 19–67, mean 42). Gastric polyps were found in eight patients (23%) of which seven were biopsied, five being hamartomas and two normal. Duodenal polyps were found in 32 patients (91%): adenomas 31, hamartomas 1; size range <1–20 mm (mean 5–7 mm). Biopsies of macroscopically normal mucosa in six patients showed microscopic adenomas in three of the duodenal adenomas, 27 were tubular (dysplasia: 25 mild, two moderate; size range <1–20 mm, mean 5–8 mm), and four tubulovillous (dysplasia: three mild, one moderate; size range 1–11 mm, mean 8–3 mm). Adenomas were commonest at the papilla.

Duodenal adenomas are probably inevitable in FAP and the papilla is particularly susceptible, perhaps stimulated by pancreatico-biliary contents. Screening should aim to identify high risk factors (? large size, villous/tubulovillous histology, degree of dysplasia) rather than whether or not polyps are present.

Increasing numbers of gastric cardial tumours are aetiological factors changing?

W ALLUM, J FIELDING, JEAN POWELL, M J S LANGMAN (Queen Elizabeth Hospital, Birmingham and West Midlands Cancer Registry) The causes of gastric cancer are poorly understood, but the assumption tends to be made that the disease can be considered as a unity. Examination of data from the West Midlands Regional Cancer Registry suggest that when tumours are considered by subsite within the stomach an increasing proportion of disease of the upper stomach is being detected. In the quinquennium 1957–61 and 1977–81 the number of tumours described as cardiac by subsite rose from 261 to 923 – that is, by 228%, whereas the numbers described as pyloric rose from 1143 to 1436 – that is, by 25%, the total numbers of tumours described for all sites being 5562 in the first and 6307 in the second quinquennium. This large and disparate increase in the proportion of disease described as cardiac was accompanied by an increase in the numbers of oesophageal adenocarcinoma (both middle and lower third) but not of squamous tumours, making spurious diagnostic re-allocation from the oesophagus unlikely. Furthermore the proportions of pancreatic tumours did not rise unduly suggesting that the slow rise in numbers of pyloric subsite does not represent preferential re-allocation to the pancreas. The data indicate possible changes in aetiological influences predisposing to upper gastric disease despite an overall fall in gastric cancer incidence as measured by age specific rates [as opposed to total case numbers which have risen slightly in association with the aging population].

Does gastrectomy for incurable carcinoma improve quality of life?

M V MADDEN, D M DENT, P M AINSLIE, S BAILEY, D J DE VILLIERS (INTRODUCED BY M R B KEIGHLEY) (Surgical Gastroenterology and Department of Surgery, Groote Schuur Hospital and University of Cape Town) When malignant disease cannot be cured by surgical intervention, quality of life after operations assumes great importance.

We assessed quality of life pre-operatively and at 1, 2, 3, 6, and 9 months in 46 patients who underwent palliative gastrectomy (35 partial, 11 total) by using linear analogue scales for 10 symptom variables. The quality of life scores (median (SD), maximum) at 0, 1, 2, 3, 6, 9 months were: Overall 59 (18), 71 (16), 80 (19), 85 (24), 75 (22), 68 (26); partial gastrectomy 54 (18), 73 (16), 80 (18), 85 (23), 78 (25), 61 (27); total gastrectomy 61 (17), 70 (18), 80 (20), 85 (27), 68 (16), 75 (26). There were no operative deaths and the median postoperative stay was 10 days. Total and partial gastrectomies had major complications in 50% and 0% respectively with minor complications in 30% and 50%. Survival at 3, 6, and 9 months was 93%, 73%, and 70% respectively.

In incurable gastric cancer, partial gastrectomy improved quality of life for at least nine months with minimal morbidity. Total gastrectomy achieved a smaller improvement in quality of life with substantial morbidity.

Is gastric carcinogenesis mediated by changes in ornithine decarboxylase activity and polyamine concentrations?

P R TAYLOR, R C MASON, G M MURPHY, S VAJA, R H DOWLING, J MCCOLL (Departments of Surgery and Gastroenterology, UMDS, Guy's Hospital, St Thomas Street, London) Surgically induced duodenogastric reflux results in adenocarcinoma of the rat glandular stomach. In tissues which have a high proliferative rate, ornithine decarboxylase (ODC) activity and polyamine concentrations are high. This study was undertaken to assess the effect of chronic duodenogastric reflux on these factors in the gastric mucosa.

Isoperistaltic gastrojejunostomy was carried out in 47 male Wistar rats and compared with 67 rats with gastrotomy alone. The animals were killed at eight weekly intervals. Gastric mucosal samples adjacent to the anastomosis or gastrostomy were excised and ODC activity and polyamine concentrations were estimated. The results show that ODC activity is significantly increased by 36% in gastrojejunostomy rats compared with gastrotomy rats (p<0.05 Mann Whitney). This is accompanied by an increase in putrescine concentration of 44% (p<0.05). No difference was found in spermidine concentrations and spermine was lower in gastrojejunostomy animals. Ornithine decarboxylase activity was always higher at each eight weekly interval in gastrojejunostomy rats with two peaks of activity at 24 and 48 weeks. These coincided with significant rises in putrescine concentration. The results suggest that duodenogastric reflux causes an increase in gastric mucosal proliferation adjacent to surgical anastomoses, and indicate a possible mechanism for carcinogenesis.

CA 72-4 in comparison with CA 19-9 and CEA

S DOMSCHKE, G HEPNER, W DOMSCHKE (Department of Medicine, University of D-8520 Erlangen, FR Germany) Immuno-histochemically CA 72-4 binds to gastric cancer (Int J Cancer 1986; 38: 643). We examined the diagnostic accuracy of CA 72-4 as a serum tumour-associated marker.

In 673 patients with benign (n=410), malignant (n=199), and without (n=64) gastrointestinal diseases, serum concentrations of CA 72-4, CA 19-9, and CEA were determined by CIS-RIAs.

64 controls, a cut off limit of ≥6.7 U/ml was established for CA 72-4. The specificity of CA 72-4 was hardly reduced by benign diseases like liver cirrhosis, cholestasis or pancreatitis (99%) in contrast with that of CA 19-9 (86%) and CEA (90%). Oesophageal carcinomas (n=24) were barely
25%, by CA 72-4 in 70%.

In the treatment of diffuse oesophageal spasm (DOS) and nutcracker oesophagus may produce disabling symptoms of chest pain and dysphagia. The response to medical treatment is variable. This work investigates the efficacy of balloon dilatation and attempts to correlate success with the presence or absence of gastroesophageal reflux (GOR). Using Castell’s criteria, the diagnosis of DOS and nutcracker oesophagus was made in 11-3% of 600 patients investigated. All patients underwent manometry (Gaeltec system) and 24-hour pH monitoring (Lectromed). Twenty five per cent of this group (17 patients) failed to respond to nifedipine and/or H₂ antagonists and underwent dilatation with a Keymed balloon dilator. Complete remission of symptoms was seen in 10 patients (60%) – 20% of these had GOR. The remaining seven had a poor response though without deterioration or complication – 83% had GOR. Mean follow up is 2½ years (four months–4 years). The presence of GOR correlates with a high incidence of poor response (p<0-02<p<0-05).

We suggest that balloon dilatation has its place in the treatment of DOS and, in the absence of GOR, has a 89% success rate.

Effect of longterm treatment with omeprazole on serum pepsinogens in reflux oesophagitis

J B M J JANSEN, E C KLINKENBERG-KNOL, I BIEMOND, H P M FESTEN, G F NELIS, P SNEL, S G M MEUWISSEN, C B H W LAMERS (Department of Gastroenterology, University Hospital, Leiden and Amsterdam and Groot Ziekenhuis Den Bosch, Sophia Hospital Zwolle, Slotervaart Hospital, Amsterdam, The Netherlands) Short term administration of omeprazole (OME) to healthy volunteers has been shown to increase both serum pepsinogen (PG) A and serum gastrin levels. Studies on the effect of longterm OME on serum PG are not available and studies on the effect of longterm OME on serum gastrin are scarce. We therefore studied serum PGA, PGC, and gastrin concentrations in 10 patients (four women, six men; age 67 (2) yrs, mean (SE)) with severe reflux oesophagitis during 18 months maintenance treatment with 20 mg OME daily. Before the start of this maintenance treatment, the reflux oesophagitis was initially healed with 40 mg OME daily for four to 12 weeks. Fasting serum PGA, PGC, and gastrin concentrations were determined by sensitive and specific radioimmunoassays before and at 3, 6, 9, 12, 15, and 18 months of maintenance treatment with 20 mg OME daily.

Serum PGA significantly (p<0-01) increased from 42 (6) to 104 (13), 94 (14), 94 (14), 100 (18), 95 (19), and 106 (21) μg/l, while serum PGC increased (p<0-01) from 19 (4) to 41 (6), 39 (7), 38 (6), 40 (4), 38 (6), and 42-8 μg/l at 3, 6, 9, 12, 15, and 18 months, respectively. Serum gastrin significantly (p<0-01) rose from 69 (13) to 198 (37), 164 (26), 271 (49), 236 (45), 265 (41), and 250 (37) ng/l, respectively.

Fasting serum PGA and PGC concentrations increased about twice in the first three months of maintenance treatment with 20 mg OME daily, while fasting serum gastrin levels increased about four-fold. When 20 mg OME treatment was continued for 18 months there were no further rises in fasting serum PGA and PGC, whereas the slight further increases in serum gastrin concentrations did not reach statistical significance. This study suggests that the serum gastrin and PGA and PGC response after three months of OME treatment is indicative of the increases to be anticipated during longterm OME therapy.

Is there a place for balloon dilatation in the treatment of diffuse oesophageal spasm and related disorders?

The British Society of Gastroenterology

M MCCULLAGH, J C LINSSELL, A ANGIANSAH, W J OWEN (Department of Surgery, Guy’s Hospital, London) Diffuse oesophageal spasm (DOS) and nutcracker oesophagus may produce disabling symptoms of chest pain and dysphagia. The response to medical treatment is variable. This work investigates the efficacy of balloon dilatation and attempts to correlate success with the presence or absence of gastroesophageal reflux (GOR). Using Castell’s criteria, the diagnosis of DOS and nutcracker oesophagus was made in 11-3% of 600 patients investigated. All patients underwent manometry (Gaeltec system) and 24-hour pH monitoring (Lectromed). Twenty five per cent of this group (17 patients) failed to respond to nifedipine and/or H₂ antagonists and underwent dilatation with a Keymed balloon dilator. Complete remission of symptoms was seen in 10 patients (60%) – 20% of these had GOR. The remaining seven had a poor response though without deterioration or complication – 83% had GOR. Mean follow up is 2½ years (four months–4 years). The presence of GOR correlates with a high incidence of poor response (p<0-02<p<0-05).

We suggest that balloon dilatation has its place in the treatment of DOS and, in the absence of GOR, has a 89% success rate.

Simultaneous monitoring of gastroesophageal reflux and respiratory function in near miss cot death infants

C W SHORE, M SAMUELS, D BENTLEY, B K SANDHU, D SOUTHAL, M J BRUETON (Department of Child Health, Westminster Children’s Hospital, London) Some studies of infants who have suffered an acute life threatening event, near miss cot death (NMCD), have shown abnormalities in respiratory function; others have showed gastroesophageal reflux (GOR). Apnoea and bradycardia may be associated with GOR in other circumstances, presumably because gastric contents stimulate chemoreceptors in the larynx or upper oesophagus, or because aspiration occurs. In order to study a possible correlation in NMCD, simultaneous 24 hour oesophageal pH and respiratory monitoring including measurement of arterial oxygen saturation, and breathing movements were carried out in 16 children of mean age 12 weeks who had presented with NMCD. Seven of these patients had significant GOR. The mean number of reflux episodes was 58 (20) (normal 27 (8-2)), the mean number of refluxes lasting more than 5 minutes was 10 (3-9) (normal 6 (2)), the mean percentage detected by CEA (<5 ng/ml; 17%) or CA 19-9 (>37 U/ml; 8%) and not by CA 72-4 (0%). Gastric cancer (n=27) was indicated by CA 72-4 in 56% of cases, by CEA in only 25%, by CA 19-9 in 52%, and by combined measurement of CA 72-4 and CA 19-9 in 70%. In pancreatic and biliary tract carcinomas (n=68 and n=21, resp) CA 19-9 (82% and 90% sensitivity, resp) was superior to CEA (47% and 62%, resp) and CA 72-4 (22% and 29%, resp). In colonic carcinomas (n=53) CEA was positive in 58%, CA 19-9 in 36% and CA 72-4 in 32%. For hepatocellular cancer the data were: 67% each for CEA and CA 19-9, 0% for CA 72-4.

A high specificity makes raised CA 72-4 concentrations relevant. CA 72-4 indicates gastric cancer best, especially in combination with CA 19-9, and may supplement usual methods of tumour search and monitoring.

Ranitidine therapy in peptic oesophagitis: doubling the dose or duration of treatment?

F PACE, G BIANCHI PORRO, O SANGALETTI (Gastrointestinal Unit, I Sacco Hospital, Milano, Italy) Several trials of the effect of conventional doses of H₂-blockers on peptic oesophagitis have shown that the healing rates after six to 12 weeks are quite disappointing when compared, for example, with those observed with the same therapy in patients with duodenal ulcer.

We have, therefore, decided to carry out a clinical single centre, double blind trial investigating the effect of doubling: (a) the study period from the usual 12 to 24 weeks, and (b) the dose of the agent, namely ranitidine (R) from 150 to 300 mg bid. Seventy six patients with oesophagitis, grade II to IV according to Savary and Miller, have been studied, 37 of whom treated with R 150 mg bid and 39 with R 300 bid. Three patients dropped out in the course of the study period.

After 12 weeks of treatment with R 300 mg; 21/37 patients had healed compared to 11/37 treated with R 600 (p<0-05); after 24 weeks the healing rate was 28/36 and 32/36 (p<0-05), respectively. As to the symptomatic response, figures were 25/37 v 22/37 (p<0-05) after 12 weeks, and 32/36 v 29/36 (p<0-05) after 24 weeks.

Protracting the full dose therapy with ranitidine from 12 to 24 weeks allows complete additional healing of 23-6% of patients; in the treatment of patients with peptic oesophagitis, no advantages emerge when the dose of ranitidine is doubled.
time the pH was >4 was 22-6 (20-5) (normal 5 (1-6)). Two of the 16 children had periods of periodic breathing, in one patient this was associated with oxygen desaturation. One of these two children also had GOR but simultaneous respiratory changes were not apparent. These observations confirm that GOR occurs frequently in children with NMCD. There appears to be no real time association between GOR and respiratory changes.

Electromyography of the oesophagus with intraluminal ring electrodes

M I MARPLES, L J HANKIN, J BANCEWICZ (Department of Surgery, Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) We have developed a simple catheter which allows oesophageal electromyography during conventional manometric studies. Bipolar ring electrodes were applied to multilumen manometry catheters in seven different configurations and assessed during 202 manometric studies in patients and normal volunteers.

The optimum design of catheter is an assembly 0-4 cm diameter with two sets of bipolar ring electrodes 0-8 cm apart at 10 cm intervals. A minimum of 8 cm catheter below the distal electrode minimised artifact. Thirty consecutive recordings made with the final catheter gave high quality recordings in 27 (90%).

The striated portion of the oesophagus showed typical high frequency skeletal muscle spike activity. In the smooth muscle oesophagus two separate spike bursts, one preceding the first upstroke of the pressure wave, the second preceding peristaltic contraction, were consistently seen in normal subjects and most patients. The latter was also seen during secondary peristalsis. In 10 normal volunteers atropine 0.01 mg/kg abolished electrical and pressure activity in response to swallows in the distal oesophagus. No spike activity was recorded distally in seven patients with achalasia, despite good electrical contact.

Oesophageal electromyography is now practical without undue discomfort to patients.

Hyperventilation (HV) increases the amplitude of oesophageal contractions in healthy volunteers: a controlled study

R M VALORI, E COLE, M LEMON, R HOWARD, R COCKEL (Department of Gastroenterology, Selly Oak Hospital and Department of Biochemistry, Queen Elizabeth Hospital, Birmingham) This study examined the effects of hyperventilation (HV) on the motor function of the oesophagus in healthy volunteers, as HV and abnormalities of oesophageal motility have been independently implicated in the genesis of atypical chest pain. Six subjects underwent a manometric study of LOS and oesophageal body function (duration, amplitude, propagation velocity and spontaneous activity) on two separate days in random order. On one day measurements were made before, during, and after enforced HV to below 3 Kpa (end-tidal pCO2). The protocol was repeated another day without HV. Venous blood was taken for pH, electrolytes, ionised calcium and inorganic phosphate during each period.

The amplitude of contractions (3, 8, and 13 cm above LOS) did not change during HV but it rose during the period after HV in all three channels in five of six subjects. The rise in the distal channel amplitude above baseline (30-7 (8-4) cm H2O; ± (SE) was significantly greater than on the control day (11-3 (5-0) cm H2O; p<0.05). No other manometric changes were observed. The only biochemical abnormality that persisted after HV was a fall in inorganic phosphate (8-2%; p<0.05). Thus during the recovery phase after HV oesophageal contractility is enhanced. The smooth muscle portion of the oesophagus appears most sensitive and the response is associated with a fall in inorganic phosphate. These findings support a causal link between HV, oesophageal dysmotility, and atypical chest pain.

Do oesophageal motor abnormalities occur in patients with proven coronary artery disease?

J S DE CAESTEKER, A PRYDE, R C HEADING (Department of Medicine, Royal Infirmary, Edinburgh) Oesophageal motor abnormalities are common in patients with angina and normal coronary arteries. Oesophageal function in 'symptom controls' is not well documented. We studied 10 patients with symptomatic coronary stenosis (shown at angiography) with oesophageal manometry (Ammeter system) and 24 hour ambulatory pH monitoring. These were from a group of 46 undergoing coronary angiography under the care of one cardiologist. The remaining 36 refused or were unable to participate. The 10 studied were not significantly different from the remainder with respect to age, sex, incidence, and frequency of heartburn, occurrence of angina at rest or previous myocardial infarction (p>0.05; χ² test with Yates' correction). Abnormal manometry was found in three patients: classical diffuse spasm (one), nutcracker oesophagus (one) – mean peristaltic amplitude >180 mmHg and duration >7 sec – and prolonged duration peristalsis (one). Abnormal acid reflux was detected in two, both with normal manometry. These were the only two with frequent (>×one/month) oesophageal symptoms. Major oesophageal abnormalities occur with surprising frequency, although our small sample size may not reflect true prevalence. These data emphasise that oesophageal abnormalities should only be regarded as significant if symptoms occur concurrently. Prolonged ambulatory motility and pH recordings may prove helpful in this respect.

Oesophageal peristaltic reflex – its application in the assessment of motility disorders

T G'HANRAHAN, J BANCEWICZ, D G THOMPSON, M MARPLES, D WILLIAMS (University Department of Medicine and Surgery, Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) The nature of many oesophageal motility disorders is poorly understood. We have studied the peristaltic reflex as an adjunct to conventional oesophageal investigation.

Eight asymptomatic volunteers, 11 patients with dysphagia and 27 with non-cardiac chest pain were studied during oesophageal manometry. Gastro-oesophageal reflux was excluded by 24-h pH recording. Eleven (28-9%) patients, but none of the volunteers, had a non-specific motility disorder.

Graded inflations of a balloon (range 1–30 ml) placed 100 cm above the lower oesophageal sphincter were performed. All but one of the volunteers showed a typical peristaltic reflex with increased motility proximal to the balloon and distal inhibition. One volunteer had no change in motility. Eight of 11 patients with dysphagia (72.7%) had an abnormal response with either no motility change (three) or a spastic reaction (five). Twenty-two of 27 with chest pain (81·5%) experienced their usual pain during inflation and 17 (63%) had an abnormal motor response (no change three; spasm 14). There was, however, no correlation between chest pain and motility disturbance.

The oesophageal peristaltic reflex may be helpful in understanding the basis of dysphagia. The nature of chest pain during balloon distension requires further elucidation.
Oesophageal manometry during eating in the investigation of patients with dysphagia

P J HOWARD, A PRYDE, R C HEADING (Department of Medicine, Royal Infirmary, Edinburgh) Although patients with dysphagia are often referred for oesophageal manometry, the response to eating is rarely examined. We studied oesophageal motility and symptoms in response to eating bread in 20 patients with gastro-oesophageal reflux and 10 with normal oesophageal motility and ambulatory pH. While no patient experienced symptoms with water swallows, one control patient experienced heartburn, without any change in motility and nine reflux patients experienced dysphagia+pain whilst eating. Oesophageal 'spasm' was evoked by eating in one of these patients. In the other eight, dysphagia was associated with aperistalsis. Comparing asymptomatic and symptomatic periods, there was a slight increase in mean swallow frequency from 7·5 to 9·0 per minute (NS; n=10). While aperistaltic swallows increased from 4·5 (0·96) (SE) to 6·2 (1·3) per minute (p<0·01; n=10) the ratio of aperistaltic to peristaltic increases from 1·5:1 to 3·5:1. Aperistalsis during symptomatic periods was due mainly to non-conducted, rather than synchronous contractions. Increased non-peristaltic swallows in these patients may be a result of short swallow intervals ('deglutitive inhibition'). Manometry while eating bread can show this symptomatic abnormality which is not revealed by conventional pressure studies.

Why measure lower oesophageal sphincter relaxation in patients with dysphagia?

P J HOWARD, L BENINI, A PRYDE, R C HEADING (Department of Medicine, Royal Infirmary, Edinburgh) Assessment of lower sphincter relaxation is considered a routine part of clinical manometry. Criteria of normal relaxation are not agreed, however, and the diagnostic significance of abnormality has not been critically assessed. We studied 97 patients referred for oesophageal function tests. Relaxation of the lower oesophageal sphincter in response to dry swallows was measured in a single channel at the point of maximum tonic pressure during a station pull through using an Arndorfer catheter. Complete relaxation, defined as a fall in sphincter pressure to intragastric pressure during both swallows, occurred in 29 of the 43 patients with dysphagia (67%) and 26 of the 44 patients without dysphagia (48%) (x²=0·018, p=0·88). Similar results were obtained when sphincter relaxation was assessed in three channels. One of the seven achalasic patients studied after pneumatic dilatation appeared to have complete sphincteric relaxation.

Assessment of lower sphincteric relaxation rarely provides useful diagnostic information except in patients with total aperistalsis. Routine studies of sphincteric relaxation should be abandoned.

Does oesophageal motor activity improve after surgical treatment of gastro-oesophageal reflux (GOR)?

G GONIS, A ANGGIANSAH, T ROKKAS, M MCCULLAGH, W J OWEN (Department of Surgery, Guy's Hospital, London) It has been reported that patients with GOR have impaired oesophageal motility but it remains unclear as to whether this is primary or secondary to GOR. The present study was initiated to investigate oesophageal motility in 18 patients suffering from GOR, pre- and post-Nissen fundoplication. Oesophageal manometry was performed with a fully computerised system (Gaeltec). Mean amplitude (mmHg) and duration (sec) of peristaltic contraction were elicited by 10 consecutive wet swallows at 5 and 10 cm above lower oesophageal sphincter (LOS). Additionally peristaltic velocity (cm/sec) and LOS pressure (mmHg) were measured. After fundoplication all patients were symptomatically relieved and 24 h ambulatory pH monitoring showed satisfactory control of reflux. Pre-operative values of LOS pressure, amplitude, duration and velocity of peristaltic waves were 10·5 (1·3), 44·38 (4·19), 3·09 (0·18), 3·46 (0·16) respectively. After the operation the respective values were 15 (2), 76·42 (10·85), 3·83 (0·22), 3·26 (0·13). The comparison of these results pre- and post-surgery showed that there was significant increase in LOS pressure (p<0·05) and in amplitude (p=0·001) and duration (p=0·009) of peristaltic activity of lower 10 cm oesophagus. Velocity was not affected. The increase in amplitude and duration of peristalsis shows improved oesophageal motility and suggests that impaired motility in patients with GOR is secondary to increased acid exposure.

An objective comparison of the Angelchik anti-reflux prosthesis and Nissen fundoplication

D F EVANS, C S ROBERTSON, D L MORRIS (Department of Surgery, University Hospital, Nottingham) Use of the Angelchik prosthesis (ACP) for gastro-oesophageal reflux (GOR) remains controversial and only one randomised study with pH monitoring has been reported and no objective assessment of swallowing was made. Seventeen patients with GOR were randomised to either Nissen fundoplication (NFP) n=9 or ACP n=8. Oesophagoscopy, oesophageal manometry, pH monitoring and marshmallow barium swallow (MMBS) were performed pre- and six months post-operatively. Median follow up in months (range) was 16 ACP (3–40), 15 NFP (6–30). Two ACP were removed at seven and 40 months for severe dysphagia and one NFP was revised at six months for persistent GOR.

Control of GOR was significantly more effective (p<0·01) after ACP than NFP (ACP preop median (range) 0·5 mins (0·3-1·5), postop eight mins (1·0), p<0·000, NFP preop 0·3 mins (0·3-1·0), postop one min (0·3-1·0), p=NS). In this series ACP was better than NFP in controlling GOR but the oesophageal transit of solids was slowed after ACP.

The Angelchik prosthesis: five years on

M DEAKIN, D MAYER, J G TEMPLE (Queen Elizabeth Hospital, Birmingham) No single operation has provided the answer for gastro-oesophageal reflux. Insertion of the Angelchik prosthesis was suggested to be an easy operation that should lead to consistent results. Although the prosthesis has been in use for 15 years there are no well documented longer term follow up studies.

Twenty two Angelchik prostheses were implanted between 1981–1982 as primary treatment for gastro-oesophageal reflux. The median age of the patients was 59 years (31–76). The results were assessed by Visick grading, manometry and oesophageal pH recording.

The lower oesophageal sphincter pressure increased from a median of 1 (0–9) to 7 (0–20) mmHg and the 24 h oesophageal pH was <4 decreased from 27 (5–94)% to 1·7 (0–40)% postoperatively (p<0·001 for both variables). There were two postoperative deaths caused by medical problems. At two years 80% of patients were Visick 1 and 20% Visick 4. Failures were the result of complications associated.
with the prosthesis, namely collar disruption, two and angulation of the prosthesis causing dysphagia, two. All four underwent reoperation. At five years three patients have died from unrelated causes. Of the remainder, 11 (65%) remain Visick 1, but three patients (18%) are Visick 2 due to occasional dysphagia.

The Angelchik prosthesis successfully controls reflux but failures are specifically associated with the prosthesis. Reoperation may be difficult. The mode of action of the prosthesis deserves further investigation but in its present form we would not recommend its use outside controlled clinical trials.

Combined pH monitoring for assessment of gastro-oesophageal reflux

C S Ball, T L Norris, L R Jenkinson, A Watson (Royal Lancaster Infirmary) Oesophageal pH monitoring is well established in the diagnosis of reflux disease. The test depends on an acid gastric pH environment, but generally this parameter is not monitored.

One hundred patients, with symptoms of reflux, were studied using gastric and oesophageal probes. pH profiles were analysed according to the percentage of time spent at each hour. pH interval and these values compared to a group of 15 control subjects. Seventy four had abnormal oesophageal acid exposure. Of the remaining 26, six had no endoscopic oesophagitis and normal gastric profile, 10 had low gastric acidity (four vagotomy or gastrectomy, two achlorhydria, four hypersecretion or bile reflux) to explain the negative test. The other 10 had mild oesophagitis but both pH profiles were normal. The incidence of gastric acid hypersecretion was 21%.

In this study, combined monitoring explained the presence of endoscopic oesophagitis in 50% of patients with normal oesophageal acid exposure. Of those with abnormal exposure, 21 (28%) had gastric acid hypersecretion. The high incidence of abnormal gastric pH profiles in reflux disease has important implications in the choice of both medical and surgical anti-reflux therapy.

What characteristics are acceptable in volunteers to establish normal ranges for 24 hour oesophageal pH monitoring?

J S de Caestecker, J A Wilson, R C Heading (Department of Medicine, Royal Infirmary and Department of Otolaryngology, City Hospital, Edinburgh) Thirty four volunteers were studied by ambulatory 24 hour pH monitoring. There were no restrictions of diet or activity, but each subject kept a diary record. Reflux was defined as a fall in pH to below 4. Twenty seven were men, and the age range was 20–66 years (median 31); 10 were smokers (three to 30 cigarettes/day, median 10). Occasional heartburn (<1 x 1/month) was reported by nine. There was no significant difference between % time pH<4, reflux frequency or mean acid clearance for upright, recumbent or total periods when either smokers or those with occasional heartburn were compared with the 15 asymptomatic non-smokers (Wilcoxon's rank-sum test) except that those with occasional heartburn had less recurrent reflux episodes (range – 0–5, median 0–0–13, median 3; p<0.05). No correlations were found between number of cigarettes smoked and number of reflux episodes for any period (Spearman rank correlation test). Duration of pH<4 did not vary with sex. Increasing age had no correlation with any reflux parameter for any study period (Spearman rank correlation). Most oesophageal laboratories will wish to establish 'normal' ranges for reflux parameters. These results show that normal values may be established independently of age (in the range 20 to 66), sex, smoking, and occasional heartburn.

Oesophageal cancer: a population based study of survival after treatment

S E Oliver, C S Robertson, R F A Logan (Departments of Community Medicine and Epidemiology and of Surgery, University Hospital, Nottingham) The place of radiotherapy in the management of squamous cell oesophageal cancer remains controversial; in many centres patients unsuitable for surgery are given radiotherapy and/or endoscopic intubation. We have carried out a population based study of the survival of oesophageal cancer patients presenting from the Nottingham area in the four years 1982–85. Of 131 patients with squamous cell oesophageal cancer, surgical resection was attempted in 43. Of the remaining 88, 31 (17 men) had endoscopic intubation alone, 29 (17 men) had radical radiotherapy alone (n=6) or combined with endoscopic intubation (n=23) and 28 had other treatment combinations, including surgical intubation and palliative radiotherapy.

Patients having intubation alone had a mean age of 75 years and were significantly older (p<0.025) with metastasis more often evident (32%) than patients having radiotherapy (mean age 69 years) of whom 14% had metastasis evident. Despite these favourable biases the Kaplan-Meier estimate of survival of the radiotherapy group (median survival 182 days, 95% confidence limit [cl] 133–253) was not significantly greater than that of the intubation alone group (median survival 99 days cl 73–155). The radiotherapy patients spent a median of 46 days in hospital compared with 24 days in the intubation alone patients. We conclude that in patients with squamous cell oesophageal cancer, unsuitable for surgery, the...
survival advantage associated with giving radiotherapy in addition to intubation is small and may be insufficient to compensate for the extra morbidity. A controlled trial of radiotherapy in such patients is now needed.

Measurement of intragastric pH: to aspirate or not to aspirate?

M J ROGERS, J H M HOLMFIELD, J N PRIMROSE, T GLEDHILL, D JOHNSTON (University Department of Surgery, The General Infirmary, Leeds) Intragastric pH (IGpH) measurements made using a non-aspiring pH sensor (NAS) correlate closely with those made by nasogastric (NG) aspiration if the NAS is fixed to the tip of the NG tube. It is thus assumed that IGpH recordings made using a NAS are also similar to aspiration studies of IGpH. When comparing IGpH recordings made by NG aspiration and by NAS, however, it is preferable not to attach the NAS to the NG tube to allow normal movement of each to occur. As gastric pH is not uniform, however, if aspiration and NAS techniques are compared, both must aim to study the same region of the stomach.

The aim of this study was to compare IGpH recorded by means of a telemetry capsule with that recorded by simultaneous NG aspiration.

Twelve healthy subjects underwent four hours IGpH monitoring with a telemetry capsule whilst having a 5 ml sample of gastric juice aspirated every 15 minutes through a NG tube. Median pH and four hour [H+] (area under the [H+] versus time curve) was calculated for each recording with each method of pH measurement.

Median (quartile) pH was 2.4 (1.8-2.5) when recorded by aspiration and 2.0 (1.6-2.1) when recorded by telemetry (0.1>p>0.05). Median (quartile) four hour [H+] was 1.2 (0.8-2.2) Mol/min when recorded by aspiration, and 3.2 (2.2-5.6) Mol/min when recorded by telemetry (0.05>p>0.025).

Thus IGpH recordings made by telemetry are different from those of aspiration and direct comparison of results from the two techniques is inappropriate.

Antral size, acid secretion and the integrated gastrin response (IGR) to food

M J ROGERS, M LAGOPoulos, M F DIXON, J PRIMROSE, T GLEDHILL, D JOHNSTON (University Departments of Surgery, Anatomy, and Pathology, The General Infirmary, Leeds)

Food stimulated acid secretion is mediated by antral gastrin release. The aim of this study was to measure the G-cell bearing area of the stomach in patients with duodenal ulcer (DU) and to relate this to acid output and the IGR to food.

Twenty nine patients referred for operation for DU had basal (BAO) and peak acid output (PAOSF and PAOPG) and IGR to a 250 g steak meal measured.

Each patient underwent highly selective vagotomy with Grassi test and biopsies were taken 2, 4, 6, and 8 cm from the pylorus along each curvature. After tissue processing, G-cells were stained immunohistochemically and their density in each biopsy assessed by an independent observer (normal density 2, absent 0, scanty 1).

Normal density G-cells extended 4 cm along both curvatures in all patients but could be found at 6 cm or more in 13 of 29 patients (Large Gastric Antrum, LGA).

Median (quartile) IGR was 5.0 ng/min (3.4-16.7) in patients with LGA and 3.7 (0.3-11.6) in those without (NS), but of five patients with a IGR greater than 15.0 ng/min four had LGA and one did not (p<0.05).

Median BAO was 2.9 mmol/h in patients with LGA and 3.6 mmol/h in patients without (NS) and PAOSF and PAOPG did not differ significantly between patients with and without LGA (median 14.8 v 16.3, 56.8 v 46.9 mmol/h respectively).

Patients with LGA have a greater IGR than patients without LGA, but their BAO and acid output to PG and SF does not differ. Intragastric titration could be used to determine if these groups differ in their acid secretory response to food.

Accurate positioning of pH electrodes

C S ROBERTSON, S LEDINGHAM, D F EVANS (Department of Surgery, University Hospital, Nottingham) Oesophageal pH probes are placed transanally often using measurements taken at gastroscopy. The difference in measurement between the oral and nasal route is not known, however, and may lead to errors in probe placement, resulting in the underestimation of acid reflux. To determine the differences between nasal and oral measurement of the lower oesophageal sphincter (LOS) 20 healthy male volunteers aged 21-36 years underwent oesophageal manometry using a triple lumen perfused catheter by the station pull through technique. Four studies were performed, two through the nose and two through the mouth.

The mean distance between the nares and upper extent of the LOS was 44.7 cm (2.0) (mean SD) in both studies. The mean distance between the incisor teeth and LOS was 42.3 cm (1.6) and 4.25 cm (1.5) for each oral manometry. The mean difference between the two routes was 2.4 cm (1.7) (p<0.001).

The difference between nasal and oral measurements will therefore lead to errors of up to 6 cm in probe placement and a correction for this difference must be made if endoscopic measurements are used.

Oesophagitis - a five year review

D L STOKER, J G WILLIAMS, R G LEECHER, D G COLIN-JONES (Royal Naval Hospital, Haslar, Gosport, Hants) This study examines the incidence of a number of diseases seen in the endoscopic practice of two adjacent district general hospitals over the past five years, with special reference to oesophagitis. Over this period, a total of 12652 upper GI endoscopies were performed, and recorded in detail on computer using the Micromed data storage system. The results of this survey are based on 8445 initial diagnostic endoscopies, representing 67% of the total number, when repeat examinations are excluded. There were 1928 cases of macroscopic oesophagitis of all grades diagnosed (22.8% of the new patient total). This compared with 1573 cases of gastritis (18.6%), 777 duodenal ulcers (9.2%), and 504 gastric ulcers excluding neoplasms (6%). There were also 254 benign oesophageal strictures (3%), and 247 cases of benign oesophageal ulceration (2.9%). In the oesophagitis group, more patients presented in the 60-70 age range than in any other. There was an increasing incidence of oesophagitis with age, starting at 14.7% in the second decade, and peaking in the eighth decade with the diagnosis being made in 26.7% of cases. These data show that oesophagitis is the commonest disease of the upper gastrointestinal tract seen in patients referred for endoscopy. It also suggests that although there is an increasing incidence of the disease with age, it is a common endoscopic diagnosis in all age groups.

Comparison of the acid/alkaline junction with the manometrically determined lower oesophageal sphincter (LOS)

D L STOKER, J G WILLIAMS, D G COLIN-JONES (Royal Naval Hospital, Haslar, Gosport, Hants) pH Probes should be placed in a reproducible anatomical position in the
oesophagus in order to make valid comparisons between patients. The acid/alkaline junction (AAJ) is often used to determine the position of the LOS when placing oesophageal pH probes if manometry is not available. We have examined 125 subjects, comparing the manometrically determined position of the LOS with the AAJ. A standard manometric technique was used to map the LOS. The mean (1 SD) length of the LOS was 3.5 cm (1-3) (range 1-7 cm). The AAJ was determined by twice withdrawing a pH probe from the stomach. In most cases there was a rapid change from pH 1-2 to pH 6-7 within 1 cm. The AAJ occurred within the sphincter zone in 72 subjects (57-6%). In 34 of these subjects the transition was at the lower end of the sphincter. In 53 cases (42-4%) the AAJ fell outside the manometrically determined LOS by 1 cm or more. Forty four (34%) cases were below the LOS (range 1-13 cm, mean 3-4 (2.3)), while eight were above (range 1-6 cm, mean 2-8 (1-8)).

The variability of the AAJ in relation to the LOS makes it an unreliable technique for accurately placing pH probes. The probable reasons for this are pH changes in the fundic gas bubble, and the occurrence of acid reflux during withdrawal of the pH probe through the sphincter zone.

Peptic activity in the refluxate of patients with uncomplicated gastro-oesophageal reflux (GOR)

D C GOTLEY, D BALL, M J COOPER (Department of Surgery and Biochemistry, Bristol Royal Infirmary, Bristol) Reflux of gastric contents into the oesophagus forms the basis of the pathophysiology of oesophagitis. Whilst acid reflux has been extensively investigated, oesophageal peptic activity has received little attention. We studied 52 patients with symptomatic GOR and abnormal acid exposure, divided into four groups: those with normal oesophageal pH, erosive oesophagitis (O), stricture (S), and Barrett’s oesophagus (B). Each patient underwent 24 hour ambulatory pH monitoring, followed by a 16 hour continuous oesophageal aspiration study with a size 14 Salem sump tube positioned 5 cm above the manometric sphincter. Specimens were collected in two-hourly aliquots (giving eight specimens/patient) and total peptic activity was determined by a haemoglobin substrate assay. Groups O, S, and B had greater acid exposure than N (p<0.001), but could not be separated from each other on the basis of pH monitoring. S and B groups, however, had significantly higher peptic concentrations than O or N (p<0.001).

Complicated oesophagitis patients have significantly higher peptic concentrations detected in the oesophagus than patients with uncomplicated oesophagitis.

Do bile acids (BA) modify the cytopathic effects of pepsin (P) on oesophageal mucosal cells?

D C GOTLEY, B FLARKS, M J COOPER (Department of Surgery and Pathology, Bristol Royal Infirmary, Bristol) The role of bile acids in reflux oesophagitis is controversial. Bile acids have been shown to inhibit peptic activity in vitro suggesting a protective role. On the other hand, bile acids and pepsin have been shown to have different sites of action on oesophageal mucosal cells, suggesting an additive effect. We have studied patients with gastro-oesophageal reflux. In a single blinded pathologist assessed each specimen at four different levels for six different parameters using a 0-4 scoring system. Minimal structural damage occurred with NS alone and at pH 2, whereas P (p<0.002) caused significant cell disruption, cytotoxicity being maximal at five min. Addition of BA to P caused no significant alteration in degree or pattern of cytotoxicity compared to that seen with P alone. ‘Physiological’ concentrations of BA do not modify the cytological damage caused by pepsin on normal oesophageal epithelium.

Prolonged intragastric pH monitoring in the diagnosis of duodenogastric bile reflux (DGR)

D C GOTLEY, A P MORGAN, M J COOPER (Department of Surgery, Bristol Royal Infirmary, Bristol) The phenomenon of ‘gastric alkaline shift’ (GAS) seen with prolonged intragastric pH monitoring has been used as a measure of DGR and gastric bile acid contamination in patients with reflux oesophagitis and biliary gastritis. This technique, however, has not been validated.

In order to determine if GAS reflects the presence of significant (>110 μmol/l) gastric conjugated bile acid (CBA) contamination, nine patients underwent simultaneous, continuous intragastric pH monitoring and gastric aspiration using a combined size 14 Salem sump tube and pH electrode. Each patient was studied for 16 hours, including a postprandial (PP) and nocturnal period, and two hourly aliquots were analysed for pH and CBA by high performance liquid chromatography (HPLC). pH traces were examined for number and duration of pH rises >3, >4, >5, and the average pH for each two hourly period.

Nine PP periods showed GAS due to buffering by food and were excluded, leaving 69 for analysis. The presence of GAS was significantly associated with intragastric CBAs (p<0.001), however, there was no relationship between magnitude, number and duration of GAS’s and level of CBA. During five periods the pH trace average was >3 pH points above aliquot pH, indicating possible probe embedding in the gastric alkaline mucus layer.

Gastric alkaline shift is a non-quantitative indicator of CBA reflux. In some patients, GAS may be misleading in the diagnosis of duodenogastric bile reflux.

The use of an ambulatory cadmium telluride detector to monitor postprandial reflux of food

N WASHINGTON, H A MOSS, C G WILSON (INTRODUCED BY R C SPILLER) (Department of Physiology and Pharmacology, Medical School, Queen’s Medical Centre, Nottingham) The assessment of gastro-oesophageal reflux by ambulatory monitoring is an established but invasive technique. Gamma scintigraphy has proved unsatisfactory, since it is difficult to provoke a reflux episode during the imaging period.

The use of a small collimated gamma probe has been investigated to detect postprandial reflux of a radiolabelled meal in six healthy female subjects. The probe was supported 5 cm above the cardia coincident with an oesophageal pH probe. Outputs from both detectors were connected to an ambulatory solid state recorder. The test meal consisted of a Spanish omelette labelled with technetium-99m (3 MBq), lemonade, apple pie, ice cream, and coffee (4648 kJ). After consumption of the meal, data were collected for four hours and transferred to a microcomputer for analysis. The reflux of the technetium was quantified and correlated with changes in oesophageal pH.
Reflex of radiolabelled food occurred between 30 and 100 minutes after the meal and was associated with a decrease in oesophageal pH. Acid reflex was not always associated with increase in oesophageal counts, however, suggesting acid does not mix uniformly with the food and is the primary aggressive agent in painful reflux.

An indirect tubeless test of gastric function

C D Johnson, P Harris, C Wastell (Department of Surgery, St Stephen's Hospital, London) Measurement of gastric function requires nasogastric intubation for aspiration of gastric juice. Gastric acid secretion entails a compensatory reduction in urinary acid output (Urao). We investigated the quantitative relationship between these two outputs to establish whether changes in Urao might be useful as a tubeless test of gastric secretion.

Gastric secretion was measured in 11 volunteers and six postvagotomy patients, using pentagastrin 6 µg/kg or shamfeeding (SF) with nasogastric intubation. Urao was measured during the gastric function tests and after a standard meal.

There was a good correlation between total gastric acid output (median 6.4 mmol/h range 0-43.3) and the change in Urao during gastric function tests (n=18, median -2.0 mmol/h, range +0.4 to -7.6; y = -0.82 -0.11x; r=0.79) and after a test meal (n=11, gastric acid median 4.8 mmol/h, range 0-14.2; change in Urao median -0.4 mmol/h, range +0.5 to -1.4; y = -0.11x; r=0.73).

Urao after SF and after a test meal identified the only postvagotomy patient with a recurrent ulcer.

We have demonstrated a linear relationship between measured gastric secretion and changes in urine acidity after a meal. This tubeless test of gastric function may be a useful screening test for the detection of incomplete vagotomy.

Validation of pH dataloggers for pharmacologic studies

D W Burget, S G Chiverton, R H Hunt (McMaster University, Division of Gastroenterology HSC-4W8, 1200 Main Street W, Hamilton, Ontario, Canada) Twenty four hour gastric aspiration studies have recently begun to be superseded by dataloggers which continuously record intragastric pH. Original reports validating dataloggers used point pH correlations in untreated normal subjects. We compared mean responses to nizatidine, ranitidine, and placebo in an actual practical pharmacological study in 15 normal volunteers. The assembly consisted of a nasogastric tube with an Ingold combined glass electrode attached with the tip adjacent to aspiration ports. Aspirates were collected at hourly intervals, and intragastric pH was recorded at 6 second intervals.

Datalogger (D) pH v aspiration (A) pH confirms a highly significant point correlation, but the slope was significantly less than 1. There was also significant correlation between D and A for mean 24-h, morning, afternoon, evening, and night pH, but the correlation was poorer during the day (r=0.51) than at night (r=0.83).

Differences between methods (D-A) during the day ranged from 0.4 to 1.4 pH units, but at night were -0.2 to +0.2 pH units. Irrespective of the technique used, however, conclusions reached on drug efficacy were similar.

These results show that datalogging devices are suitable for the evaluation of drug effect on 24 hour gastric acidity, but that the results, especially during the daytime, may substantially differ from those obtained by aspiration, and cannot therefore be directly compared.

24-hour intra-gastric pH profile in healed and in active duodenal ulcer disease

B K Kapur, K D Bardhan (District General Hospital, Rotherham, South Yorkshire) Little is known of changes in the intragastric pH profile in duodenal ulcer (DU) when active and when healed. We therefore measured the 24-hour intragastric pH profile under standard conditions and off all drugs using a validated ambulatory monitoring system in 22 healthy volunteers (HV), in 55 patients with healed DU (H-DU) and in 30 patients with active DU (A-DU). Arcsine transformation was used to normalise the data and the mean percentage (and 95% confidence limits) of day time and night time spent at pH <2 and pH >4 were calculated.

The only significant difference (p<0.01) (analysis of variance) was observed at night (2400-08.50 h). The time spent at pH <2 was in; HV 46% (30-63), H-DU 59% (49-69), A-DU 80% (71-88); and at pH >4 was, respectively, 35% (20-53), 23% (15-32), and 8% (4-13). During the day (08.50-2400 h) the time at pH <2 was in; HV 61% (46-75), H-DU 63% (55-70), A-DU 66% (53-77); and at pH >4 was, respectively, 11% (4-21), 14% (10-18), and 18% (8-30).

Thus the 24-hour pH profile in patients with healed DU is normal whereas in active DU the gastroduodenal mucosa is exposed to a greater acid concentration only at night. This abnormality emphasises the need to selectively suppress nocturnal acidity to heal DU.

Investigation of gastrointestinal motility with echo planar magnetic resonance imaging (EPI)

D F Evans, M K Stehling, G Lamont, R Coxon, A M Howseman, R J Ordridge, J D Hardcastle, P Mansfield (Departments of Physics and Surgery, Nottingham University, Nottingham) Magnetic resonance imaging (MRI) is not suitable for dynamic studies of the gastrointestinal tract because of long image acquisition times and subsequent image blurring and artefact. The EPI variant MBEST produces images in only 64 msecs allowing rapid sequential quantitation of gut wall movements.

We have evaluated EPI to image gastrointestinal motility in four volunteers. Three fasted subjects were imaged at the transpyloric plane or ligament of Treitz before and after a test meal, after preloading the stomach with 1 l tap water to improve contrast. One subject was similarly imaged after 10 mg metoclopramide im. Movie loops of 40 images/min were produced to identify gastroduodenal peristalsis. Visible peristalsis was seen in the antroduodenal region after the test meal with a frequency of two/min. Food stimulated duodenal peristalsis was seen with a wave velocity of 0.64 cm/sec and a frequency of six/min. Metoclopramide maximally stimulated antroduodenal peristalsis after 20-25 mins with a wave velocity of 9 cm/sec and a frequency of two to three/min.

Echo planar imaging is an exciting new extension to MRI and shows great potential in the non-invasive dynamic imaging of gastrointestinal motility.

Non-invasive assessment of antral motor function by high resolution real-time ultrasound in normal subjects and functional dyspeptic patients

D G Thompson, K Gaits, H Mambraka (Departments of Medicine and Radiology, Hope Hospital, Eccles Old Road, Salford) We used high resolution real time ultrasound (Acuson-128) to assess antral capacity and peristaltic function following a standard 400 ml soup meal in eight normal subjects, and in seven patients with functional dyspeptic symptoms (normal endoscopy and biliary investigations). Antral area was measured at
at 15 minute intervals (using the inbuilt plotter) during and between peristaltic waves. In normal subjects, the time to 50% reduction of post meal antral area was 62.7 (3.4) min (mean (SE)), % reduction at 90
minutes was 65.6 (3.1). In seven normal subjects repeated studies (x3) showed high reproducibility (mean coefficient of variation of t2 8.4%). Values for dyspeptic patients were significantly different, time to 50% antral area reduction was 78.2 (4.5) min, p<0.02, % reduction at 90 minutes 50.2 (5.9), p<0.05. Aborally synchronised peristalsis was identifiable in all normal subjects and patients (irrespective of emptying impairment). The % change in antral area with a peristaltic wave was similar in both normals (51.1 (10.3)) and dyspeptics (51.4 (5.1)) p>0.1, indicating similar peristaltic amplitudes. These changes were unrelated to time after meal ingestion. Peristaltic frequency was also similar in both groups, 3.25 (0.3)/min (normal subjects) v 3.0 (0.4)/min (dyspeptics) p>0.5.

Real time ultrasound is a convenient, reproducible, non-invasive method for clinical assessment of antral function and identifies abnormalities in functional dyspepsia patients which are missed by routine investigation.

Can ultrasound detect gastroduodenal disease?

S H SAVERYMUTU, A E A JOSEPH, J D MAXWELL (St George's Hospital, London) Increasing numbers of patients are being investigated for suspected gastroduodenal disease and are found to have a normal endoscopy. To reduce the negative endoscopy rate there is a need for a screening investigation. Ultrasound has been reported to be abnormal in a variety of gastroduodenal diseases but has not been systematically compared with endoscopy. We have compared ultrasound with endoscopy in 146 patients – major pathology was present in 54 patients – 22 gastric tumours, 14 duodenal ulcers and 18 gastric ulcers and minor pathology in 34 patients – 27 with gastric erosions or gastritis and seven with duodenal erosions. Fifty eight had normal endoscopies. Ultrasound of the stomach and duodenum was abnormal in 87% of major pathology including all gastric tumours, 91% gastric ulcers, 64% duodenal ulcers and 72% of minor pathology. Both major and minor pathology caused gastroduodenal wall thickening and disruption of mucosal folds but fixed air collections in ulcer craters and mass lesions were only found in major pathology. Twelve of 54 patients with normal endoscopies, however, had abnormal ultrasound (specificity 78%). Ultrasound can detect a high proportion of gastroduodenal pathology and therefore may be able to screen patients for endoscopy.

ENDOSCOPY

Endoscopy in the Trent region

B B SCOTT, M ATKINSON (County Hospital, Lincoln and University Hospital, Nottingham) A survey of gastrointestinal endoscopy in the Trent region was made in 1981. A continued increase in demand was predicted and deficiencies were highlighted. It was therefore thought timely to make a further review. Questionnaires relating to 1986 were completed by all gastroenterologists in the region. Upper G-I endoscopy had doubled to 7-6/1000 of the population/year (as many as barium meals). There had been a large increase in the proportion (27%) done by surgeons. Colonoscopy had increased from 0-40 to 0-94/1000. There were 0-37 ERCPs/1000 being done in six of the 12 districts; over half being done in Leicester. There were 0-17 variceal sclerotherapy procedures/1000 being done in five districts; over half being done in Sheffield. There was widespread dissatisfaction with the provision of facilities and staff for endoscopy. This included lack of a separate unit in seven of 18 hospitals. Designated nurses were found in only 10 hospitals, secretaries in two, and GPCAs for endoscopy in seven. Planning groups should be created in each district to ensure provision of a well staffed and financed endoscopy unit, to rationalise the endoscopy service and determine the techniques to be done locally.

Gastric epithelial dysplasia: a prospective multicentre follow up study

INTERDISCIPLINARY GROUP ON GASTRIC EPITHELIAL DYSPLASIA (IGGED), F FARINATI, ET AL (INTRODUCED BY PROF R NACCARATO) (Cattedra Malattie Apparato Digerente Policlinico Universitario, Università di Padova, Italy) The evolution in time of gastric dysplastic lesions has not been fully ascertained. We report here the results of a prospective multicentre follow up study of gastric epithelial dysplasia carried out according to a standardised protocol that calls for repeated endoscopies at intervals of three, six, and 12 months depending on the degree of the lesion. Each biopsy is reviewed by a panel of pathologists. So far, 114 patients (89 men, 25 women, mean age 59, range 29–83, 0-4% of all patients undergoing endoscopy over the same period of time) have been diagnosed and 80 have at least two examinations. Mean follow up is 17 months (range 3–68), mean number of endoscopies 3-5 (2–10). Dysplasia was of mild degree (MiD) in 69 patients, moderate (MoD) in 30, Severe (SD) in nine, and non evaluable (NVD) in six. Gastric ulcer (32%), chronic atrophic gastritis (50%), polyps (4%), gastrectomy (7%) were the associated lesions (no lesions 7%). For the 80 cases currently being followed up, this is the evolution observed: MiD regression 73%, persistence 19%, progression 8% (two of four cases to cancer); MoD reg 64%, pers 9%, progr 27% (six of six cases to cancer); SD reg 9%, pers 9%, progr 72% (five of five cases to cancer); NVD reg 100%. Of the 13 cases of cancer, six were early. All had gastric ulcer. Mean time to diagnosis was 9.5 months, mean number of endoscopies 3.4. Ten of 13 were diagnosed within one year of follow up (diagnostic delay), three after 18, 24, and 40 months. In conclusion, gastric epithelial dysplasia is an infrequent finding; MiD and MoD most frequently regress or are no longer detectable. Association with or evolution to cancer is observed in the great majority of SD patients, who require surgery, but may be observed even in MiD and MoD, thus indicating the need for careful follow up. Such an approach seems to facilitate the diagnosis of gastric cancer in its early stage.

Fragmentation of gall stones using pulsed laser light

N MITCHELL, R NOVAK, M MCLAUGHLIN, J HEGARTY, J G LUNNEY, O CORRIGAN, W VAN DER PUTTEN, P W N KEELING (Trinity College, Dublin 2, Ireland) Gall stones were fractured by irradiations with pulsed excimer, ruby, and Nd:YAG lasers. Fracturing occurred by the generation of shock waves in the material as a result of plasma production at the irradiated surface by short (30 nsec) intense pulses. The gall stones were mounted on a piezoelectric detector which was used to monitor the acoustic pulses produced. With the excimer laser, 100–300 pulses were necessary for breaking in air. Less than 10 pulses from the ruby laser directed at the gall stone in water was sufficient to cause fracturing. Pulses from a Q-switched Nd:YAG laser were able to destroy dark, pigmented stones in water.
Palliative endoscopic Nd:YAG laser treatment of rectosigmoid carcinoma

L A LOIZOU, D GRIGG, P B BOULOS, C G CLARK, S G BROWN (National Medical Laser Centre, Department of Surgery, University College Hospital, London) Forty patients with rectal or distal sigmoid carcinomas considered inoperable because of old age, significant concomitant disease or advanced tumour stage underwent endoscopic Nd:YAG laser treatment for palliation of symptoms: diarrhoea, rectal bleeding and discharge, tenesmus and obstruction. Fourteen (35%) of the lesions extended above the peritoneal reflection. Five patients had tumours <3 cm in diameter; all these patients derived significant improvement which was maintained by repeated treatment over a mean follow up period of 40 weeks. In two patients complete macroscopic and histological elimination of the tumour was achieved. The remaining 35 patients had more extensive tumours – 30 circumferential, five involving 1⁄3–2⁄3 of the intestinal circumference. Twenty eight patients (80%) derived significant symptomatic improvement over a mean follow up period of 23 weeks; mean survival of patients who died during this period was 16 weeks. All treatment failures occurred in patients with extensive circumferential tumours; five were early failures (three in patients with obstruction and two in patients with incontinence) and two late failures (both in patients with obstruction). Of the early failures, only one was considered fit for surgery the remaining patients receiving terminal care; both late failures were managed by defunctioning colostomy. There were no treatment related deaths; bowel perforation however, occurred in two patients. Treatments were performed with simple bowel preparation and minimal sedation and repeated at mean intervals of eight weeks. Patients required an average of 2-5 treatments in order to maintain symptomatic improvement; ambulant patients were treated on an outpatient basis.

Laser tumour photoablation provides good quality longterm symptomatic palliation in patients with inoperable rectosigmoid carcinomas with low associated morbidity.

The British Society of Gastroenterology

Colorectal

Low dosage 5-ASA enemas in the treatment of distal ulcerative colitis

G BIANCHI PORRO, R FASOLI, M PETRILLO, S ARDIZZONE (Gastrointestinal Unit, L Sacco Hospital, Milano, Italy) Recent studies suggest that low dosage 5-ASA enemas are as effective as hydrocortisone enemas in treating distal ulcerative colitis of mild to moderate activity. We have compared a low-dosage (1 g/day) rectal preparation of 5-ASA in slightly acidic buffered suspension (Pentasa) with a hydrocortisone 100 mg/day enema (Cortenema) in 41 patients with mild to moderate distal ulcerative colitis in a randomised double blind three week study. The two groups were comparable with regard to age, sex, maintenance therapy, as well as pretreatment clinical, endoscopic, and histologic activity. After three weeks, both types of treatment resulted in a statistically significant improvement of clinical and endoscopic activity; histology improved only in the group treated with Pentasa. As regards the comparison between the two drugs, no significant difference was observed, although a numerical trend in favour of Pentasa was evident both in clinical (95% v 75%) and in endoscopic (76% v 60%) activity. No side effects were reported in either group.

Our experience confirms that a short term topical treatment with a low-dosage 5-ASA is at least as effective as 100 mg hydrocortisone enemas in treating mild to moderate distal ulcerative colitis, and generally well tolerated.

Detection of malignant change in ulcerative colitis by brush cytology of the colon

D M MELVILLE, P R RICHMAN, N A SHEPHERD, C B WILLIAMS, J E LENNARD-JONES (ICRF Colorectal Cancer Unit, St Mark's Hospital, City Road, London) Surveillance programmes for patients with longstanding ulcerative colitis rely on mucosal biopsies for the detection of the premalignant changes of dysplasia. Such biopsies only sample a very small part of the mucosa and may miss focal dysplastic changes. Cytology has not been routinely used in patients with ulcerative colitis because of previous reports that the histological changes of neoplasia are mimicked by reactive hyperplasia associated with acute inflammation. In a prospective study of 100 patients with ulcerative colitis, 82 of whom had extensive colitis, carcinoma and dysplasia could be distinguished cytologically from reactive hyperplasia. There were six patients with carcinoma complicating colitis, and satisfactory samples were obtained from five. The cytological appearances were interpreted as carcinoma in three and as dysplasia in two. There were 78 patients who had not developed carcinoma or dysplasia; the cytological appearances were interpreted as negative for dysplasia in 75, and indefinite for dysplasia in three. In patients who had developed dysplasia, the changes appeared to be more widespread on cytology than on histology. Brush cytology may complement histological assessment in patients with ulcerative colitis who have developed strictures or in whom there is a high suspicion of neoplastic change.

Defunctioned proctitis: a diagnostic dilemma

M C WINSLET, M R KEEGHLY (The General Hospital, Birmingham) Proctitis in the defunctioned rectum may represent a normal physiological response or the onset of inflammatory bowel disease. It is a common indication for not restoring intestinal continuity. The aim of this study was to investigate the cause, diagnostic criteria and effect of restoring intestinal continuity in this condition. Eighteen patients underwent colonic diversion and 10 had intestinal continuity restored for a non-inflammatory condition. Macroscopic inflammation occurred in 10 patients (55%) within three months of colonic diversion with histological confirmation in five. Five patients showed macroscopic and histological improvement in restoring continuity. There was no significant difference in mucosal indices between the proctitis (P) and non-proctitis (NP) group (Crypt cell production rate: P=2.5±0.7, NP=2.9±0.9 cells/crypt/h). Glucosamine synthetase: P=14.3±3.3, NP=14.7±2.6 mmol/h/g. Mucosal lymphocytes: P=1.1×10³, NP=1.9×10³ cells/g. The flora of the excluded colon (aerobic and anaerobic species carriage rate, organisms (P=6.8%, NP=3.0%) and species count (P=4, NP=4) was not significantly different in the two groups. Colonic permeability was similar (P=8.5% for both). Defunctioned proctitis is a common complication after faecal diversion of unknown aetiology. Its only diagnostic
feature, to date, is resolution after resection of continuity. It presence is not a contraindication to stoma closure.

Cephalic phase of colonic motility

J ROGERS, A H RAIMUNDO, J J MISIEWICZ (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) To test the existence of a cephalic phase to food induced increase in colonic activity five normal subjects (mean age 22-6 yr (22-24), were studied, on six separate occasions in random order, by intraluminal pressure recording in the unprepared sigmoid colon. After a 60 minute basal period one of five food related cephalic stimuli of 30 minute duration or control stimulus was given and recording continued for 120 minutes. The pressure records were analysed in 10 minute periods as a study segment (sum of all four channels), for activity index (AI=area under curve, mmHg/min) by fully automated computer analysis. Constant gastric aspiration by NG tube was done to measure the effect of the stimuli on gastric acid secretion. Food discussion (FD) significantly (p<0.01, t-test) increased the mean colonic pressure activity compared to control discussion (781 (129) mean AI (SD) v 340 (65)) and was the best stimulus compared with slight only, smell only, sight and smell, or sham feeding of the subjects favourite meal. Increase in colonic pressure activity following FD correlated significantly (r=0.56, p<0.01) with volume of gastric juice aspirated. There was no correlation in the control study. These data show that there is a cephalic phase to food induced increase in colonic pressure activity and suggests it may be related to increased production of gastric acid.

Pseudo-diarrhoea in the irritable bowel syn-
drome: patients' records of stool form reflect transit time while stool frequency does not

L J O'DONNELL, J VIRJEE, K W HEATON (Departments of Medicine and Radiology, University of Bristol, Bristol Royal Infirmary, Bristol) Patients with IBS often complain of increased stool frequency and urgency and this is easily interpreted by patient and doctor as diarrhoea. Experienced gastroenterologists know that frequent stools can be formed or even hard suggesting intestinal transit is normal or slow but evidence for this is scanty.

Twenty three unselected IBS patients (16 women, 7 men; age 18-68 yr) recorded the form and time of evacuation of six consecu-
tive stools. Stool form was enumerated from a newly-devised 7-point scale in which the stool is classified according to cohesion, surface cracking, and consistency. Simultaneously, whole gut transit time (WGTT) was measured by ingestion of 20 radiopaque markers daily on four consecutive days followed by an abdominal radiograph on day 5 (Gastroenterology 92: 40). Median stool frequency was 1.7/24 h (range 0-3-5). Urgency was recorded by 74% of patients. WGTT ranged from 6 to 96 h. WGTT did not correlate with mean stool frequency (r=−0.22; NS). It correlated well, however, with mean stool form (r=−0.81; p=0.001).

These data show that patients' records of stool form can be used as a guide to transit time and indicate that in IBS 'diarrhoea' is often pseudo-diarrhoea. As patients with slow and fast transit may respond differently to high fibre diets or bulking agents, assessment of transit time by patients' records of stool form may be a simple and useful guide to management options.

Association between tumour development and plasminogen activators in the human colon

P A F DE BRUIJN, H W VERSPAGET, G GRIFFIOEN, H F E M VAN DEN INGH, J H VERHEYEN, G DOOIJEWALD, C B H W LAMERS (Department of Gastroenterology and Hepatology, Department of Pathology, University Hospital and Gaubius Institute TNO, Leiden, The Netherlands) Changes in plasminogen activator (PA) content have been implicated in the aetiology of malignancy. We studied PA activities by a spectrophotometric assay and antigens by ELISA in homogenates of adenomatous polyps (n=48) from the colon and compared the results with other malignancy parameters. Twenty five pairs of normal mucosa/carcinoma served as controls. Results, activities in mIU/mg protein and antigens in ng/mg protein, are expressed as mean (SE).

Activity of u-PA in adenocarcinomas (126 (21), p=0.001) was three times higher than in the normal mucosa (39 (66)), while u-PA antigen even showed a ten-fold increase (respectively 10-7 (1-1) v 1-0 (0-1), p<0.001). The adenomatous polyps contained u-PA activity (59 (5)) and antigen (4-4 (0-4) intermediate to, and significantly (p<0.01) different from those of normal mucosa and carcinomas. t-PA antigen in adenomas (3-8 (0-2)) and carcinomas (4-6 (0-4)) were significantly (p<0.001) lower than in the normal mucosa (7-9 (0-4)). Also noticed in t-PA enzyme activity (respective 612 (46), 594 (77) v 1948 (257)). When severely dysplastic polyps with invasive growth were compared with the other polyps, u-PA antigen was significantly (p=0-005) higher and similar to that in the carcinoma group. No relation was found between PA and histological type or polyp size.

In colon carcinogenesis (normal mucosa adenoma carcinoma), two discrete changes in PA content can be distinguished: one, a decrease of t-PA and an increase of u-PA when an adenoma develops; two, a second increase of u-PA at the appearance of invasive growth. These results point to an important role for u-PA in colonic carcinogenesis.

Evaluation of a biopsy gun for guided biopsy of impalpable lesions using intraoperative ultrasound

R M CHARNLEY, J P SHEFFIELD, J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Intraoperative ultrasound can detect occult liver metastases in up to 10% of patients who undergo curative resection for colorectal cancer. Identification of these impalpable lesions relies not only on imaging the lesions but also on gaining histological evidence by biopsy which can be technically difficult using conventional biopsy needles. We have evaluated a biopsy gun which can be operated with one hand by performing guided biopsy of impalpable liver metastases at necropy.

Twenty impalpable liver metastases between 2 cm and 5 cm from the liver surface were identified at necropy by contact ultrasound using an intraoperative ultrasound probe. Each lesion was individually measured using the light pen attachment on the ultrasound machine and was then biopsied under ultrasound control using a biopsy gun (Biopsy-Radiplast AB, Uppsala, Sweden). The 20 core biopsies were individually analysed histologically for the presence of carcinoma.

Of the 20 impalpable lesions (median diameter 12 mm; range 9-18 mm) histology was positive for carcinoma in 18 (90%).

Biopsy of impalpable liver metastases down to a diameter of 9 mm is possible using a biopsy gun under intraoperative ultrasound control.

Palliation of colorectal cancer with the Nd: YAG laser. Which patients are palliated?
Validation of the motor and sensory tests of anorectal function: a repeatability study

J Rogers, S Lauberg, J J Misiewicz, M M Henry (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London and Department of Physiology, St Marks Hospital, London) Anorectal physiology, used in the management of patients, has not been validated. Sixteen subjects (mean age 50.7 yr (12-8), three men) were studied on two separate occasions by two independent investigators in random order with anatomical, manometric, and electrophysiological assessment of anorectal motor and sensory function. There was no significant difference between the results obtained by the two investigators in the six separate tests of anorectal function. Bias between investigators for each variable, 95% CI of the bias; ±2 SD (limits of agreement) and the average range of values by both methods follow: Peri-anal descent (cm): -0.07, -0.47 to 0.31; ±1.3, [0.5-2.4]. Anal canal length (cm): -0.1, -0.2 to 0.4; ±1.0, [2-4]. Resting pressure (cmH2O): -10, -25 to 4.7; ±4.2, [30-130]. Squeeze pressure (cmH2O): 9, -32 to 14; ±6.5, [40-250]. Pubococcygeal muscle latency (ms): 0-1, -0.3 to 0.2; ±0.6, [1.7-2.7]. Fibre density: 0.26, -0.04 to 0.57; ±0.35, [1.83-2.58]. Mucosal electrosensitivity (mA): 0.5, -3.3 to 4.3; ±1.9, [1.75-23.6].

Repeatability for the calculation of fibre density derived from single muscle fibre EMG was assessed with each investigator analysing the others' tracings blind and showed no significant difference, bias -0.003, -0.07 to 0.06 95% CI.

In this study the standard tests of anorectal sensorimotor function show a high degree of repeatability between different investigators. These tests are validated and allow comparison of data obtained in different centres employing the same techniques.

Prolonged ambulant anorectal motility in chronic idiopathic constipation

D J Waldron, D Kumar, N S Williams, R Hallan (The Surgical Unit, The London Hospital, Whitechapel, London) Laboratory anorectal manometric studies report variable results in chronic idiopathic constipation (CIC) some showing a high pressure zone in the anal canal. Six subjects with CIC and 14 controls were studied in an ambulant situation for 18-2 and 20-3 hours (mean) respectively, using a Gaetelc anorectal probe containing pressure-sensitive microtransducers placed 10 cm apart to lie in the rectum and anal canal.

Sampling reflexes occurred significantly less often in CIC, 2-4 (0-3)/hour (mean (SEM)), compared with controls, 7-4 (2-0)/hour, (p<0.05). Rectal contractile events, frequency two to three minute, occurred at intervals of 60-90 minutes in both groups with post prandial contractile frequencies of five to six minute occurring at shorter intervals (20-30 minutes). Such events were less frequently seen, however, and were of lesser amplitude in the constipated group.

Episodic rises in anal canal resting pressure, mean amplitude increase of 12.0 (0-8) mmHg and duration 5.1 (0-7) minutes, occurred 1-1 (0-2) times/hour only in the constipated group. Otherwise resting anal canal pressure was not different between both groups.

These results indicate that rectal contractile events and sampling episodes occur less often in CIC compared with controls. Demonstration of episodic variations in the anal canal resting pressures in CIC may explain inconsistencies in previous laboratory studies and highlights the importance of more physiological prolonged ambulant studies.

Posterior pelvic floor repair – a new surgical approach for outlet obstruction constipation (obstructed defecation)

I G Finlay, D Brown (Department of Surgery, Royal Infirmary, Glasgow) Outlet obstruction constipation (OOC) is associated with puborectalis paradox (1). We reported that (a) unobstructed defecation requires lifting of the posterior pelvic floor (PPF) before puborectalis relaxation (2), (b) patients with OOC collapse the PPF on straining at stool (3).

An operation has been performed in 12 female patients with classical OOC which is designed to support the posterior pelvic floor using a porcine dermis implant. After an intersphincteric dissection the graft is sutured to the sacrum and to the origin of the levator ani muscles.

Videoprogctography was used to study the position of the anorectal junction (ARJ) and the lowest point of the posterior pelvic floor with reference to the puboccygeus line. The mean descent of the ARJ pre-operatively was 2.2 cm (0-3) (mean(SE)) and compared with 1.4 cm (0-3) one month after surgery, p=0.1. The corresponding values for the mean descent of the posterior pelvic floor were 3.5 cm (0-5) and 1.6 cm (0-4) respectively, p<0.001.

All patients were asymptomatic for three months. Three have developed minor symptoms in the fourth month of follow up.

These results suggest that posterior pelvic floor repair may be of value in patients with outlet obstruction constipation.
monitor the disease course. The Acute Physiology and Chronic Health Evaluation (APACHE II) scoring system overcomes some of these problems but is not a widely accepted means of assessing severity in acute pancreatitis. We have prospectively evaluated this system in 155 consecutive patients with acute pancreatitis. Thirty eight (24.5%) had a complicated attack (including 12 deaths (8%)), the remainder having an uncomplicated course.

The admission APACHE II score distinguished complicated from uncomplicated attacks (mean scores 10.9 ± 6.3, p < 0.001 Mann-Whitney U test). An admission score of >5 predicted severe attacks with a sensitivity of 95% and had an overall correct prediction of 64%. A score of >29 during the first three days predicts severe attacks with a sensitivity of 82%, specificity of 74% and overall correct value of 76%. This is comparable with the existing systems.

APACHE II provides continuity of assessment. All laboratory investigations are available as part of the ‘out of hours service’ and the scores calculable within a few hours of admission.

Changing incidence and mortality from acute pancreatitis

C. W. Wilson, C. W. M. Re (Department of Surgery, Royal Infirmary, Glasgow) Few studies have examined the changing incidence and mortality trends from acute pancreatitis. Studies from Bristol showed an increasing incidence over the 30 year period 1950–1979, although case mortality remained unchanged at around 20%. Data on hospital admissions in Scotland have been recorded since 1961 as the Scottish Hospital In-Patient Statistics, permitting analysis of such trends.

The annual admissions for acute pancreatitis in men have increased 11-fold from 69 cases/year in 1961 to 750 cases/year in 1985 and in women has increased four-fold from 112 cases/year to 484 cases/year respectively. This increase was seen particularly in young and middle aged adult men (20–59 years) and in elderly women (≥60 years). A corresponding change was not seen in mortality which increased only two-fold in men from 15 cases/year to 30 cases/year and in women from 29 cases/year to 37 cases/year.

The largest increase in admissions occurred in the six year period after 1971 coincident with the introduction of the Phadebus amylyase test (Pharmacia). It is suggested that much of the apparent increase in incidence of acute pancreatitis may be attributed to an increased diagnostic rate caused by greater clinical awareness and the availability of a simple reproducible diagnostic test.

The tumour marker CA195 predicts duration of survival in pancreatic cancer

O. M. Taylor, E. H. Cooper, M. J. McMahan, E. A. Benson (The Department of Surgery and The Unit For Cancer Research, The General Infirmary, Leeds) The carbohydrate antigen CA195, a tumour associated antigen, may be raised in the serum of patients with carcinoma of the exocrine pancreas. Using an immuno-radiometric assay (Tandem IRMA Kit) we have determined the serum CA195 concentrations in 35 patients with histologically proven pancreatic carcinoma. All cases were staged using combinations of ultrasound, computed tomography, and laparotomy. Twenty four cases were followed up at monthly intervals until death (median survival = 75 days; quartiles = 27–112). Samples were obtained for CA195 assay at each review.

Analysis of the data (using χ² with Yates correction) suggested that a cut-off CA195 level of 1000 U/ml distinguished both metastatic status and survival of less than three months. Of 35 samples taken within three months of death (median = 38 days, Q1:Q3 = 22:67), 25 had CA195 > 1000 U/ml, but of 19 samples taken before this time, only three had such high levels (p < 0.001).

Only three of 21 cases without metastastic disease had CA195 > 1000 U/ml, compared with 10 with levels above this value, of 14 with metastases (p < 0.001). Comparing metastatic metastatic status with survival, we found only two of 13 with metastases lived for more than three months (median = 50 days, Q1:Q3 = 26:75), compared with the survival of 12 patients without metastases (median = 102 days, Q1:Q3 = 70:141) of whom eight lived for longer than three months (p < 0.05).

In patients with pancreatic adenocarcinoma the CA195 level seems to be a better indicator of duration of survival than metastatic status. Its assay may be useful both clinically and in the study of this disease.

Pancreatic adenomas are induced by duodenogastric reflux

P. R. Taylor, R. C. Mason, T. Palmer, D. C. Hanley, G. M. Murphy, R. H. Dowling, I. McColl (Departments of Surgery, Histopathology and Gastroenterology, UMDS, Guy’s Hospital, St Thomas Street, London) The factors controlling pancreatic growth are poorly understood. Transplantation of the jejunum between the stomach and duodenum (pancreatobiliary diversion) causes pancreatic hyperplasia. We describe a new model to induce pancreatic hyperplasia and adenoma formation.

Male Wistar rats underwent either a simple gastrojejunostomy or a 'split' gastrojejunostomy where the jejunum was divided and the two limbs implanted into the stomach 1 cm apart. When killed at 56 weeks the mean body weight of the 'split' gastrojejunostomy rats was significantly lower (495 g) compared to those with a simple gastrojejunostomy (643 g, p < 0.001 Mann Whitney). The 13 simple gastrojejunostomy rats had no hyperplasia of the pancreas or small bowel, and the jejunal villous to crypt ratio was 1:55, reflecting the jejunal atrophy associated with this operation. All 10 'split' gastrojejunostomy rats had pancreatic hyperplasia with nodule formation. Five animals had hyperplastic nodules, four animals had both hyperplastic and adenomatous nodules, and one rat had enlarged lymph nodes. Both the afferent and efferent limbs of the gastrojejunostomy were grossly enlarged and the villous to crypt ratio was 3:65.

This study shows that separation of the limbs of a gastrojejunostomy in the rat is associated with autonomous pancreatic growth and jejunal hyperplasia.

Assessment of exocrine pancreatic function after gastrectomy

S. Domschke, G. Heptner, W. Domschke (Department of Medicine, University of D-8520 Erlangen, FR Germany) Gastrectomy may lead to pancreaticocytocytic asynchronia and impair the diagnostic accuracy of established indirect pancreatic function tests. We compared intra-individually the specificity of these tests with that of our new plasma amino acid consumption (PAAC) test before and after gastrectomy.

In 10 patients (three men, seven women; aged 20 to 68 years) a normal pancreatic function was affirmed by the secretin–pancreozymin test, preoperatively. Before and three months after total (n = 4; Roux-Y type) or subtotal (n = 6; Billroth II) gastrectomy, in each patient the Pancreolauryl test (PLT), the NBT-PABA test, the fecal Chymotripsin (Ich) determination and the PAAC test were carried out.

Before gastrectomy only one patient had a falsely pathological result in the PLT test.
Exocrine and endocrine function in chronic pancreatitis: relation to pancreatic surgery

J C Thow, T Hawkins, K G M M Alberti, R Taylor, C Venables (Departments of Medicine and Surgery, University of Newcastle upon Tyne) Chronic pancreatitis is associated with progressive loss of endocrine and exocrine function but it is not known to what extent this decline is influenced by pancreatic resection. Fifty-two patients with chronic pancreatitis were studied, of whom 25 (48%) had undergone pancreatic surgery (18 distal pancreatectomy (DP); seven Whipple's pancreaticoduodenectomy (WP)). Exocrine and residual β-cell function were assessed by the p-amino benzoic acid (PABA), test (normal range 0-67-1-09) and fasting C-peptide concentration (normal range 0-18-0-52 nmol/l) respectively. There was a significant reduction in C-peptide in DP and WP groups (0-22 (0-04) SE v 0-24 (0-05) nmol/l; NS) compared with the non-operated group (0-44 (0-04) nmol/l). p<0.001 and p<0.01 respectively. There was a significant reduction in PABA results in the DP and WP groups (0-54 (0-07) v 0-43 (0-14); NS) compared with the non-operated group (0-83 (0-04); p<0.01 and p<0.05 respectively).

There was a close correlation between PABA and C-peptide in the operated subjects (R=0.66, p<0.01) but poor correlation in the non-operated group (R=0-34; NS). Diabetes was more common in both DP and WP groups compared to the non-operated group (66, 57, and 23% respectively; χ²=9.4; p<0.01). These results quantify the consequences of surgery on exocrine and residual β-cell function and show that resection of the distal pancreas and more extensive surgery carry similar consequences.

Distal pancreatic resection in benign pancreatic disease

S Shankar, R G Russell (Department of Gastroenterology, The Middlesex Hospital, London) Distal resection has become unpopular, yet in patients with defined ductal disease the results appear good. To test this hypothesis 121 patients operated upon between 1976 and 1988 are reviewed. Resection was elective in 110 patients. The dominant indication was uncontrolled pain with narcotic abuse in 43, steatorrhea 33 and loss of work 23. Forty patients had acute pancreatitis at first presentation, 20 had non-resolving acute pancreatitis and the remainder chronic disease. ERCP was successful in 102, showing duct obstruction in 53, duct disruption in 18, and diffuse disease in 31. The resection included splenectomy in all and a pancreaticocolonostomy in 50. Mean length of stay was 24 days, operative mortality was nil and late deaths were three. Using the Visick grading 53 patients had good results (I and II), 10 fair (III), and 27 poor (IV). Twenty-three patients were excluded as they were not seen in the last two years, and eight were operated on within the last six months. Good results were seen in those with duct obstruction or disruption, and poor results in those without a defined duct abnormality, 21 of whom went on to have a total pancreatectomy.

It is concluded that distal resection should be performed in these patients with a defined and localised duct abnormality as shown on the pancreatectogram.

Efficacy of quantitative hepatobiliary scintigraphy (QHS) for evaluating a large series of patients with suspected partial common duct obstruction

J S A Collins, W J Dodds, J E Geenan, W J Hogan, R Darweesh, B D Collier, E T Stewart (Departments of Radiology and Medicine, Medical College of Wisconsin, Milwaukee, USA) Quantitative hepatobiliary scintigraphy (QHS) may be a promising method for evaluating suspected partial common bile duct obstruction. During the past three years, we obtained QHS exams in 100 non-jaundiced, cholecystectomised patients with unexplained upper abdominal pain. The patient group consisted of 80 women and 20 men, age 52 ± 15 SD yrs. DISIDA was given iv and the time of peak isotope activity and isotope clearance curves were derived from a region over the hepatic hilum. Values from patients were compared with those from 22 asymptomatic cholecystectomised controls. The 'truth' about each patient was derived from an ERCP, accompanied by sphincter of Oddi (SO) manometry in those with possible cryptic obstructive SO dysfunction (SOD). Of the 100 patients, 31 were judged true positive and 69 true negative. The positives included 17 patients with common duct stones (CDS), 10 with SOD and four with benign stricture, tumour or choledochocele. The SOD cases consisted of patients with sphincter stenosis or dyskinesia. Overall sensitivity was 78%, including 76% for CDS and 80% for SOD. False positive findings occurred in 14% of the true negatives for a specificity of 96%. We conclude that: (1) QHS is useful for evaluating patients with suspected partial common duct obstruction. (2) The test is applicable in cholecystectomised patients without significant liver dysfunction. (3) In some cases, QHS may obviate the need for SO manometry.

Endoscopic stenting for malignant biliary obstruction: how good really? – a review of 641 consecutive patients

J F Dowsett, A Polydorou, D Vaira, S R Cairns, J Croker, P B Cotton, R G Russell, A R W Hatfield (Departments of Gastroenterology and Surgery, The Middlesex and London Hospitals, London) During the last five years at the Middlesex and three years at the London, 641 patients had attempted permanent palliation of unresectable malignant biliary obstruction by the endoscopic placement of 10 or 12 Fr endoprotheses. Ninety four of these patients had attempted combined endoscopic-percutaneous procedures. The patients were divided by origin of malignancy (primary or secondary) and level of blockage (ampullary, common bile duct, or hepatic duct). Hepatic duct strictures were further separated into Types I, II, and III (after Bismuth). Only one stent was placed for hepatic duct lesions, unless evidence of sphincter in undrained segments developed before the initial placement. All patients received prophylactic antibiotics and had decompression assessed by serum bilirubin estimation and ultrasound.

There were 37 ampullary, 337 low, 43 Type I, 62 Type II, and 68 Type III primary malignancies and nil (−) ampullary, 23 low, 26 Type I, 21 Type II, and 24 Type III secondary malignancies. For primary malignancies, the success rates were 97%, 84%, 94%, and 85%, the complication rates were 32%, 19%, 13%, 18%, and 23%, the 30 day mortality rates were 3%, 17%, 10%, 12%, and 28%, and the median survivals were 9, 4-5, 5-5, 4, and 3 mths. For secondary malignancies, the success rates were −.
Endoscopic stenting is a successful means of providing permanent palliation for both primary and secondary malignant biliary obstruction but overall, the results vary considerably with the site and cause of obstruction.

Wide bore self expanding stainless steel endoprostheses: a new approach for percutaneous stenting of biliary strictures

A GILLAMS, R DICK, K E HOBBS, J S DOOLEY (Royal Free Hospital and School of Medicine, Pond Street, London) The treatment of biliary strictures by the insertion of an endoprosthesis (EP) either percutaneously or endoscopically is handicapped by the size of EP that can be used, and the problem of stent blockage. We have therefore used a self expanding stainless steel braid endoprosthesis (Medinvent, Lausanne, Switzerland) which is inserted percutaneously in a compressed form (catheter diameter Fr 7) and expands to a diameter of 8–10 mm when released in the stricture. Of 25 patients treated (mean age 65 yr, range 44–84), 21 had a malignant and four a benign stricture. A total of 31 EP were used (three patients received three EP). There were two serious early complications: acute renal failure and a blood stained pleural effusion. Three patients (12%) died within 30 days of the procedure. Biliary decompression was successfully achieved in 21 of the 22 remaining patients. During follow up, available in 20 patients (mean 2.6 m; range 1–7 m), two patients required a further drainage procedure at 1-0 and 5 months. This new design of EP provides a considerably wider lumen for bile drainage than other currently available types without increasing the complication rate of insertion. Further follow up is necessary to establish longterm patency.

Near infra-red reflectoscopy (NIR): a simple and accurate method for faecal fat measurement

L BENINI, S CALIARI, I VANTINI, G TALAMINI, M G GUIOTTO, M RAMPANELLI, C SEMBENINI, L A SCURO (Medical Clinic and Department of Gastroenterology at Valeggio s/M, University of Verona, Italy) Standard methods for faecal fat analysis are complex, unpleasant, and rarely performed. A method has been recently described to measure in less than one minute fat concentration on a small faecal sample by infrared reflectance close to the visible. To evaluate its accuracy we have studied faecal fat balance in 118 inpatients, admitted for suspected malabsorption or for diseases possibly causing it. Faecal fat was measured by near infrared reflectance, by the Van De Kamer titrimetric method and, in the last 40 pats, by the Sobel gravimetric method. The linear correlation coefficient r was calculated after logarithmic transformation of the data to normalise them (as confirmed by a non-significant Kolmogorov-Smirnov test). In our patients median faecal fat excretion was 10.5 g/24 h (range 1–95). A good correlation between the methods was found (r=0.92 and 0.95 for NIR v titrimetric and gravimetric method respectively; r=0.94 for gravimetric v titrimetric method; p always <0.001). On homogenised faeces (12 patients measured three times) a mean coefficient of variation of 2.1% (SD 1.7) was found. On non-homogenised faeces (30 samples from three patients) a CV of 11.2, 9, and 8.3% was obtained. In conclusion, the NIR method is simple, well accepted by laboratory staff and well correlated with the established methods; repeated readings can avoid the unpleasant faecal homogenisation.

Modification of jejunal ion transport and luminal eicosanoids by dietary fat

F A SAGHER, R MOORE, J A DODGE (Department of Child Health, The Queen’s University of Belfast) Diarrhoeal conditions may be provoked or mediated by prostaglandins and ameliorated by increasing dietary fat. To study the effects of dietary fat on ion transport and luminal PGs. Three week old Sprague Dawley rats were weaned onto isocaloric diets in which 40% of the total calories were given as fat: either butter (high saturated), olive oil (high mono-unsaturated) or corn oil (high poly-unsaturated) with a control group on standard low fat (10% of total calories) laboratory diet.

During jejunal in vivo perfusion studies we found that polynsaturated fat increased the jejunal absorption of water (p<0.05 v control), Na⁺ (p<0.05 v olive oil, p<0.005 v butter), and Cl⁻ (p<0.025 v butter group). Saturated fat markedly reduced the absorption of water Na⁺ and Cl⁻ (p<0.025 v controls). Luminal PGE₂ and PGF₂α were found to be raised only in the olive oil group (p<0.005, p<0.025 v control group respectively).

We conclude (i) that feeding rats polyunsaturated fat increased the small intestinal permeability to water and sodium, and (ii) the production of luminal PGs from arachidonic acid can be inhibited by linoleic acid or enhanced by oleic acid.

Congenital microvillous atrophy (CMA), new methods of diagnosis

I R SANDERSON, v V SMITH, B D LAKE, G W ANDERSON, M MALONE, P J Milla (Hospital for Sick Children, Great Ormond Street, London) Congenital microvillous atrophy (CMA) is an unusual enteropathy that often presents in the neonatal period. Diagnosis is dependent on ultrastructural studies of jejunal mucosa but frequently cannot be made at presentation as the infants are too small or ill for a jejunal biopsy to be done or electron microscopy is not available. We have studied four children who had neonatal CMA and characteristic changes of a disrupted brush border, intracellular secretory granules and microvillus involutions on electron microscopy of jejunal mucosa. We used a histochemical method to examine the intracellular localisation of brush border alkaline phosphatase (AP) in paraffin wax embedded sections of jejunal biopsies in three and in post mortem jejunum in one. In all four cases patchy but intense intracellular AP activity was found in the apex of villous enterocytes only whereas in age matched controls activity was confined solely to the villous brush border. In two of four rectal biopsies were examined both by electron microscopy and for AP activity. Characteristic ultrastructural changes were found but only in surface epithelial cells and were patchy in distribution. Abnormal AP activity could be detected in both these biopsies. These data show that the diagnosis of CMA can be made retrospectively in paraffin embedded jejunal mucosa. In some children the disease process is not restricted to the small intestine and may effect other regions of the gut, in such infants a rectal biopsy done at presentation may reveal the diagnosis and prevent many months of parenteral nutrition and false hopes of a ‘cure’.

Intra-uterine malnutrition impairs the development of pancreatic exocrine function (PEF) in man

Paediatric posters

The British Society of Gastroenterology

A1459
controls (group C). Before treatment at gastroscopy group A showed: four peptic oesophagitis (PO), seven antral gastritis (AG), three antral ulcers (AU), six duodenal ulcers (DU); group B showed: two PO, four AG, four AU, four DU; group C showed: six PO, one AG, two AU, nine DU. Serum PG I levels (mean (1 SD)) before treatment in group A and B were comparable and significantly (p<0.001) higher than in group C (group A: 89 (30), group B: 79 (22), group C: 53 (13) ng/ml). After treatment serum PG I significantly (p<0.001) lowered to 58 (19) ng/ml, a value comparable with control levels, in CP-cleared group A, while in CP-persisting group B it did not change significantly (84 (31) ng/ml).

Our data seem to suggest that in children a raised serum PG I might be a marker of Campylobacter pylori infection.

**LIVER POSTERS**

**Computer diagnosis of jaundice (‘Soluble’)**

**F R VICARY, E W F W ALTON, N NEWMAN, J HOOPER (Department of Gastroenterology, Whittington Hospital, Highgate Hill, London)** We have developed a software program (Soluble) for the diagnosis of the jaundiced patient. The mathematical program, although based on Bayes’ theorem, contains a number of mathematical innovations.

A database of 397 patients has been entered and the diagnostic ability depends solely on this database. There are 24 diagnostic categories. There is a second programme (Auxible) which automatically updates the database every week and assesses the performance and accuracy of the Soluble program. The software programs are running in the Dept of Gastroenterology on an IBM compatible microcomputer.

Fifty new patients were entered prospectively into the programme. Thirty seven (74%) were diagnosed accurately, with 47 (94%) placed in the three most likely diagnoses. One hundred patients were entered prospectively at a nearby teaching hospital: 72% were diagnosed accurately and 90% were in the first three places.

Soluble will give reasons for its diagnosis and suggest further relevant investigations. The average time needed to enter data and for the houseman to receive a diagnosis is five and a half minutes.

**Is an isolated rise in gammaglutamyltranspeptidase (γ-GT) an indication for liver biopsy?**

**A IRELAND, L NEVILLE, A CARMICHAEL, J D MCgee, J M Trowell, R W Chapman (Gastroenterology Unit, John Radcliffe Hospital, Oxford)** γ-GT is often the only abnormality detected on screening of a patient with alcoholic liver disease. In order to determine whether an isolated rise of γ-GT is sufficient for a liver biopsy, we have analysed the records of 117 consecutive alcoholic patients (65 men, 52 women; aged 23–78 years) biopsied between 1983 and 1987. They were divided into three groups, based on liver function test abnormalities. Group 1 (n = 17) had an isolated raised γ-GT; group 2 (n = 34) had a raised aspartate aminotransferase (AST); 32 of whom also had a raised γ-GT, and group 3 (n = 66) had, in addition, abnormalities of other liver function tests. The groups were of comparable age. Liver biopsies were assessed for steatosis, ballooning, megamitochondria, Mallory’s hyaline, inflammatory infiltrate, fibrosis, hyaline sclerosis and cirrhosis. In group 1, γ-GT level ranged from 42–255 IU/l (normal <40 IU/l). Three of 17 biopsies were normal, and in the remainder changes seen on biopsy included steatosis, megamitochondria and Mallory bodies. In group 2, AST level ranged from 40–358 IU/l (normal <35 IU/l), and γ-GT level ranged from 14–739 IU/l. In addition to the above, changes, six of 34 had evidence of hepatitis, 11 fibrosis, and three cirrhosis. In group 3, 19/66 had evidence of hepatitis, 22 fibrosis, and 15 cirrhosis. Thus, raised γ-GT reveals only reversible changes on biopsy. However, if AST is also raised, >50% show fibrosis, hepatitis or cirrhosis.

**Interferon mediated impairment of hepatic oxidative drug metabolism in rats**

**S J WILLIAMS, P J CRAIG, E CANTRILL, G C FARRELL (INTRODUCED BY A R W HATFIELD) (Liver Research Group, Department of Medicine, University of Sydney at Westmead Hospital, Sydney, Australia)** We have previously reported that recombinant human alpha interferon (rIFN-αA) significantly impairs antipyrine (Br J Clin Pharmacol 1986; 22: 610–2) and theophylline (Lancet 1987; ii: 939–41) clearance in man. In the present study an animal model was developed to examine the nature of this interferon mediated impairment of hepatic oxidative drug metabolism. Rats were injected intramuscularly with...
either rIFN-αA, recombinant human IFN-γ (rIFN-γ), recombinant rat IFN-γ or vehicle and experiments performed 24 h later. In intact animals, theophylline clearance (CL\textsubscript{t}) was determined twice 10 days apart; once after IFN (2-7.5×10\textsuperscript{9} U in 0.2 ml H\textsubscript{2}O) and once after vehicle (0.2 ml H\textsubscript{2}O). CL\textsubscript{t} was also determined in the isolated perfused rat liver (IPRL) following IPN (2×10\textsuperscript{9} U) or vehicle. Androst-4-ene-3,17-dione (androstenedione) hydroxylation pathways were used to assess possible IFN effects on the activities of individual cytochrome P-450 isozymes.

Rat IFN-γ significantly reduced CL\textsubscript{t} in the intact animal (2.62±1.25 v 3.76±2.03 ml/kg/min, p<0.05) and in the IRPL model (0.98±0.14 v 1.32±0.18 ml/min/kg, p<0.05) but human rIFN-αA and rIFN-γ had no effect on CL\textsubscript{t} in either system. Rat IFN-γ alone resulted in decreased levels of total P-450 (0.60±0.10 v 0.7±0.11 nmol/mg protein, p<0.05) and reduced androstenedione 16β-hydroxylation (0.17±0.04 v 0.22±0.06 nmol product formed/mg protein, p<0.05); three other principal hydroxylated metabolites of androstenedione also appeared reduced (NS).

In the rat, autologous but not heterologous IFNs impair hepatic oxidative drug metabolism. The reduction of P-450 produced by IFN appears to be caused by suppression of multiple isozymes.

**Gastric mucosal blood flow in portal hypertension**

J T WALKH, H L SMART, W B TINDALE, D R TRIGER (University Departments of Medicine and Medical Physics, Royal Hallamshire Hospital, Sheffield) Gastric mucosal bleeding in portal hypertension (PH) is increasingly recognised but poorly understood. We have investigated the role of gastric mucosal blood flow (GMBF) by studying 28 patients with oesophageal varices (19 with congestive gastropathy); 12 patients with endoscopic negative dyspepsia acted as controls. Both groups were well matched for age, sex and weight. Gastric mucosal blood flow was measured using a \textsuperscript{111}\textsubscript{Tc}-pertechnetate clearance technique involving simultaneous gastric juice and venous blood sampling following the injection of 5 MBq of tracer at the start of a standard pentagastrin test. Overall, GMBF was significantly (p<0.05) lower in patients with PH [13.5 (3.7–55.6) ml/minute] than in controls [25.8 (10.7–49.1) ml/minute] (values as median and range). This finding was unrelated to the presence of congestive gastropathy and independent of the severity of liver disease.

In patients with varices treated by injection sclerotherapy (15), however, GMBF was significantly (p<0.05) reduced [12.8 (3.7–46.0) ml/minute] when compared with those who were untreated [19.0 (6.9–55.6) ml/minute]. Portal hypertension is associated with diminished GMBF. This is related more to bleeding oesophageal varices or their treatment by sclerotherapy than to the presence of congestive gastropathy. This finding may be pertinent to the factors predisposing to variceal haemorrhage.

**Non-invasive diagnosis of portal vein occlusion by radionuclide angiography**

P MACMATHUNA, M K O’CONNOR, D HAMILTON, P W N KEELING (Departments of Clinical Medicine and Nuclear Medicine, Trinity College, St James’ Hospital, Dublin, Ireland) The diagnosis of portal vein occlusion (PVO) as a cause of extra hepatic portal hypertension (PH) has relied predominately upon invasive mesenteric angiography (IMA). We have developed a novel non-invasive radionuclide angiographic (RA) technique to indirectly estimate portal venous (PV) and hepatic arterial (HA) contributions to total liver perfusion. The aim of this study was therefore to evaluate the accuracy of RA in detecting PVO.

Group I, 10 patients (mean age 47 yrs, M/F 5/5) with PVO (including three patients with cavernous transformation (CVT)) confirmed by TMA. Group II, 25 cirrhotic patients without PVO (Child A n=7, B and C n=18) and group III, 26 control subjects with no evidence of liver disease of PH.

After an overnight fast, Tc 99m was injected rapidly into a peripheral vein and isotope flow curves (IFC) generated for 100 sec at 0.5 sec intervals over the liver and spleen together with heart lung and kidneys. Using computer assisted deconvolutional analysis and gamma variate fit, and assuming that splenic arterial (SA) flow resembles that of the HA, the SA IFC was superimposed upon the total liver IFC to yield the HA contribution and hence indirectly PV flow. Results for each group were expressed as the mean HA/PV ratio.

Controls: 22/78 consistent with known physiological estimates; cirrhotics: Child A: 28/72, B and C: 56/54 consistent with decreased PV inflow with increasing severity of disease. PVO group: 97/3 consistent with negligible PV flow and PV and CVT: 81/19 indicating residual collateral PV flow.

Our results show that non-invasive RA provides a safe and accurate method of evaluating portal vein patency, to complement existing radiological techniques.

**The effect of carbon tetrachloride (CCl\textsubscript{4}) on the copper-laden rat liver**

L BARROW, M S TANNER (Department of Child Health, University of Leicester, Leicester) Copper is believed to be hepatotoxic in Wilson’s disease and Indian childhood cirrhosis. In rats, however, whose liver copper was raised from 75±13 to 461±13 μg/l dry weight by copper acetate supplementation of drinking water, hepatic damage was confined to a mild focal hepatitis with minimal rise of transaminases. The hypothesis was therefore advanced that a second hepatic insult may precipitate or perpetuate liver injury in a copper laden liver.

In non-copper-dosed rats CCl\textsubscript{4} 10 mmol/Kp iv produced raised serum transaminases (aspartate aminotransferase, aST, 809±298 IU/l, control 20±5 and alanine aminotransferase, ALT, 295±157 IU/l, control 6±1). Liver histology showed extensive necrosis, portal inflammatory infiltration and periportal fat deposition. In copper-loaded rats CCl\textsubscript{4} produced much smaller increases in AST (492±80 IU/l) and ALT (172±57 IU/l) and a mild focal necrosis. Fat deposition was, however, not reduced.

The previous copper loading of rats unequivocally protected against CCl\textsubscript{4} induced liver necrosis, showed biochemically and histologically, although triglyceride accumulation was apparently unaffected. By interfering with arachidonic acid metabolism, copper may reduce prostaglandin mediated inflammation. Copper cytotoxicity may be an insufficient pathological explanation of copper storage disorders.

**Antibodies against the hepatic asialoglycoprotein receptor preferentially coat periportal hepatocytes in the in situ perfused rat liver**

B M MCFLARANE, J SIPOS, C D GOVE, C G MCSORLEY, I G MCFLARANE, R WILLIAMS (Liver Unit, King’s College Hospital, Denmark Hill, London) Antibody-dependent, cell-mediated cytotoxic (ADCC) reactions may contribute to hepatocellular injury in autoimmune (AI) and hepatitis B virus (HBV) related chronic active hepatitis (CAH). Circulating autoantibodies against the hepatocyte specific, cell surface expressed asialoglycoprotein receptor (HL) have been described in both AI- and HBV-CAH and correlate with severity of portal liver
damage. We have investigated the hypothesis that periportal hepatocytes are exposed to high concentrations of anti-HL in afferent blood, rendering them particularly susceptible to ADCC damage. Eight antegrade (portal vein) and seven retrograde (hepatic vein via vena cava) in situ perfusions of rat livers were performed at 10°C with 50 ml/kg Krebs-Ringer, then 12 ml guinea-pig anti-rabbit-HL or monoclonal anti-human-HL or control guinea pig sera washed through with 50 ml Krebs-Ringer. The distribution of anti-HL in cryostat sections of the snap-frozen livers was determined by a sensitive enzyme-avidin-biotin immunohistochemical technique. In all experiments with anti-HL the antibody was found to be prominently and almost exclusively deposited on periportal hepatocyte surfaces, regardless of the direction of perfusion. This preferential coating of periportal hepatocytes is therefore not related to their location relative to high concentrations of anti-HL in the afferent circulation but apparently to their particular capacity to bind the antibody and, in vivo, it might account for the characteristic histological lesion of CAH.

Down-regulation of the hepatic steroid 16α-hydroxylase, cytochrome P-450 UT-A in male rats with portal bypass

E CANTRILL, M MURRAY, I MEHTA, G C FARRELL (Liver Research Group, Sydney University and Westmead Hospital, Westmead, NSW 2145, Australia) Hepatic microsomal steroid hydroxylase activities were determined in control and portal vein ligated (PVL) male rat liver to test the hypothesis that oestriadiol (E2) accumulation after portal bypass is related to altered regulation of sex-dependent cytochrome P-450 (P-450) isozymes (JCI 1988; 81: 221). With androstenedione as substrate, total hydroxylation of androstenedione (AD) was reduced in PVL liver. This was due to reduction of 16α hydroxylation (to 55% of control, p<0.05); 7α hydroxylation (catalysed by P-450 UT-F), 6β hydroxylation (P-450 PCN-E), 16β hydroxylation (P-450 PB-B), and total oestrogen formation were unaltered. Despite normal total oestrogen production from AD, there was a sevenfold greater accumulation of E2 by hepatic microsomes after portal bypass. Experiments measuring E2 hydroxylation directly showed that, after PVL, 16α hydroxylation of E2 (to oestriol) was decreased (to 44% of control, p<0.02); 17α hydroxylase formation and 17α hydroxylation were not affected. In male rats, 16α hydroxylation of both AD and E2 is catalysed by P-450 UT-A. Accordingly, the content of P-450 UT-A was quantified in hepatic microsomes by immunoblotting; in PVL it was 56% of control levels (p<0.05). Hence down-regulation of P-450 UT-A occurs in portal bypass. This finding suggests a role for portal hypertension in mediating the altered drug and steroid metabolism which occur in cirrhosis (Mol Pharm 1987; 31: 117). Enhanced E2 production after portal bypass, however, does not arise from hepatic aromatisation of androgens. Instead, impaired 16α hydroxylation of AD may enhance extrahepatic metabolism of androgens by pathways which include E2 formation. The reduced hepatic 16α hydroxylation of E2 further enhances the accumulation of this biologically more potent oestrogen at the expense of oestriol, a less potent metabolite. Supported by the NH and MRC of Australia.

Serial prothrombin ratios: a prognostic indicator in paracetamol-induced acute liver failure

P M HARRISON, G J ALEXANDER, J G O'GRADY, R KEAYS, ROGER WILLIAMS (Liver Unit, King's College Hospital and School of Medicine and Dentistry, London) Mortality in grade 3 or 4 paracetamol induced acute liver failure (P-ALF) remains high (48%), despite improved intensive care. Ethical reservations have discouraged liver transplantation, in such cases, although it is of proven value in viral ALF (71% survival in 33 patients). Peak prothrombin time (PT) >180 and acidosis on admission have been shown to identify patients with P-ALF who are at particular risk; those with acidosis are poor candidates for transplantation because of their rapid deterioration. To investigate whether serial estimation of PT complemented peak PT in identification of high-risk groups, 100 consecutive patients with P-ALF were studied retrospectively. The association between peak PT and mortality was confirmed (PT ≥180, 95% mortality; PT 120–179, 45% mortality; PT 90–119, 46% mortality; PT <90, 27% mortality). A rise in PT between days 3 and 4, after overdose, indicated a poor prognosis, irrespective of absolute PT (86% mortality compared to 27% if PT falls, p<0.001). Changes in PT on other days, up to day 7, were uninformative. An increase beyond day 7 was uniformly fatal and indicated sepsis. These data indicate that the peak PT >180 or an increase in PT on day 4 from overdose identify, at an early stage, those patients with a less than 15% chance of survival. In selected cases meeting these criteria liver transplantation should be considered while sufficient time remains to locate a donor.

Anorectal varices: prevalence in a cirrhotic population

S W HOSKING, H L SMART, A G JOHNSON, D R TRIGER (University Surgical and Medical Departments, Royal Hallamshire Hospital, Sheffield) Anorectal varices (ARV) are usually asymptomatic, but sometimes they bleed catastrophically. Unlike oesophageal varices (OV), their prevalence in cirrhotic patients is unknown. Furthermore, the relationship between ARV, haemorrhoids and portal hypertension is undocumented.

One hundred consecutive patients presenting with either newly diagnosed liver disease, first GI bleed (13), or OV rebleeding (29) were examined for ARVs by anorectoscopy. ARVs were diagnosed either by the presence of external compressible anal varices and/or the presence of dilated varicosities within the anal canal and rectum. Forty four patients had ARVs (six anal, 16 anorectal, 22 rectal). They were unrelated to age, sex, or Child's grading. ARVs coexisted with haemorrhoids in 30% of all patients, but were present without haemorrhoids in 14%; 33% had haemorrhoids alone, while 23% had neither. In those patients without oesophageal varices, ARVs were present in 20%, in patients with non-bleeding OVs, 37%, and this increased to 63% in patients with bleeding OVs. Of those with ARVs and OVs (n=40), previous oesophageal sclerotherapy had been performed in 45%. ARVs become commoner as complications of portal hypertension develop. They do not indicate severity of liver disease and their presence is not caused by previous oesophageal sclerotherapy. The natural history, however, remains unknown and merits prospective longitudinal study.

Bleeding varices in the elderly – well worth treating

S W HOSKING, N C BIRD, D R TRIGER, A G JOHNSON (University Surgical and Medical Departments, Royal Hallamshire Hospital, Sheffield) Bleeding from peptic ulcer carries a worse prognosis in elderly patients and this influences management. In contrast, variceal bleeding in the elderly has been barely studied, leaving clinicians often unsure of appropriate management. Since 1980 we have admitted 217 patients (146

The British Society of Gastroenterology
Primary biliary cirrhosis – its prevalence and variceal haemorrhage

H L SMART, D BULLMORE, M S LOSOWSKY, D R TRIGER (University Departments of Medicine, Royal Hallamshire Hospital, Sheffield and St James’s Hospital, Leeds)

Primary biliary cirrhosis (PBC) is uncommon, shows variable geographical prevalence and features infrequently in reported series of variceal haemorrhage from either Europe and North America. We have examined its occurrence as a cause of portal hypertension in patients admitted to two referral centres with bleeding oesophageal varices. Over a seven year period, 162 patients were admitted to the Royal Hallamshire Hospital Sheffield, and 136 to St James’s Hospital, Leeds with endoscopically proven variceal haemorrhage. Case note review revealed that overall PBC was second only to alcoholic cirrhosis as a cause of portal hypertension in Leeds (15% and 36% respectively) and Sheffield (15% and 39% respectively). This finding could not be accounted for by supradistinct referrals. Moreover, in women, PBC was the single most important underlying cause of variceal haemorrhage in both centres (Leeds 32%; Sheffield 31%). The known high prevalence of PBC in Sheffield contributes significantly to the incidence of variceal haemorrhage. That a similar proportion of variceal bleeds in Leeds are due to PBC suggests that there is a similar prevalence of advanced PBC in the nearby Yorkshire region. The geographical variation in the prevalence of PBC would appear to be related to the diagnosis of cases before the onset of significant portal hypertension.

Psychometric deficits and MRI brain scan abnormalities in non-encephalopathic patients with cirrhosis

A A DUNK, J MOORE, H DEANS, F SMITH, J BESSON, T S SINCLAIR, N A G MOWAT, P W BRUNT (Departments of Medicine, Neuropsychology, Radiology, Nuclear Medicine and Mental Health, Royal Infirmary, Aberdeen) Latent hepatic encephalopathy is not detectable by current bedside techniques. Nineteen cirrhotic patients with no overt evidence of encephalopathy have undergone psychometric testing and magnetic resonance imaging (MRI) of the brain, in order to determine the frequency of latent encephalopathy in the ‘healthy’ cirrhotic population and whether this disorder is associated with measurable changes in cerebral morphology. Most patients were Pugh grade A (n=17), 17 had varices, and three had previously been encephalopathic. All alcoholics (n=10) were abstinent. Compared with matched controls with normal liver function, visual memory and reaction times to light sound and choice stimuli were all significantly impaired in cirrhotics, irrespective of aetiology. Sixteen

Diethylaminoethyl-dextran (DEAE-Dextran) for itching in primary biliary cirrhosis: a double blind trial

A FLOREANI, M CHIARAMONTE, M ZAGOLIN, R NACCARATO (Department of Gastroenterology, Institute of Internal Medicine University of Padova, Italy) In an attempt to find a bile sequestering substance as an alternative to cholestyramine, which may have significant side effects, we studied DEAE-Dextran (a MW 500000 polysaccharide) in a double blind crossover trial v placebo. Twelve female PBC patients with severe pruritus entered the study. DEAE-Dextran or placebo were given alternatively for 15 days at a dosage of 1000–2000 mg three times daily. Pruritus was assessed by an intensity scale. Total bile salts were assayed at the beginning and the end of each cycle.

During placebo no changes in itching were observed. With DEAE-Dextran, five patients experienced complete disappearance of pruritus, two showed a decrease, and five showed no changes. In the seven patients who received placebo first, no significant modification of bile salts was observed after placebo, while bile salt levels decreased significantly after DEAE-Dextran (from 29-37 (15-98) to 20-2 (12-78) μmol/l, p<0.05). In the five patients who had DEAE-Dextran first, a slow decrease followed by a rebound after placebo was observed. The five patients with no relief from itching did not show any decrease in serum bile acid levels.

In conclusion, DEAE-Dextran was effective in controlling pruritus in 40% of the patients; the introduction of higher dosages should increase its efficacy.

Enhanced survival of hepatocyte implants in bile-duct obstructed rats

V JAFFE, H DARBY, H J F HODGSON (Departments of Surgery and Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road, London) In syngeneic animals ectopically implanted hepatocytes survive and proliferate despite an intact recipient liver. An initial phase of hepatocyte loss is succeeded by proliferation. In this study we examined the fate of implanted hepatocytes in animals with severe hepatic dysfunction. Sixteen August rats were randomised to bile duct ligation and transection or sham surgery and 2 x 10⁶ isolated syngeneic hepatocytes implanted in the spleen 24 hours later. They were killed after six weeks, and ligated animals had massive bile duct dilatation, compressing adjacent liver, and portal venous collaterals. In eight animals studied by quantitative splenic histology, there was a striking increase in cells counted (hepatocytes per 15 random sections; bile duct ligated, mean 8752 ± 2507 cf sham operated, 856 ± 235; p<0.05). Histological assessment showed a marked difference in architecture in the areas of hepatocyte colonisation. In obstructed animals, in addition to cords or markedly polyploid hepatocytes, well-formed ductules with a characteristic biliary epithelium were prominent. Biliary obstruction therefore promotes survival of implanted hepatocytes and modulates their growth pattern. The relative roles of obstructive jaundice, diminished hepatocyte reserve and portal hypertension in this modulation is uncertain but this greatly enhanced survival of cells in obstructed animals encourages further exploration of hepatocyte transplantation for the treatment of chronic liver disease.
of 19 cirrhotics failed two or more of the seven performance based psychometric tests, compared with 0/19 in the control group, and by the criteria of Schomers et al. most cirrhotics would be considered unfit to drive. Several statistically significant morphological differences between the brains of cirrhotics and controls were found on MRI. These changes, indicating cerebral atrophy, were more apparent in alcoholic than in non-alcoholic cirrhotics. The degree of association between psychometric performance and changes in cerebral morphology was poor, suggesting that latent encephalopathy is likely to be a metabolic disorder.

Does HIV infection affect loss of HBeAg among homosexual men with chronic hepatitis B?

R H T LOKE, N DAYTON, J C COLEMAN, K MACRAE, J M MURRAY-LYON (Departments of Gastroenterology and Virology, Charing Cross Hospital, London) Our aim was to see if HIV infection alters the natural history of chronic hepatitis B as reflected by loss of HBeAg.

One hundred and nine male homosexuals with chronic hepatitis B (HBsAg positive greater than six months), followed up at three to six monthly intervals for a median of 33.5 months (range 5-174). Prospective and retrospective testing of HBsAg, HBeAg, anti-HBe, anti-HBs, and anti-HIV were performed using commercially available kits. Date of entry taken as six months from first documented positive test for HBsAg. Data analysed using SPSS-X programme.

Median age at entry, 31 years (range 17-64), with anti-HIV positive group younger (p=0.001). Forty eight of 109 (44%) were anti-HIV positive with median duration of 27 months (range 1-77), of which 10 lost the HBeAg compared with 27 of the 61 anti-HIV negative subjects (p=0.022). Life-table analysis (Lee-Desa statistic), however, did not show any statistically significant difference (p=0.107). Of the anti-HIV positive subjects, 10 developed the persistent generalised lymphadenopathy syndrome, four developed the AIDS-related complex and nine developed AIDS.

HIV does not affect loss of HBeAg in chronic hepatitis B.

A comparison of albendazole, mebendazole, and praziquantel in echinococcus multilocularis

D H TAYLOR, D L MORRIS (Department of Surgery, University Hospital, Nottingham) E multilocularis (alveolar hydatid disease) remains an almost invariably fatal disease. This is the first comparison of mebendazole (MEB), albendazole (ALB), and praziquantel (PRAZI) against E multilocularis infections in vivo. Fifty infected gerbils (three months post inoculation) entered, 10 were killed to assess parasite weight at week 0, 10 controls (CONT), 10 MEB 50 mg/kg/day, 10 ALB 50 mg/kg/day, and 10 PRAZ 500 mg/kg/day gavage for 25 wks. Animals weighed weekly. In week 25 surviving animals underwent necropsy, parasite material removed and weighed, protoscolex viability assessed. Cyst weight compared with week 0 material. CONT and PRAZI had more material (p>0.01), MEB and ALB not significantly different. ALB material weighed less than CONT, MEB, and PRAZI (p<0.01, 0.05, and 0.001 respectively). MEB had less material than PRAZI though not of CONT (p>0.01 and 0.1). PRAZI no different to control. In mean weight gain of the entire animal during the period week 10-25, ALB was less than CONT, MEB, and PRAZI (p<0.001), MEB was less than CONT and PRAZI (p<0.01). PRAZI not less than CONT (p>0.01). Percentage viabilities of protoscoleces were CONT 95%, MEB 67%, ALB 25%, and PRAZI 82%.

Praziquantel is able to kill protoscoleces of E multilocularis in situ, but not inhibit growth of cysts. Albendazole is better than mebendazole or praziquantel in preventing growth and is therefore the drug of choice.

IBD POSTERS

**Indium leucocyte scintigraphy: a simple test for assessing patients with Crohn's disease unresponsive to therapy**

J G WHEELER, A DUNCAN, N F SLACK, R F HARVEY (Frenchay Hospital, Bristol) Patients with active Crohn's disease respond poorly to treatment with corticosteroids if they have developed an intra-abdominal abscess, a complication which is often difficult to confirm clinically. Seventeen patients with Crohn's disease unresponsive to therapy underwent **indium leucocyte scintigraphy in an attempt to differentiate between active bowel inflammation and abscesses. All patients also had barium and/or computed tomography studies, mostly within two weeks of **indium leucocyte scintigraphy.

Thirteen patients subsequently underwent laparotomy. After reinjection of **indium oxine labelled autologous leucocytes, gamma camera images were accumulated at approximately four, 24, and 48 hours. Images were reviewed to assess: (i) The relationship between the extent of active disease shown by **indium leucocyte scintigraphy and that shown on barium studies. (ii) The presence of intra-abdominal abscesses.

**Indium leucocyte scintigraphy invariably demonstrated the presence of active bowel disease, but underestimated its extent in two patients and overestimated it in three. It correctly identified and localised each of six confirmed intra-abdominal abscesses; computed tomography identified five. There were no false positive results. Abscesses were consistently distinguishable from inflamed bowel.**

**Indium leucocyte scintigraphy accurately differentiates between inflamed bowel and abscesses in patients with unresponsive active Crohn's disease, contributing significantly to the management of these patients.**

Enhanced interleukin 1-β (IL1-β) production by mononuclear cells (MNC) isolated from inflammatory bowel disease (IBD) mucosa

Y R MAHIDA, K WU, D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) Interleukin 1 mediates a wide variety of biological functions during inflammation. Interleukin 1-β production by MNC isolated from six normal and 11 IBD colonic mucosal specimens was studied. Mononuclear cells were isolated by EDTA-collagenase. EDTA-collagenase. 10* MNC (in 1 ml) were incubated for 45 hours with or without 10 μg lipopolysaccharide (LPS). Supernatant was collected and stored at -70°C. Interleukin 1-β was measured by ELISA and results expressed as median (range) IL1-β in pg/ml.

There was significantly more IL1-β produced spontaneously by MNC from active IBD mucosa (190 (45-700)) compared with MNC from normal mucosa (20 (0-165)). Stimulation with LPS significantly enhanced IL1-β production by MNC from IBD mucosa (250 (70-790)) but not from normal mucosa (35 (0-145)). In three colons with distal ulcerative colitis, there was more IL1-β produced by MNC from inflamed mucosa (500 (95-700)) compared with MNC from non-inflamed mucosa (35 (25-120)). When MNC were depleted of macrophages by panning with monoclonal anti-
body 3C10, less IL1-β was produced. Enhanced IL1-β production by MNC from IBD mucosa is likely to play an important role in mediation of many inflammatory responses. The enhanced production is likely to be due to a recruited population of cells as MNC from normal colonic mucosa appear to be 'desensitised' to the effect of LPS.

Faecal lysozyme excretion and alpha-1-antitrypsin clearance in the assessment of disease activity in inflammatory bowel disease

G E GRAMA-BOHBOUTH, I BIEMOND, A S PEÑA, I T WETERMAN, H W VERSPAGET, J BROUWER, C B H W LAMERS (Department of Gastroenterology and Hepatology, University Hospital, Leiden and Department of Immunology, SSDZ Delft, The Netherlands) We have investigated the value of faecal lysozyme excretion and alpha-1-antitrypsin (α1-AT) clearance in the assessment of inflammatory bowel disease (IBD) using the results of faecal Indium-111 excretion as golden standard of gut inflammation. Sixty patients with IBD (37 women, 23 men) were studied. Thirty-three had Crohn’s disease (CD) of the small bowel and 27 had IBD with colonic localisation. Patients were divided into mild, moderate and severe according to their disease activity. Ten patients without intestinal inflammation were used as a control group.

The mean faecal lysozyme excretion was significantly higher (p<0.001) in patients with colonic (18.4 mg/24 h) and small bowel disease (1.3 mg/24 h) than in the control group (0.28 mg/24 h). However, after division for disease activity only the patients with moderate and severe colonic disease had significantly increased lysozyme excretion when compared with controls (p<0.01). Only colonic disease showed a significant correlation with the 24 h faecal Indium-111 excretion (r=0.58, p<0.001). The mean α1-AT clearance was significantly (p<0.001) higher in IBD patients with either localisation (182.5 ± 109.4 ml/24 h) than in the control group (141 ± 24 ml/24 h). For both localisations α1-AT correlated significantly with 24 h faecal Indium-111 excretion (r=0.50 and r=0.71; p<0.01, p<0.001). Patients with moderate and severe activity but not those with mild disease had independent of the localisation an increased α1-AT clearance when compared with controls (p<0.0001).

The present study shows that both faecal lysozyme excretion and α1-AT clearance represent simple and safe methods to assess disease activity in IBD. Compared with faecal Indium-111 excretion, they have the advantage to be less expensive and devoid of radiation exposure.

Intrajejunial prostanooid release in response to deoxycolic acid: an adaptive intestinal mechanism to irritative stimuli?

F CASELLAS, F GUARNER, R RODRIGUEZ, J R MALAGELADA (Digestive System Research Unit, Hospital General Vall d’Hebron, Barcelona, Spain) We hypothesised an adaptive mechanism of the intestinal mucosa to luminal irritants and tested it by quantifying prostanooid release in response to deoxycolic acid (DCA) perfusion in healthy man. In seven volunteers, we placed a triple lumen tube in the jejunum. At the angle of Treitz, we infused at 5 ml/min an isosmotic solution of mannitol 180 mM, xylose 100 mM, and PEG-4000 2 g/l, with or without DCA 2.5 mM. This concentration of DCA is similar to that found postprandially in man. Through the aspiration port (60 cm distally, with air-vent) we collected luminal contents continuously by siphonage, pooled it at 10 min intervals and measured PEG (by turbidometry), 6 ketoPGF1α, TXB2, and PGE2 by specific RIA’s. In each volunteer we randomly perfused solution with or without DCA for 70 min each (30 min equilibration, 40 min test) with 30 min rest period in between.

During perfusion without DCA appreciable quantities of all three prostanooids were constantly released into the lumen. With DCA perfusion, PGE2 release increased markedly and steadily over time (p<0.05), while changes in TXB2 or 6 ketoPGF1α were not significant. With DCA, intestinal net flow almost doubled from 2.54 ml/min (without DCA) to 4.58 ml/min, p<0.05 6 ketoPGF1α, TXB2, and PGE2 are normally released into the intestinal fluid. Intestinal PGE2 release increases markedly in response to low concentration of DCA as fluid secretion is induced. These results support the existence of an adaptive mechanism to physiologic irritants such as DCA.

Faecal and mucosa associated flora in Crohn’s colitis

M C WINSLET, D J YOUNGS, D W BURDON, M R KEIGHLEY (General Hospital, Birmingham) The beneficial effect of metronidazole and salazopyrine in Crohn’s colitis suggests that disease relapse may be associated with abnormal colonic flora. This study compared the mucosa associated (MAF) and faecal flora (FF) in patients with active Crohn’s colitis (n=20) and a control group (n=10).

A rectal biopsy and adjacent faecal sample were taken. The biopsy was washed (x6) in isotonic diluent and macerated. The viable count of MAF and FF was assessed by single drop dilution (10⁻¹-10⁻⁷) onto selective and non-selective media. Comparison of matched mucosal and faecal samples revealed similar carriage, viable aerobic and anaerobic counts but a reduction in the number of mucosal aerobic species (median MAF=2, FF=4, p<0.05) and total species (p<0.05) in Crohn’s colitis and controls. There was no significant difference in the mucosal or faecal species carriage rate or quantitative aerobic and anaerobic viable count between Crohn’s colitis and controls (control faeces 2.7⁰ (1.1⁰–7.0⁰); colitis faeces 2.3⁰ (1.3⁰–1.1⁰) NS. Control mucosa 1.3⁰ (1.3⁰–3.3⁰); colitis mucosa 2.0 (3.9⁰–2.6⁰).

This study suggests that mucosa associated flora represents an independent ecosystem rather than simple contamination from adjacent faeces. This study does not support the hypothesis of an abnormal colonic flora in active Crohn’s colitis.

Candidacidal activity of Crohn’s disease neutrophils

F T CURRAN, D J YOUNGS, R N ALLAN, M R B KEIGHLEY (The General Hospital, Birmingham) We have investigated the ability of Crohn’s disease neutrophils to kill Candida albicans. Neutrophils were isolated from the peripheral blood of 20 patients with Crohn’s disease and 15 healthy volunteers and suspended in phosphate-buffered saline at 5×10⁶ cells/ml. Candida albicans was grown to a stationary phase in broth culture and suspended in phosphate-buffered saline at 10⁷ organisms/ml. Neutrophils and Candida were then incubated together at 37°C in a shaking water bath in the presence of fresh serum. At 30 and 60 minutes samples were withdrawn, neutrophils lysed and candida survival assessed by colony counting. Results were compared with control suspensions of candida incubated with serum alone. After 30 and 60 minutes in the presence of autologous serum normal neutrophils killed a mean of 58.7% and 75.2% of candida respectively and Crohn’s neutrophils 36.0% and 51.9% respectively. The results did not alter significantly when normal neutrophils were incubated with candida in the presence of Crohn’s disease serum and Crohn’s disease cells in the...
High dose methylprednisolone in the treatment of active ulcerative colitis

A Ireland, W Rosenberg, D P Jewell (Gastroenterology Unit, John Radcliffe Hospital, Oxford) Pulsed high dose methylprednisolone therapy is effective in various immunologically mediated diseases. As there has been no recent improvement in the standard treatment of severe ulcerative colitis (UC), a pilot study was set up to examine the role of high dose methylprednisolone in this group of patients.

Twenty consecutive patients with severe active UC were entered. There were nine men and 11 women. Severe disease was defined as eight or more stools/day with blood and mucus, plus evidence of systemic upset. Five patients had total UC, 10 left sided and five proctitis. After baseline measurements, all patients were placed nil per mouth for five days. One gram of methylprednisolone was given daily iv for the first three days, followed by 100 mg hydrocortisone six hourly for days 4 and 5 of the regime. All patients received a 100 mg hydrocortisone rectal drip twice daily.

Eight of 20 patients failed to respond to iv steroids and underwent surgery. The remainder settled well on treatment. The surgery group tended to be younger, male, and with more extensive disease. The surgical rate in this unit has been constant at 20–25% during the last 15 years. Hence, the surgical rate of 40% was unexpected and has not encouraged a controlled trial to be set up.

Elemental diet reduces intestinal inflammation in Crohn’s disease

I Bjarnason, K Teahan, G Zanelli, P Smethurst, A J Levi (MRC Clinical Research Centre, Watford Road, Harrow, Middlesex) Elemental diet (Vivonex) is an effective form of treatment for acute Crohn’s disease. We studied 18 consecutive hospitalised patients with acute Crohn’s disease, before and after four to six week treatment with Vivonex, with 111Indium leucocytes, including a four day faecal collection which provides an objective index of intestinal inflammation, to assess whether clinical relapse is associated with reduced inflammatory activity.

Seventeen patients improved clinically: Harvey and Bradshaw decreasing from 8 (1) (mean (SE)) to 3 (1) (p<0.05). This was matched by a significant decrease in the faecal 111Indium excretion. 11-4 (1-8)% to 2-2 (0-7)% (p=0.001. N=1-0% of these two had low initial excretion values (1-2 and 1-6% respectively) both of whom required surgery for strictures. One patient, who improved clinically, had significant post-treatment inflammatory activity (faecal 111Indium excretion values (13-3% and 19-0% pre- and post-treatment).

(1) These studies confirm that clinical improvement in Crohn’s Disease after elemental diet is associated with reduced inflammatory activity. (2) Persistently high post-treatment 111Indium excretion values may predict an early relapse. (3) The use of 111Indium leucocytes may help in determining the potential reversibility of radiological strictures.

Rectal mucosal blood flow is increased in proctitis

G L Lamont, J D Harrison, D L Morris (Department of Surgery, University Hospital, Nottingham) Rectal mucosal blood flow has been measured in a group of normal patients (n=12) and compared with a group with active proctitis (n=18) to assess differences between the groups. Additionally, the effect of enema administration on rectal mucosal blood flow has been measured in some normal patients (n=23). Statistical comparison was made using the Mann-Whitney U test.

Mucosal blood flow was measured in 53 patients before sigmoidoscopy at 10 cm from the anal margin on the posterior wall of the rectum. Measurements were made using a ‘Laserflo’ laser Doppler probe (TSI Inc) interfaced to a BBC microcomputer to give a continuous reading.

The mean blood flow in mls/100 g tissue/min, was significantly higher in active proctitis (Blood flow, median (range): 39-04 (14-2–93-3)) than in patients with no rectal pathology (17-2 (10-7–31-2); p<0.02). Patients who had received an enema before sigmoidoscopy also showed a significant increase in blood flow when compared with those without enema preparation (34-4 (13-3–70-1) v 17-2 (10-7–31-2); p=0-02).

Rectal mucosal blood flow has been shown to be increased after bowel preparation, and in patients with active proctitis, and may be a useful index in monitoring inflammatory bowel disease.

The next operation for Crohn’s disease will not be needed sooner if strictureplasty is used rather than resection

J Sayfan, J Alexander-Williams, A Allan, H Andrews (The General Hospital, Birmingham) Crohn’s disease is a chronic disease characterised by frequent exacerbations and often complicated by stenosis and characterised by the need for repeated operations. We have used strictureplasty for Crohn’s disease strictures since 1981. It has been shown to be feasible, safe and suitable for multiple strictures but the long-term results await evaluation. Therefore, we have compared the disease free interval between either resection of strictureplasty and the need for another operation for a lesion (usually stenotic) at the site of the original strictureplasty or anastomosis.

In 82 patients, having 130 strictureplasties and 221 resections these criteria were met; 41 having resection with mean follow up of 17-4 years and 41 having a combination of resection and strictureplasty or strictureplasty alone, with mean follow up of 15-2 years.

After resection the mean surgery free interval was significantly longer (7-9 years) than after strictureplasty (2-9 years). This trend was confirmed by an actuarial cumulative curve of the re-operation rate.

The groups did not have similar disease distribution or operation indications so conclusions must be guarded.

We conclude that, for an intestinal stenosis, when the operative choice is between resection or strictureplasty a new stricture is likely not to necessitate re-operation much sooner if strictureplasty is chosen.
glucagon, we have investigated the possible involvement of glucagon on the stomach to caecum transit time (SCTT) during the progression of experimental diabetes in the rat. Adult Sprague-Dawley rats were injected with streptozotocin (60 mg/kg iv) which induced glycosuria after two days. Stomach to caecum transit time was measured using the non-invasive breath hydrogen technique. Diabetic rats were studied one, two, four, and eight weeks after injection and normal SCTT was established in age matched controls. A third group of rats received a single (ip) dose of either 50 μg or 75 μg pancreatic glucagon or its diluent.

In diabetic rats, SCTT was prolonged by 46% at one week, 61% at two weeks, 45% at four weeks, and 64% at eight weeks. At all time points studied SCTT was significantly prolonged in comparison with controls (p<0.01). In normal rats, glucagon injection was associated with delayed SCTT by 25% (50 μg) and 32% (75 μg) in comparison with diluent (p<0.05). Autonomic neuropathy is unlikely to account for delayed SCTT in early stages of diabetes in the rat and it is possible that hyperglucagonaemia may be involved.

Proximal duodenal secretion in the acutely undernourished rat

M C PEREIRA, A YOUNG, R J LEVIN (Department of Biomedical Science, The University, Sheffield) After starvation for 72 h, the proximal duodenum (D) becomes hypersecretive to secretagogues both in vivo and in vitro, resulting in increased electrogenic HCO₃⁻ and Cl⁻ secretion. The effect of acute dietary restriction (8 g/d for nine days, 33% of normal intake) on secretion in the D was investigated. Electrogenic ion secretion across sheets of D removed from anaesthetised rats and stripped of external muscle was monitored as the short circuit current (Isc). Both basal Isc and maximal increases above basal level (ΔIsc) were measured. Secretagogues used were dibutyryl cAMP (cAMP, 1 mM); 5-hydroxytryptamine (5-HT, 50 μM); acetylcholine (Ach, 1 mM); prostaglandin E₂ (PGE₂, 28 μM) and forskolin (F, 5 μM). No differences in basal Isc between fed controls and the acutely undernourished (AU) animals were seen, but all of the secretagogues induced a significantly greater response in the AU group (cAMP +57%, p<0.05; 5-HT +88%, p<0.01) Ach +77%, p<0.001; PGE₂ +73%, p<0.01; F +74%, p<0.001). Thus reduced or absent food intake hyper-sensitises the electrogenic component of duodenal secretion to secretagogues.

Hypersecretion induced by staphylococcus aureus enterotoxin B in the rat intestine

A YOUNG, HELEN C NZEGWU, R J LEVIN (Department of Biomedical Science, The University, Sheffield) A major cause of death in human famine or malnutrition is diarrhoea. Little is known about the effects of bacterial enterotoxins on intestinal secretion in the malnourished or starved state. We have investigated the action of S aureus enterotoxin B (ET-B, Sigma) on electrogenic secretion in the rat proximal duodenum (D), jejunum (J), ileum (I), most proximal colon (MPC), midcolon (MC), and distal colon (DC) removed from fed controls and 72 h starved rats. Electrogenic ion secretion was monitored in vitro as the short circuit current (Isc, cm⁻² serosal area) measuring maximal changes above basal level (ΔIsc) in response to mucosal ET-B challenge. At 5 μg/ml, ET-B had no effect on Isc but significant increases were seen with 10 μg/ml. In controls, the ΔIsc never exceeded 5 μA cm⁻² but in the starved group the D, J, I, and MC all gave responses above 10 μA cm⁻² significantly greater than the fed controls (D, J, and I, p<0.001; MC, p<0.05). The MPC and DC had similar responses in fed and starved groups (both, p>0.05). The intestinal hypersecretivity to a bacterial toxin may represent an important factor in the aetiology of the diarrhoea of malnutrition or famine.

Diet deficient in linoleic acid reduces gastric and duodenal mucosal eicosanoid synthesis in the rat

J P KEATING, I TAYLOR (University Surgical Unit, Level F, Centre Block, Southampton General Hospital, Tremorana Road, Southampton) Patients with duodenal ulcer have a reduced ability to synthesise gastric and duodenal mucosal prostaglandins compared to non-ulcer control patients. The aim of this study is to investigate the effect of an essential fatty acid deficient diet on mucosal eicosanoid synthesis.

Male Wistar rats were raised on a standard diet containing 0-56% of linoleic acid and 0-5% of saturated fats. The rats were then fed an essential fatty acid deficient diet containing 10% hydrogenated coconut oil and no linoleic acid for six weeks and thereafter replaced on the standard diet for four weeks. Eight rats were killed at the start of the study and at two weekly intervals for 10 weeks. Measurement of eicosanoids in the mucosal incubates was by radio-immunoassay. After six weeks on the deficient diet gastric prostaglandin E₂ production fell from a mean of 9-24±2-5 ng/mg protein to 1-14±0-42 ng/mg protein, gastric thromboxane A₂ from 3-71±1-27 ng/mg to 0-37±0-13 ng/mg and gastric prostacyclin from 29-03±9-60 ng/mg to 3-02±0-83 ng/mg. Similar changes occurred in the duodenal mucosa. Replacing rats on the standard diet reversed the fall in eicosanoid synthesis. A low dietary intake of essential fatty acids may explain the reduced capacity of duodenal ulcer patients to synthesise prostanoids.

Breath hydrogen testing: an indicator of small bowel overgrowth following ileoanal pouch formation

W KMIOT, J D O’BRIEN, M R KEIGHLEY (The General Hospital, Birmingham) The absolute number of bacteria per gram of ileal chyme and the anaerobic: aerobic ratio increases after ileal reservoir construction. The production of hydrogen by anaerobic fermentation is a recognised measure of small intestinal bacterial overgrowth.

After restorative proctocolectomy 30 patients performed a series of breath hydrogen estimations at five minute intervals for one hour. A further 30 age/sex matched controls were also tested. All subjects remained fasted for a minimum of 20 hours.

Patients with ileal reservoirs had a higher mean fasted breath hydrogen value than control subjects (16-4 v 5-7 parts per million (ppm), p<0.05). Six pouch patients did not exhibit a breath hydrogen rise either on repeated tests or on instillation of isotonic glucose directly into the pouch. The remaining 24 pouch patients exhibited rises of at least 20 ppm. All patients with a fasting breath hydrogen level of >10 ppm had anaerobic bacterial pouch overgrowth (>10⁷ cfu/g), compared with none of the remainder (p<0.05). There was no relationship between ileal overgrowth and the frequency of defection. This study confirms that fasting non-invasive breath hydrogen sampling acts as a sensitive indicator of ileal bacterial overgrowth after pouch formation.

Esfamol is trophic to the rat small intestinal mucosa

A P JENKINS, M A GHATEI, S R BLOOM, R P H THOMPSON (Gastrointestinal Laboratory, Rayne Institute, St Thomas’ Hospital
Mucosal changes in elderly patients with small bowel bacterial overgrowth

N Y HABOUBI, G S LEE, P ASQUIT (Department of Geriatric Medicine, Maelor Hospital, Wrexham and Metabolic Unit, East Birmingham Hospital, Birmingham) Small bowel bacterial overgrowth is recognised as an important cause of malabsorption in the elderly.

Sixteen elderly patients, four men (mean age 78 years) with proven small bowel bacterial overgrowth were studied. Endoscopic small bowel mucosal biopsies were examined morphometrically before and four to six months after cyclical courses of amoxycillin-clavulanic acid. They were compared with biopsies from 23 controls, nine men (mean age 81 years). Mean villous height was significantly lower in the pre-treatment group (82.9 μm) than in the post-treatment (128.3) and control groups (132.9), (p<0.001). Similar significant differences were also found in mean crypt and total mucosal heights in these groups.

In contrast, the mean intraepithelial lymphocytes number was higher in the pre-treatment group (23.5) than the post-treatment (10.3) and the control groups (12.4), (p<0.01, and <0.001 respectively).

These changes could be due to bacterial autigenic stimuli of the small intestinal mucosa. The marked and relatedly rapid response to therapy demonstrated the reversibility of these changes when bacteria was eliminated or reduced in number.

Role of superoxide radicals in gut peptide release from refurred ischaemic intestine

L MELEAGROS, R A SPOKES, M A GHATEI, S R BLOOM (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London) Reperfusion of the ischaemic intestine causes severe vascular and mucosal injury due to the generation of superoxide radicals (SO) and is accompanied by the release of the powerful vasodilator gut peptides vaso-active intestinal polypeptide (VIP) and b-calcitonin gene related peptide (b-CGRP) and the mucosal trophic peptide enteroglucagon (EG). Involvement of these peptides in refurrence of injury was investigated using allopurinol (Ap) to suppress SO and prevent injury. The superior mesenteric artery (SMA) was occluded for 20 minutes in four groups of anaesthetised Wistar rats (n=6 per group) in two experiments. The gut was refurred for 2 in the first (groups A1, B1) or 20 minutes in the second (A2, B2) experiment and arterial blood was collected. Plasma peptides (pmol/l) were measured by radioimmunoassay and results were analysed by ANOVA. Control rats (C1, C2, n=6 in each) had no SMA occlusion. Groups B1 and B2 received Ap orally (50 mg/kg/day) for three days and iv (50 mg/kg) before SMA occlusion. Plasma peptide levels (mean(SE)) rose in A1 and A2, VIP was unaffected by Ap. However, Ap abolished the late rise in both-CGRP: A1 38 (4)*, B1 27 (5)*, C1 6 (1) (**p<0.005 v C1); A2 37 (7)*, B2 18 (4)* C2 15 (4) (*p<0.01 v C2, ’p<0.02 v A2) and reduced both the early and late rise in EG: A1 205 (38)*, B1 104 (8)*, C1 67 (6); A2 135 (11)*, B2 65 (10)*, C2 38 (1) (**p<0.005 v C1 or C2, *p<0.05 v A1 or A2, C1 or C2). Therefore SO may mediate their vascular effects by causing release of peptides such as b-CGRP, which is inhibited by allopurinol. Enteroglucagon may be involved in post-injury mucosal regeneration as its plasma levels relate to the severity of injury.

Effect of age on small bowel adaptation and growth after proximal enterectomy

G J POSTON, T SAYDIARI, J P LAWRENCE, R W ALEXANDER, C M TOWNSEND, J C THOMPSON (INTRODUced by I S BENJAMIN) (University of Texas Medical Branch, Galveston, TX, USA) Massive enterectomy may be necessary for Crohn's disease in younger patients, and intestinal infarction in older patients. Nothing is known, however, on the effect of age on the capacity of the small bowel to undergo adaptive changes following massive enterectomy.

Thirty three month old and 20 month old F344 rats were studied. Half of each group underwent a 60% proximal small bowel resection with end to end anastomosis and the other half underwent midsmall bowel transection with reanastomosis. Five, 14, 21 days, 14, and 21 days after surgery five rats from each age group were killed. All the ileal mucosa from the transected rats and the distal 40% of small bowel mucosa from the control rats, were scraped and analysed for DNA content.

All rats lost weight immediately after surgery but by 21 days both groups of younger rats achieved similar increases in body weight from preoperative values. Older rats continued to lose weight. Young rats completed their post resectional small bowel adaptive hyperplasia by 14 days but comparable adaptation was not achieved until 21 days in the old rats.

The capacity for bowel mucosal growth and adaptation after enterectomy is preserved into old age, but is significantly delayed and associated with a continuing loss of body weight at a time when younger rats are increasing body weight after surgery.

Complement dependent antiepithelial cytotoxic antibodies are present in the serum of patients with endemic tropical sprue

GEORGE KURIAN, D W BROWN, J R DANIEL, V MATHAN (INTRODUced by PROFESSOR M S LOSTOWSKY) (Department of Gastroenterology and The Wellcome Research Unit, Christia Medical College and Hospital, Vellore 632 004, India) Histological similarities in the small intestinal lesion between tropical sprue (TS) and graft versus host disease, where antiepithelial antibodies probably have a pathogenic role, initiated a search for similar antibodies in the sera of patients with endemic tropical sprue. Using two colon carcinoma cell lines (SKCO-1, HT-29) and a control non-epithelial rhabdomyosarcoma cell line.
jejunal biopsy cases dependent cytotoxic activity against (RD), 29-9.4% of Medicine), were enumerated with cytotoxic cells, indicating that the cytotoxicity was specifically against epithelial cells. (c) Both IgG and IgM fractions, separated on a sucrose gradient, had similar cytotoxic activity. These results suggest that anti-epithelial cytotoxic antibodies may play a role in the pathogenesis of the mucosal lesion in tropical sprue and may contribute to the persistence of the lesion leading to the chronic nature of the disease.

WITHDRAWN—The role of the TNF β (lymphotxin) in the pathology of coeliac disease

A new diagnostic test of gluten sensitivity: a prospective study of rectal gluten challenge

D E loft, M N Marsh, P T Crowe (Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) We previously showed (Gut 1987; 28: A1392) that instillation of Faerz fraction III (FF3) increases rectal crypt epithelial lymphocytes (CEL) of treated coeliac patients (TCD) six hour post-challenge. Since these data indicated that a 10% increase in CEL would have a predictive value of 100%, we evaluated this index prospectively in screening for untreated coeliac disease (UCD) and as a confirmatory test for TCD.

Forty three subjects referred consecutively for jejunal biopsy were studied. On the same day as jejunal biopsy, a rectal biopsy was taken before and six hour post-challenge with 2 g FF3 instilled rectally. Total CEL overlying 10° µm² muscularis were enumerated by computerised image-analysis.

There were 21 non-CD, 13 TCD and nine UCD established by the ‘gold standard’ jejunal biopsy criteria. There was no difference in the pre-challenge CEL (means: SE: non-CD 46 (3); TCD 41:1 (5-6); UCD 52 (7)). Non-CD did not respond to FF3 (% change −9-4 (3)); CD responded to FF3 (% change TCD 127 (25) p<0-005; UCD 29 (10) p<0-005). The specificity=90%. Sensitive TCD=92%; UCD=88%. CD nor control subjects responded to β lactoglobulin.

Rectal gluten challenge is a simple, safe, reliable test of gluten sensitivity with high sensitivity and specificity. It provides rapid confirmation of gluten sensitivity in TCD and a screening test where jejunal biopsy may be difficult or hazardous.

Evidence against the involvement of adenovirus 12 in the pathogenesis of coeliac disease

PD Howdle, ME Blair Zajdel, CJ Smart, L K Tedosiewicz, G E Blair, M S Losowsky (Department of Medicine, St James’s Hospital and Department of Biochemistry, University of Leeds, Leeds) The description of an amino acid sequence homology between the E1B-58kDa protein of adenovirus 12 and gliadin led to the suggestion that previous infection by this virus and subsequent exposure to gliadin could trigger the development of coeliac disease in susceptible individuals as a result of immunological crossreactivity. Coeliac patients were subsequently shown to have (i) raised titres of neutralising antibodies to the whole virus and (ii) a cell mediated immune reaction to a synthetic peptide containing the sequence homology. We sought to measure specific antibodies to the E1B-58kDa protein in coeliac patients and normal subjects.

Sera were obtained from seven untreated and 16 treated adult coeliac patients and 10 normal subjects. They were analysed by radioimmunooprecipitation using metabolically labelled adenovirus 12-transformed rat cells (which express the E1B-58kDa protein), followed by separation on polyacrylamide gels. None of the sera had antibodies to the E1B-58kDa protein. Eight of 23 coeliac sera had, however, raised titres of anti-gliadin antibodies, of which only one had a raised titre to a homologous synthetic peptide of gliadin and the E1B-58kDa protein. These data suggest that coeliac patients show little evidence of humoral immunity to the specific adenovirus 12 E1B-58kDa protein implicated in the aetiology of coeliac disease.

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

RG P Rees, JJ Payne-James, GK Grimble, DH Halliday, DBASILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London and Clinical Research Centre, Harrow) Although the value of glycine nitrogen for protein synthesis is disputed, it still represents a significant proportion of total nitrogen in some amino acid solutions used in TPN. Previous data demonstrated that there was no nutritional disadvantage with regard to either nitrogen balance or plasma protein concentrations for parenterally fed patients when up to 23% of total amino acid N was provided as glycine. In the present five-day randomised cross-over study, four metabolically stable patients (26–76 years) with gastrointestinal disease, and requiring TPN, received daily either Vamin 14 or Aminofusin L Forte supplying 13-5 and 13-7 g N containing 8% and 25% of amino acid N as glycine respectively in a 2400 kcal lipid/glucose nutritive mixture. Twenty-four hour total urinary nitrogen was measured continuously for nitrogen balance, and on day 5 of each amino acid infusion, total body protein turnover was measured using a primed constant-infusion of the stable isotope L-(1-14C) leucine. Results (mean (SE)) for the four patients for Vamin and Aminofusin respectively were: net total body protein synthesis rate (mg/kg/h) −6-1 (6-3) v +1-0 (5-8); nitrogen balance (last three days and corrected for blood urea nitrogen) (g N/d) +0-1 (1-3) v 1-7 (1-2). These results provide further evidence to indicate that there is no significant nutritional disadvantage to using amino acid solutions for TPN that contain high concentrations of glycine.

Colonic inflow and small bowel motility during intraduodenal enteral nutrition

AH Raimundo, T Rogers, G Grimble, E Cameron, B SILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London) Diarrhoea occurs in up to 20% of patients receiving enteral nutrition, but the pathogenesis is not clear. The aim of this study was to measure the effect of enteral nutrition on colonic inflow of fluid and small bowel motility in seven normal subjects (mean age 22 yr, 21–25) during constant intraduodenal infusion of an energy dense polymeric diet. Using an oro-caecal 11-lumen tube, 3H-PEG was infused at 1 µl/min into a 20 cm segment terminal ileum just proximal to the caecum. After a steady state, flows were determined at 30 min intervals for four hours before and after continuous intraduodenal infusion (2-8 ml/min) of the enteral diet (7-8 gN/1, 1500 kcal/1). Small bowel motility was recorded proximally at six sites (30 cm apart), spanning 150 cm of tube. Mean terminal ileal flow rates increased significantly (p<0-001) during the diet infusion (20-4 ml/30 (3-8) mean (SE) v 100-7 (7-9)). In the fasting
period phase III migrating motor complexes (MMC’s) occurred predominantly in the proximal small bowel. Total number of MMC’s were significantly reduced during diet infusion (5 (1-8) v 1.6 (0-2)). Postprandial colonic inflow from these data is equivalent to 4-8 l/24 h which is less than the total absorptive capacity of the normal human colon. These data show intraduodenal infusion of energy dense diets convert the small intestinal motility from fasting to fed pattern and the rate of colonic inflow does not exceed the normal absorptive capacity of the colon.

Effect of prefeeding lipid on energy intake from a meal

C P SEPPLE, N W READ (Sub-dept Human Gastrointestinal Physiology and Nutrition, University of Sheffield, Royal Hallamshire Hospital, Sheffield) Infusing lipid into the human small intestine reduces food intake and induces early satiety and is also associated with a delay in gastric emptying. A soup homogenised with 60 g of fat can delay the emptying of a meal fed 20 minutes later. We investigated the effect of feeding the high fat soup on the intake of either a low fat solid meal (2-2 g fat/100 g) or a preselected appetising meal, in six volunteers. The meals were fed 20 minutes after the soup. We measured the time taken to complete the meal, the amount of food and drink consumed and the rate of eating. Subjective sensations of hunger and fullness were measured using visual analogue scales. Further experiments investigated the effect of feeding a high fat breakfast (65 g fat, 927 kcal) v a low fat breakfast (8-1 g fat, 418 kcal) on food intake of a preselected appetising meal at lunchtime. The two breakfasts were similar in appearance and in protein and carbohydrate content. Feeding high fat soup had no effect on the amount consumed from either meal and did not influence sensations of hunger and fullness. The high fat breakfast significantly reduced the amount of meal eaten at lunchtime (p<0.02), the total energy intake of this meal (p<0.05) and the rate of eating (p<0.05) compared with the lunch eaten after the low fat breakfast. Subjects felt significantly less hungry at lunchtime after the high fat breakfast than after the low fat breakfast. Thus, although prefeeding lipid as a soup does not appear to inhibit energy intake from a subsequent solid meal, eating a high fat breakfast inhibits energy intake from an appetising meal consumed at lunchtime.

Postoperative fatigue – even more real than apparent

S E STOCK, M B CLAGUE, J D A JOHNSTON (Departments of Surgery, University of Newcastle upon Tyne and Newcastle General Hospital) Postoperative fatigue is a well recognised but poorly understood phenomenon. Ambulatory monitoring of posture and mobility, using skin sensors and recording of signals on magnetic tape, was carried out over 24 hour periods on 80 patients in their homes before and after abdominal surgery. Fatigue was also assessed subjectively by patients.

Patients spent more time lying at 2 (11.56 (2-70) h; p<0.01; mean (SD)) and four weeks (10.83 (2.50) h; p<0.01) than preoperatively (9.57 (2.01) h), taking less steps at two (533 (8121); p<0.01), four (7872 (6984); p<0.01), and six weeks (9278 (6999); p<0.05) than before surgery (11 267 (8464)), returning to preoperative values at 12 weeks. Although patients’ assessment of fatigue showed an increase at two weeks (5-05 (1.95-5.95); p<0.02; median and interquartile range) than before surgery (4-90 (1-20-5.70)), values reduced thereafter and were significantly less at 12 weeks (1-95 (1-08-5.00); p<0.007).

Postoperative fatigue is a real and measurable phenomenon which may be underplayed by the feeling of wellbeing experienced by patients recovering from surgery.

Evaluation of a hypotonic oral rehydration solution (ORS) in mammalian models

J B HUNT, A F MALIM, A V THILLAINAYAGAM, S CARNABY, E ELLIOTT, M L CLARK, M J G FARKING (Department of Gastroenterology, St Bartholomew’s Hospital, West Smithfield, London) Controversy continues regarding the ideal composition of ORS. The majority of ORS are hypertonic but our previous work suggests that hypotonic ORS are more effective. Using steady state intestinal perfusion of (1) normal human jejunum (n=7-9), (2) normal and cholera toxin (CT)-treated entire small intestine (n=9-12), and (3) rotavirus (RV) infected neonatal rat intestine (n=6-8), we compared the most commonly used ORS in the UK (BNF-ORS Na 35, glu 200 mmol/l; 310 mOs/mkg), with a hypotonic ORS (HYPO-ORS Na 60, glu 90 mmol/l; 240 mOs/mkg) and WHO-ORS (Na 90, glu 110 mmol/l; 331 mOs/mkg). HYPO-ORS promoted more water absorption than BNF-ORS or WHO-ORS in all model systems (p<0.05). Differences were particularly striking in rat CT model (HYPO-ORS +105±4.1 ul/min/36 g; BNF-ORS +2.2±6.9; WHO-ORS +37.3±7.7) and rat RV model (HYPO-ORS +68.7±1.24; BNF-ORS –38.2±8.4; WHO-ORS +5.7±4.9). Similar profiles were found in normal rat and human small intestine. HYPO-ORS promoted approximately two-fold greater water absorption in normal rat small intestine than BNF-ORS or WHO-ORS.

These findings confirm parallelism between human and rat small intestine and suggest that (1) normal and “diseased” intestinal model systems are useful in screening new ORS and (2) that water absorption is improved from hypotonic ORS. These studies provide the rationale for clinical trials of HYPO-ORS in man.

Practical aspects of home enteral nutrition

R H R PARK, A GALLOWAY, R I RUSSELL (Gastroenterology Unit and Department of Dietetics, Royal Infirmary, Glasgow, Scotland) We investigated the practical aspects of home enteral nutrition (HEN). Eleven patients (10 had Crohn’s disease) received HEN for a mean of eight months (range two to 14 months). Technical instruction was given to patients and the time taken for training ranged from one to two days (nine patients) to seven days (two patients). All patients apart from one was on nightly HEN. Only two patients required assistance from a relative. Ten patients used the Flexiflo pump system. Time to set up the enteral feed took five minutes (two), 10 minutes (five), and 15 minutes (four). Four patients found the Flexiflo pump to be heavy at the start of the feed and one found it to be noisy. Nine patients considered the Flexiflo pump to be accurate delivering 95% (three), 100% (six) of the feed over the determined infusion time. Only four patients (36%) found their sleep was interrupted more often when on the enteral feed by sounds of the pump. No patient had experienced symptoms suggestive of reflux or aspiration. Six patients (55%) considered that HEN had produced an improvement in their lifestyle, with a reduction in hospital admissions (three), improvement in symptoms (six), and improvement in daily activities (five). Four patients had not noticed any change, and one patient felt worse. Home enteral nutrition offers a method of long-term nutritional support which does not require extensive training, is acceptable to patients, who require little assistance, and is free from complications. Most patients...
found an improvement or stabilisation in their lifestyle.

**Total parenteral nutrition: a metabolic study**

E PULICINO, M ELIA (INTRODUCED BY G NEALE) (Department of Gastroenterology and Clinical Nutrition, Addenbrooke's Hospital, Cambridge) The optimal rate of nutritional rehabilitation with total parenteral nutrition is uncertain. We took the opportunity of making detailed measurements of energy expenditure and tissue deposition in a cachectic male patient with widespread but inactive Crohn's disease. The patient (weight 53 kg) was studied sequentially as energy intake was increased from 10-85 MJ/day to 23-21 MJ/day in three increments (nitrogen intake 12-2 g/day). Total parenteral nutrition was given 15 h/day for 62 days. Basal metabolic rate and body composition were measured at the beginning and end of the study and resting energy expenditure (REE) on 48 occasions on and off feed using a computerised ventilated hood technique. The patient received 1040 MJ (total) of which about 380 MJ was deposited as body tissue (8.5 kg fat; 10.7 kg fat free mass). Resting energy expenditure accounted for a little over half of the energy infused. Each increment in energy intake (ΔEi) produced a progressive increase in REE (ΔREE); ΔREE/ΔEi=0-12-0.26. The respiratory exchange ratio exceeded unity throughout the whole period of high energy intake implying lipogenesis from glycogen when not being fed. This study shows that (1) a cachetic subject can be readily repleted using high energy infusions; (2) net lipogenesis from carbohydrate persisted during the off feed period; (3) increases of REE are largely explicable by increases in body mass and the cost of tissue deposition.

How can selenium deficiency be detected in patients on home parenteral nutrition?

J L SHAFFER, H CHAMSI-PASHA, M STOKES, A SHENKIN, M H IRVING (Departments of Medicine and Surgery, Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) Patients on longterm parenteral nutrition are at risk from developing skeletal and cardiac myopathies. Selenium (Se) deficiency has been implicated. The currently accepted methods for assessing selenium status, monitoring plasma levels of selenium and the selenium dependent enzyme, red cell glutathione (RCG) peroxidase are not widely available. We have used M-mode echocardiography (Hewlett Packard) to assess cardiac muscle function.

In 32 patients (16 men, on HPN 0-5-8 yrs) the mean Se was 0-69 μmol/l (95% confidence limits 0-6 to 0-78) and RCG 11-4 U/g Hb (10-12-8). Mean percentage fractional shortening was 32-6% (30-4-34-8), and ejection fraction was 60-5% (57-2-63-8). There was a significant correlation between Se and fractional shortening percentage (r=0-448, p<0-005, Spearman) and ejection fraction (r=0-448, p<0-005) but not red cell glutathione peroxidase with the two cardiac parameters. Nineteen patients had a low ejection fraction (<64%), 17 of these had a low Se (<8-0 μmol/l). None of the remaining 13 had an abnormal ejection fraction of plasma Se (specificity 87%, sensitivity 100%).

Echocardiography is a widely available non-invasive test that appears to predict the effects of selenium status on cardiac muscle function. Many patients on home parenteral nutrition have subnormal cardiac performance.

**Intestinal mucosal enzyme deficiency in IgA nephropathy (Berger's disease)**

FIONA M STEVENS, E LAVELLE, M KEARNS, P F FOOTRELL, B DUFFY (Departments of Medicine and Biochemistry, University College, Galway, Ireland) An association between coeliac disease (CD) and IgA nephropathy (IgAN) is well recognised. A gluten free diet reduces the level of circulating immune complexes even in non-coeliac patients with IgAN, resulting in decreased urinary protein loss and improved renal function. A study has been undertaken to determine the frequency of intestinal abnormalities in IgAN. Thirty one unslected patients, with IgAN on renal biopsy, had small intestinal biopsies performed. No patient had intestinal symptoms or metabolic deficiencies suggestive of CD. Intestinal biopsies were examined histologically and biochemically (lactase, sucrase, and alkaline phosphatase activity). The enzyme results of biopsies (histologically normal) from 31 age/sex matched symptomatic controls undergoing investigation to preclude CD were available for comparison. One patient with IgAN had a flat biopsy compatible with untreated CD. A further 16 IgAN patients (51%) had a reduction of at least one mucosal enzyme activity compared with five (16%) controls. The difference is statistically significant. There is no difference in intraepithelial lymphocyte counts.

These findings show there is a widespread enteropathy in IgAN and this may be of aetiological significance.

**OESOPHAGO-GASTRODUODENAL**

**Standardised method of expression of the normal range of oesophageal body peristalsis**

S ATWOOD, T NORRIS, L JENKINSON, C BALL, A WATSON (Royal Lancaster Infirmary, Lancaster) Much controversy surrounds the diagnosis of oesophageal motility disorders arising from a lack of agreed normal values. Few publications have addressed this issue, these being mainly confirmed to the distal oesophagus. The present study was undertaken to establish a standardised form of manometric assessment of peristaltic amplitude based on the study of the whole oesophagus.

Thirty asymptomatic volunteers (age range 19-74 yrs) underwent standard perfusion manometry and peristaltic amplitude was measured in each of six segments in the oesophageal body. To express peristaltic amplitude we compared means (standard deviation) with median values and percentiles for swallows within each patient and for the group as a whole.

The optimal method of analysis was the median value of a series of swallows and the range of normality best expressed as within the 10th and 90th percentiles in the form of a bar chart which represents a 'motility map' of the oesophagus.

This method produces a quick and easy reference of normality when plotting patient data. It can be readily applied to computer assisted analysis which eliminates observer variation and enables standardisation of measurement technique. This allows direct comparisons of patient data with accepted normal values.

**Oesophageal cancer – an epidemiological study in Transkei**

P M SAGAR, E A BENSON (The General Infirmary at Leeds, Great George Street, Leeds) Oesophageal cancer (OC) has its highest incidence in Transkei, a South African homeland state, where, in certain areas, it is the most common cause of death in adult men. High cereal intake and soil trace element deficiencies have been impli-
cated but, of greater aetiological significance, are the smoking and drinking habits. Locally grown tobacco ('Dacca') is highly mutagenic and pipe stem juice ('Injonga') and home brewed maize beer both have a high nitrosamine content. The dietary and smoking habits of a consecutive series of 17 patients who presented with OC in a 10 week period to one hospital were recorded and compared with a group of 200 control patients who attended the hospital in the same period. Study and control groups were similar with respect to age, sex, race, geographical origin and cultural background. Regional prevalence in one 2000 km² district was investigated in a retrospective study of 234 cases of OC. Patients with OC had both a significantly higher intake of beer (p<0.001) and a greater consumption of tobacco (p<0.01) than the control group. There was no correlation between OC prevalence and varying soil trace element deficiencies. Beer and tobacco consumption in Transkei have a potent carcinogenic effect.

Tryptic and peptid activity in oesophageal refluxate

D L STOKER, J G WILLIAMS, L J CHUBB, J A BILLINGS, D G COLIN-JONES (Royal Naval Hospital, Haslar, Gosport, Hants and Queen Alexandra Hospital, Cosham, Portsmouth) The effects of acid, and bile salts on oesophageal mucosa are well documented. There are, however, no data available on the presence of potentially damaging proteolytic enzymes in the human oesophagus. The aim of this study was to measure the activity of trypsin and pepsin in oesophageal refluxate. Samples of oesophageal refluxate were collected from 42 fasted, symptomatic patients, using an endoscopic aspiration technique previously described. The pH of each sample was measured, and these were then centrifuged to remove debris, and frozen at −20°C before assay using standard laboratory techniques. In 32 cases (76%) there was related, endoscopically proven oesophagitis. Twenty one of 42 samples fell into the pH range 4–7. Tryptic activity was present in 24 (56%) of the samples (median 1.5, range 0.1–19.6 IU/l). There was a positive correlation between increasing trypsin activity and rising pH (r=+0.60, p<0.0005), with negligible levels below pH 4. Pepsin activity was present in 32 (76%) samples (median 27, range 0–250 IU/l). There was negligible peptic activity above pH 5. The study shows that there are duodenal and gastric proteolytic enzymes present in oesophageal refluxate, and at pH levels which may be ignored by conventional pH monitoring. Such enzymes may have a role in the aetiology of reflux oesophagitis.

Does the timing of the evening meal affect the pattern of 24 hour intragastric acidity?

S LANZON-MILLER, R E POUNDER, R L MCSAAC, J R WOOD (Academic Department of Medicine, Royal Free Hospital School of Medicine, London and Department of Gastroenterology, Glaxo Group Research Ltd, Greenford, Middlesex) Control of nocturnal acidity has been shown to be an important factor in duodenal ulcer healing. Food not only buffers intragastric acid but it also stimulates acid secretion. The aim of the study was to determine the effect of varying the time of the evening meal on 24 hour intragastric acidity.

Ten healthy volunteers were each studied on three occasions when dietary and environmental conditions were identical except for the timing of the evening meal—1715 h (E=early), 1915 h (N=normal), or 2115 h (L=late). Each of the studies was performed in a predetermined random order. Hourly gastric studies aspirates were obtained to measure intragastric acidity.

There was no significant difference in the integrated 24 h acidity between the three study days (E=1044; N=906; L=941 mmol/l). The early meal resulted in little afternoon acidity (115 mmol/l), however, but considerable evening and nocturnal acidity (746 mmol/l); conversely, a late meal resulted in higher acidity in the afternoon and early evening (360 mmol/l), less nocturnal acidity (476 mmol/l), and a delayed nocturnal peak of intragastric acidity.

Altering the time of the evening meal causes major changes in the pattern of intragastric acidity. Regimens using short acting H₂ receptor antagonists may need to take account of the patient’s dietary habits, to provide optimal control of intragastric acidity.

Early gastric carcinoma with particular reference to the significance of intestinal metaplasia as a marker of increased cancer risk

T ROKKAS, M J FILIPE, A SANDEY, G E SLADEN (Gastroenterology Unit and Department of Histopathology, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals, London) Despite a decline in the incidence of gastric cancer (GC) the prognosis is usually poor. Between 1976 and 1987 there was a progressive decline in the number of GC operations performed each year (n=718). However, the percentage of early gastric carcinomas (EGC) (n=24, 17 M/F, mean age 68.4 (2-4) SE) increased from 1-6% for the period 1976–82 to 5.6% for the period 1982–87 (p<0.01). This increase was associated with a prospective study on gastric biopsies, started in 1982, to assess the incidence and distribution of intestinal metaplasia (IM) types and to establish their value in the selection, for endoscopic surveillance, of patients at high risk of developing cancer. All gastric biopsies were examined by the same histopathologist, Extensive IM was present in 20/24 (83%) of the cases and it was of incomplete type IM (sulphomucin secretion) in 17/20 (85%). In five resected specimens (20%) there was submucosal infiltration and in 4 (16-6%) involvement of lymph nodes. Survival data after surgery were available in all 24 EGC patients. Twenty one (81%) patients were alive, followed for a mean 5 (0-54) yr (range 1–9) after surgery. Of the three deaths, two were cancer related (both one year after surgery) and one was cancer related. Neither submucosal infiltration nor positive nodes significantly reduced survival.

EGC is diagnosed with increasing frequency and this is associated with closer endoscopic surveillance of patients with type III incomplete IM. EGC is associated with good prognosis despite submucosal invasion and node involvement in some cases.

Effect of a defined policy on the outcome of bleeding peptic ulcer disease

K E WHEATLEY, P W DYKES, M R B KEIGHLEY (The General Hospital, Birmingham) Bleeding peptic ulcer disease is a common problem, with mortality rates of over 10% frequently reported. Mortality has remained around this level for three decades, largely due to increasing age of patients. Since 1984 we have had a stable defined policy for the management of patients with bleeding peptic ulcers. Patients are admitted to a centralised unit and managed by a team comprising physicians, surgeons and an endoscopist. Early endoscopy is practised and there are defined criteria for the timing of surgical intervention. Non-resectional surgery for GU is performed where possible. In a four year period we admitted 30...
patients with bleeding from proven peptic ulcers, 60% were over age 60, and 11% over 80 years old. Twelve patients died (overall mortality 4%). No patients died under the age of 50, one under 60 years, and thereafter the mortality rose steadily with age. Sixty eight (22%) patients received emergency operations with only two postoperative deaths. Vagotomy and pyloroplasty was the commonest operation for DU, and 22 of 36 patients with GU did not receive a gastrectomy.

With our defined policy we have maintained a low overall and operative mortality of 4% and 3% respectively.

Endogenous gastric prostaglandins do not protect the human gastric mucosa

H W Grant, K R Palmer (Gastrointestinal Unit, Western General Hospital, Crewe Road, Edinburgh) Polysaturated fatty acids increase gastric prostaglandin secretion and reduce acid output, suggesting that dietary fat could influence the natural history of peptic ulcer. In this study the gastric mucosal properties of linoleic acid (LA) were measured in normal subjects. Gastric mucus output was measured on two occasions in nine volunteers. The mean volume of mucus (the dialysable, solid component of gastric juice), increased from 432 (47) mg/hour (SE), when subjects had been taking a normal diet, to 593 (83) mg/hour (p<0.05) after a 14 day period of supplementation with LA, 3 g daily.

Gastrointestinal bleeding was measured in 12 volunteers whose red blood cells were labelled with Cr<sup>51</sup>. In a randomised cross-over study, mean faecal blood loss was 35 (5) ml/week whilst taking aspirin 1-2 g 8 hourly, and 36 (6) ml/week when each dose of aspirin was preceded by 1 g of LA. 60 ml 80% ethanol was infused endoscopically onto the gastric antrum of six normal subjects on two occasions separated by 14 days. On one occasion each subject was pretreated with 1 g of LA. Endoscopies over 90 mins showed similar degrees of ulceration and haemorrhage in both situations. Mucosal biopsies from the damaged area were incubated with H<sub>3</sub> thymidine and subjected to autoradiography. The % nuclei in 'S' phase invariably fell transiently after ethanol but labelling indices were similar whether or not LA had been given.

Although LA increases gastric mucus secretion, it does not protect the stomach against the damaging effects of aspirin or ethanol. This questions the 'cytoprotective effect of endogenous gastric prostaglandins.'

Symptomatology in C pylori-positive and negative non-ulcer dyspepsia

B J Rathbone, J Wyatt, R V Healey (Departments of Medicine and Pathology, St James's University Hospital, Leeds) The role of C pylori associated chronic gastritis in causing dyspeptic symptoms is at present unclear. To investigate whether CP-positive dyspeptics differ in their symptom complex from CP-negatives, 193 consecutive dyspeptic non-ulcer patients from general practice were studied by structured history, endoscopy and biopsy. C pylori colonisation was assessed by a modified Giemsa stain on antral and body sections. One hundred and five patients were CP-positive (mean age 48-7 years), 88 were CP-negative (mean age 39-7 years). There was no significant difference in presenting symptoms, nor smoking nor drinking habits between the two groups. In the CP-positive group, previous episodes of dyspepsia were more common, together with a past history of previous upper GI investigation. Detailed examination of other symptoms demonstrated that only oesophageal reflux symptoms were significantly more common in the CP-positive group. There was, however, no significant difference between endoscopic or histological oesophagitis in the positive and negative groups.

This study confirms the high prevalence of CP positivity in non-ulcer dyspepsia. The data show, however, that non-ulcer dyspeptic patients do not have sufficiently distinct symptomatology to separate them clinically from CP-negative dyspeptics. The frequency of reflux symptoms in CP-positive patients is of interest and warrants further investigation.

Why do patients with ulcerative colitis relapse?

S A Riley, V Mani, M J Goodman, L A Turnberg (University Department of Medicine, Hope Hospital, Salford and Leigh Infirmary and Bury General Hospital, Manchester) In order to determine the factors responsible for ulcerative colitis relapse we have studied a cohort of 92 patients (18 to 78 years, 50 men) with clinically inactive disease over 48 weeks.

At 12 weekly intervals patients were asked by means of standardised questionnaires about infections, drug ingestion, anxiety, depression, stressful life events and diarrhoeal episodes in the four weeks before attendance. Thirty five patients (38%) relapsed after a mean interval of 17 weeks (range three to 44 weeks). Relapers and non-relapers were comparable for age, sex, duration, and extent of disease.

A clear seasonal pattern of ulcerative colitis relapse emerged. Only nine patients relapsed from February to July whereas 26 relapsed from August to January (p<0.005) with a peak incidence in September and October. Upper respiratory tract symptoms also showed a seasonal pattern but these peaked in January.

Of the events that preceded colitis relapse between and within group comparisons revealed that infections, antibiotic ingestion, analgesic intake, stressful life events and diarrhoeal episodes were no more common in the four weeks prior to relapse than during remission. Anxiety and depression ratings were similar in the two groups.

We conclude that seasonal factors may be responsible for ulcerative colitis relapse.
Antigen presenting activity of mononuclear cells (MNC) from normal and inflammatory bowel disease (IBD) mucosa

Y R MAHIDA, K WU, D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) The capacity of mononuclear cells (MNC) from normal (7) and IBD (7) colonic mucosa to stimulate purified T cells in an allogeneic mixed lymphocyte reaction was studied as a means of assessing antigen presenting activity.

Mononuclear cells were isolated by EDTA-collagenase and treated with mitomycin C. Purified, resting, allogeneic T cells were obtained from peripheral blood MNC by adherence to plastic and nylon wool and complement lysis with monoclonal antibodies to monocytes, B cells, and HLA-D. The allogeneic T cells were used as responders and intestinal MNC as stimulators. Mixed lymphocyte reactions were performed in triplicate and incubated for six days. Results are expressed as mean (SD) proliferation per 100 stimulator cells.

There was greater proliferation induced by MNC from IBD mucosa compared with MNC from normal mucosa (34-8 (17) v 22-8 (3-7)), but this did not reach statistical significance. In three colons with distal ulcerative colitis, significantly greater proliferation was induced by MNC from inflamed mucosa compared with MNC from non-inflamed mucosa (48-5 (8-2) v 25-8 (1-7)).

Mononuclear cells isolated for active IBD mucosa have enhanced antigen presenting activity, which we have previously shown to be mediated by cells with characteristics of macrophages.

Faecal elastase in inflammatory bowel disease

E O ADEYEMI, H J F HODGSON (Department of Medicine, RPSM, Hammersmith Hospital, Du Cane Road, London) Plasma neutrophil elastase complexed to alpha-1-protease inhibitor (EPIC), rises in active inflammatory bowel disease but not always in active ulcerative colitis.

We therefore assessed the usefulness of EPIC levels in fresh stool samples in IBD as a specific correlate of inflammation in gut mucosa. Using an ELISA technique, EPIC and CRP levels were determined in plasma samples of 80 controls, 14 CD patients, 16 patients with UC, and EPIC in stool supernatants.

Plasma EPIC and CRP were raised in 50% of UC patients. Median stool EPIC in 10 controls was 0.0 ng/ml (range 0.0–20), in small bowel CD 168 ng/ml, Crohn’s colitis 1015 ng/ml, and in active UC 1159 ng/ml. Median stool EPIC levels in active UC and Crohn’s colitis were each significantly higher than in small bowel CD (p=0.0014 and 0.0024 respectively). Stool EPIC measurements in UC correlated significantly with a numerical activity index (r= 0.87, p=0.001), but not with ESR, WBC, and plasma CRP. Stool EPIC in Crohn’s colitis correlated significantly with CDAI (r=0.78, p=0.05), ESR (r=0.74, p=0.05), and plasma CRP (r=0.9, p=0.003) but not with WBC.

Stool EPIC may better characterise inflammation in colitics, when plasma EPIC and CRP levels are not raised.

Azathioprine in resistant ulcerative colitis

P N FOSTER, A J LOBO, D A BURKE, D JOHNSTON, A T R AXON (Gastroenterology Unit and Department of Surgery, The General Infirmary, Great George Street, Leeds) The use of azathioprine in ulcerative colitis is controversial; our policy is to give azathioprine in difficult cases. We present the details and outcome of 46 patients who received azathioprine for either (i) severe, resistant disease otherwise requiring surgery (28) or (ii) steroid dependence/intolerance (18) and who have been followed up for at least 12 months. On introduction of azathioprine the disease extended beyond the splenic flexure in 30 and was total in 22; in the remainder the disease was confined to the rectum (three) or left side of the colon (13). Duration of treatment ranged from one week to 66 months (median 12 months) and the mean daily dose was 1.9 (0.3) mg/kg. Of the patients in group (i), 14 (50%) achieved remission, 11 of whom had not relapsed during a median follow-up of 22 months (range 12 to 58) and 14 underwent surgery one week to 12 months (median five weeks) after commencing azathioprine. In group (ii), steroids were withdrawn or reduced in 10 (55%) patients and four patients required colectomy. Side effects necessitating withdrawal of azathioprine occurred in 12 patients: haematological (six), gastrointestinal (four), others (two). Two patients required a reduced dose of azathioprine because of leucopenia. We conclude that azathioprine is a valuable therapeutic option in selected patients with ulcerative colitis, obviating surgery, and sparing steroids, but regular blood counts are essential.

Eleven years experience of elemental diet in acute Crohn’s disease

K TEAHON, I BJRNMASON, A J LEVI (MRC Clinical Research Centre, Watford Road, Harrow, Middlesex) Elemental diet is an effective form of treatment for acute Crohn’s disease. Previous studies have been too small to assess the overall success rate, predictions of success and the long term prognosis. We reviewed 107 Crohn’s patients treated with an elemental diet (Vivonex) at Northwick Park Hospital over 11 years. Eighty seven per cent obtained remission, characteristically within 10 days, regardless of the site and severity of the disease. Thirteen per cent did not improve but there were no predictions of a poor response. Follow up of successfully treated patients (M: 45 months) shows that 75% of patients with diffuse small intestinal involvement maintained remission and the 25% who relapsed (DEF: clinical change resulting in alteration of management) did so within five months. The more distal the disease the greater the relapse rate; 90% of perianal disease or fissures relapse within two months. Longterm follow up (>five years) of patients treated initially and temporarily with elemental diet (n=16), steroids (n=12), or surgery (n=31) shows that 38%, 20%, and 50% respectively maintain a remission at five years.

(1) Treatment with elemental diet achieves a 87% remission rate regardless of site and severity of disease. (2) The more proximal the disease the greater is the duration of remission. (3) Distal disease and fistulae require additional treatment. (4) Elemental diet does not appear to alter the natural history of Crohn’s disease.

Conservative proctocolectomy – is it an option in ulcerative colitis?

R W TALBOT, J K RITCHIE, J A NORTHOVER (St Mark’s Hospital, City Road, London) A conservative proctocolectomy (CP) preserves the anus whilst removing all rectal mucosa and allows a subsequent restorative procedure to be performed should this be indicated. Between 1975–1987, 22 patients underwent CP for ulcerative colitis (n=18). Crohn’s disease (n=3), or familial adenomatous polyposis (n=1). The longterm outcome of this operation had been studied. Healing was uncomplicated in four patients including one after removal of an incontinent ileoanal pouch. A persisting discharge from a sinus at the top of the anus occurred in 18 and nine of these had a chronic abscess cavity. Four of these 18
patients healed after a mean of two years but the remainder are still unhealed six months to 10 years later (median three years). Eight patients have undergone a total of 17 operations including six sphincter divisions and two anal excisions. Only one patient has healed after sphincter division alone. Two patients with a discharging sinus have had a successful ileal pouch anal anastomosis. These results compare unfavourably with the healing of perineal wound after intersphincter excision of the rectum at our institution. Conservative proctocolectomy cannot be recommended as a definitive operation for ulcerative colitis even though it may permit a subsequent restorative procedure.

Faecal challenge as a predictor of the effect of restoring intestinal continuity in defunctioned Crohn’s colitis

M C Winset, M R B Keighley (The General Hospital, Birmingham) The effect of restoring intestinal continuity in patients with defunctioned Crohn’s colitis is unpredictable. The aim of this study was to assess whether preoperative faecal challenge of the defunctioned colon with ileostomy effluent can predict those patients likely to suffer an early disease relapse.

Nine patients (four men, mean age: 39 years) with Crohn’s colitis for restoration of intestinal continuity, had a mean volume of 120 (60–280) ml ileostomy effluent inserted into the efferent limb of their loop ileostomy daily for seven days.

The median time to defecation was 1 (1–2) day. Four patients developed diarrhoea (≥5–10/day) with systemic symptoms and were considered unsuitable for stoma closure. Two patients developed mild diarrhoea whilst three were asymptomatic. Five patients had intestinal continuity restored and all remain in clinical remission at six months. Changes in serum and mucosal indices of disease activity after faecal challenge and restoration of continuity were similar.

Faecal challenge produces results similar to restoration of intestinal continuity. It is a useful method of predicting patients likely to suffer an early relapse in whom intestinal continuity should be avoided.

Six hour post-prandial pH monitoring: an adequate test for gastro-oesophageal reflux in childhood

J Panayotou, S Devane, P J Milla (Hospital for Sick Children, Great Ormond Street, London) Twenty four hour ambulatory pH monitoring is the ‘gold’ standard for detecting gastro-oesophageal reflux (GOR) but requires an overnight admission. In children there are few studies of abbreviated pH monitoring suitable for day patient use. As in infants GOR is mostly postprandial abbreviated postprandial pH monitoring may be a suitable test. We investigated 45 patients by 24 hour (24) and six hour postprandial (6PP) ambulatory pH monitoring using a naso-oesophageal probe with its tip 5 cm above the lower oesophageal sphincter and a Synectics Digitrapper. Twenty five patients were investigated for vomiting, eight with feeding problems and 12 respiratory symptoms. All were endoscoped and 10 had oesophagitis. Acid exposure time was calculated as the proportion of time with pH below 4. A total acid exposure greater than 7% was found in 36/45 on 24 and 33/45 on 6PP with a correlation of r=0.78 between tests. There were three false negatives, two with only <10% reflux. On 6PP there was a good correlation between total time and upright or supine reflux (r=0.75 and 0.72 respectively). Those with oesophagitis had longer acid exposure and as many had upright as supine reflux seven of 10 and nine of 10 were detected by 24 and 6PP respectively. Those with severe reflux; (≥20%) five of 36 were detected by both tests but upright five of 36 was better than supine three of 36. Four of six patients with feeding problems refluxed and were predicted by both tests. The results indicate that 6PP is as good as 24 at predicting severe reflux and an adequate prediction of the degree of acid reflux demonstrable in a 24 hour period for those with moderate reflux.

Non-specific abdominal pain in childhood. Can serology detect those with campylobacter pylori (CP) associated gastritis?

G Oderda, D Vaira, J Holton, J Dowsett, N Ansaldi (introduced by N I Mcneil) (Pediatric Gastroenterology Section, University of Torino, Department of Gastroenterology and Microbiology, The Middlesex Hospital, London) Fifty one consecutive children median age 11 years (range 1–18), who presented with recurrent abdominal pain were investigated for CP associated gastritis by upper GI endoscopy with antral biopsies. The specimens were evaluated by microscopy, culture, and urease testing. Serum IgG, IgA, and IgM antibodies to CP were also measured by ELISA technique, using a sonicated antigen and the results expressed as optical density measurement.

Nineteen children showed no histological gastritis nor presence of CP on microscopy, culture and/or urease test. Thirty two children showed histological gastritis. All those 32 had CP on microscopy. Culture was also positive in 29 and urease test was positive in 24. The sensitivity, compared to microscopy of culture and urease testing was 90% and 74% respectively. The specificity was 100% and 100% respectively. The mean IgG, IgA levels in the 19 children with no histological, microbiological and no urease testing evidence of CP were 97 and 34 respectively, and in the 32 patients with histological gastritis and associated CP on microscopy, culture and/or urease test were 253 and 72 respectively. Both levels were significantly higher in the CP positive group (IgG: p<0.001; IgA: p<0.01). No difference was found in IgM titres (mean value 100 in the positive group and 99 in the negative group respectively).

The serum IgG and IgA assay for CP may correctly identify those children with CP associated gastritis, and can be used to screen non-invasively children for the condition before endoscopy.

Epigastric impedance (EPI) studies: a clinically useful method of measuring gastric emptying in children (GE)

H L Smith, G W Hollins, S J Newell, I W Booth (Institute of Child Health, University of Birmingham, Francis Road, Edgbaston, Birmingham and the Department of Medical Physics, Birmingham Maternity Hospital) A non-invasive non-isotopic means of measuring GE in children has not been available until recently. We have therefore evaluated the measurement of GE in children using EPI. Forty five normal subjects (1–18 y, median 12.9 y; 27 men, 18 women) and 13 cystic fibrosis patients (7–18 y, median 14 y; seven men, six women) were each studied fasting. Baseline EPI was stable and did not correlate with age, weight, triceps skinfold thickness (TSF), or body surface area (BSA). Ingestion of orange squash (400 ml/m² BSA) in 50–100 ml increments, revealed a highly significant correlation between volume ingested and stepwise increases in impedance (r>0.95, p<0.01). ΔEPI showed a close, negative curvi-linear
relationship with BSA, weight, age, and TSF. Mean time to half-emptying (t½) in normal subjects was 14.5 min (SD 6.6) and in CF patients was 16.5 min (SD 6.5); t½ did not correlate with age or sex. The test was well tolerated and was capable of: (i) discriminating between test meals of differing viscosity (± Carobel 1%), and caloric density (± Calogen 2.5%) (ii) identifying an infant with post-fundoplication dumping syndrome (t½ four min).

Experimental rat rotavirus infection: a new animal model for studying efficacy of oral rehydration solutions (ORS)

A F M SALIM, J A WALKER-SMITH, M J G FARTHING (Departments of Gastroenterology and Child Health, St Bartholomew's Hospital, London) Although oral rehydration therapy with glucose electrolyte solutions is of proven efficacy in RV diarrhoea, the optimal composition of ORS had not been established. We have developed a model of RV infection using eight day old neonatal rats inoculated orally with rat RV. Rats were anaesthetised and the entire small intestine was perfused with a plasma electrolyte solution (PES), (Na 140, K 4, HCO₃ 40 mmol/l; 300 mOsm/kg), WHO-ORS (Na 90, K 20, HCO₃ 30, Glu 111 mmol/l; 331 mOsm/kg) and an isotonic experimental (EXP) ORS (Na 60, K 25, citrate 10, Glu 111 mmol/l; 289 mOsm/kg) at 18, 24, 48, 72, and 96 h after infection. Net water secretion occurred with PES at 18, 24, and 48 h (± 20±9±6±8, ±19±5±7±1, ±19±12±6±3 μl/min/g dry wt, respectively; n=6). This was reversed to absorption by both ORS but EXP-ORS produced more water absorption than WHO-ORS at 18, 24, and 48 h (p<0.01), the most impressive difference being at 48 h (+58±7±5±8 vs +8±6±4±6; p<0.001). Following resolution of diarrhoea at 72 h and 96 h net water absorption occurred from PES (19.9±5±0) and there was no difference in the efficacy of WHO and EXP-ORS. In these studies sodium movement paralleled water movement. This study shows that the rat RV model closely mimics human RV infection and may be used to compare the efficacy of ORS. Our findings in this model indicate that the isotonic EXP-ORS is more effective in promoting water absorption than the WHO-ORS.

A comparison of a casein hydrolysate formula with a standard rehabilitation milk in the management of chronic diarrhoea and malnutrition in Gambian infants

P B SULLIVAN, G NEALE, A K J GOKA, M J G FARTHING (Dunn Nutrition Laboratory, University of Cambridge and Department of Gastroenterology, St Bartholomew's Hospital, London) Infection with Giardia is highly prevalent in many underdeveloped countries, but assessment of its clinical impact has been limited by the unreliability of diagnostic methods. This was confirmed when 120 stool samples from 31 malnourished Gambian children were examined microscopically in the routine MRC laboratory; none were reported positive for Giardia. Twenty five of these patients underwent jejunal biopsy and in 11 Giardia trophozoites were identified. Anti-Giardia antibodies (IgM, IgA, and IgG) were sought by ELISA; 16/31 had IgM anti-Giardia antibody titres >500 and of these nine were biopsy positive. IgM was found to be a better indicator of active infection than either IgA or IgG anti-Giardia antibody. Detection by ELISA of Giardia antigen in faeces was not helpful in diagnosis. Thus 52% (16/31) of patients with chronic diarrhoea were considered to be infected with Giardia, either by direct parasite identification or positive IgM response. Furthermore serial biopsies and serology were performed and of 16 positive cases nine were found to have evidence of persistent infection with Giardia the three weeks later despite apparently adequate treatment with metronidazole. This may relate to the poor nutritional state of these children and associated impaired secretory immunity. This study demonstrates the difficulties associated with diagnosis of giardiasis and confirms the value of specific serum IgM responses in detecting active infection.

Risk factors in Gastrointestinal complications in children after orthotopic liver transplantation

D A KELLY, S S KAUFMAN, B SHAW, P WOOD, D J SCRIVNER, M BROWN, J GUEST, D L ANTONSON, J A VANDERHOOF (University of Nebraska Medical Center, Omaha, Nebraska, USA) Gastrointestinal (GI) complications after orthotopic liver transplantation (OLT) are common in children at this centre. To identify risk factors, all children were graded according to nutritional status and hepatic dysfunction at OLT. From 1985–87, 53 children were transplanted. Thirty four children (64%) developed GI complications. Ninety one per cent had behavioural feeding problems. Seventeen of 34 developed small bowel or colonic perforations. GI bleeding was present in 12/34 children, 11 of whom had acid-peptic disease and one died. Infectious colitis developed in 17/34 children and pneumatisis intestinalis in nine of 34. Twenty two had previous abdominal surgery, 12 of whom developed intestinal perforation. Children with GI complications were more likely to have had previous surgery (67%), be malnourished (60%), and to have decompensated liver disease (69%) than those who did not (52%, 35%, and 37% respectively). There was no significant difference in immunosuppression between the groups. Thus, children with decompensated liver disease who are malnourished are at risk of GI complications with substantial morbidity.
but low mortality. The risk of perforation is increased with previous surgery.

Does intensive enteral feeding in children with advanced cirrhosis cause nitrogen intolerance?

C P J CHARTLON, M A EDWARDS, A BAKER, E BUCHANAN, C HOLDEN, A GREEN, I W BOOTH, M J TARLOW (Liver Unit, Birmingham Children’s Hospital, Institute of Child Health, University of Birmingham) We have previously demonstrated that intensive enteral feeding of malnourished children with advanced cirrhosis can dramatically improve nutritional status. Concern has been expressed, however, about the biochemical effects of increasing the dietary protein load by a mean of 33% (range 5%–54%). Fasting blood ammonia and quantitative aminoacid concentrations were therefore measured before and at the end of eight weeks enteral feeding in 10 children with advanced cirrhosis. Initially ammonia concentrations were raised (>40 μmol/l) in eight of 10, and rose significantly with feeding (before feeding: mean 59±3 μmol/l, range 38–86 μmol/l; after eight weeks: mean 77±1 μmol/l; range 50–141 μmol/l; p<0.05). This increase was not, however, associated with any deterioraion in cognitive function and parents actually reported increased well being.

Despite the use of a formula containing 31% of total N as branched chain amino acids (normal diet 15–20%), plasma levels of these were not significantly raised during the study, suggesting that branched chain amino acids are well metabolised in these patients. Other amino acids (particularly methionine, tryosine, phenylalanine, lysine, and threonine) were generally high, although no consistent trend related to feeding was observed. These data confirm the biochemical safety of nutritional support in 10 children with advanced liver disease, and the ability of the patients, despite a severely compromised liver, to metabolise high concentrations of branched chain amino acids. We recommend that blood ammonia levels be regularly monitored in these patients.

First measurement of gastric juice ascorbic acid levels

G M SOBALA, C J SCHORAH, M SANDERSON, P GODWIN, M F DIXON, A T R AXON (Gastroenterology Unit and University Departments of Microbiology, Chemical Pathology, and Histopathology, The General Infirmary, Leeds) Ascorbic acid may protect against gastric cancer by inhibiting intragastric nitrosation, being oxidised to inactive dehydroascorbic acid as it destroys nitrite. Only gastric juice total vitamin C (GVC), however — that is, ascorbic acid plus dehydroascorbic acid, has been measured before. In this study gastric juice ascorbic acid (GAA) was quantified for the first time, together with GVC, plasma vitamin C (PVC), and dietary intake of vitamin C in 75 patients endoscoped for dyspepsia. Patients with chronic gastritis had lower GVC and GAA than normals (medians: GVC: 0.95 mg/dl v 2.45; p<0.001; GAA: 0.40 v 1.79; p<0.001), but not PVC or intake. The ratio of GVC to PVC was significantly greater than unity only in normals (mean ratios normals: 3:28; p<0.02; gastritis: 1:125; p>0.2). The proportion of GVC that was present as GAA was lower when gastric juice pH >4 (medians 11% v 62%; p=0.0001).

These results suggest that there is active vitamin C secretion in normal subjects, but this is impaired in patients with chronic gastritis. In hypochlorhydric subjects, very little of the vitamin C present is ‘useful’ ascorbic acid and this suggests that oxidation by nitrite has already occurred. Thus low levels of ascorbic acid in gastric juice may contribute to the increased cancer risk in chronic gastritis and hypochlorhydria.

Somatostatin (SMS 201.995) reduces growth of human gastric cancer (MKN45) xenografts

D L MORRIS, S A WATSON, J D HARRISON, L DURRANT (Department of Surgery, University Hospital, Nottingham) We have previously reported that gastrin stimulates in vivo growth of human gastric and colorectal cancer cells. MKN45, a human gastric cancer cell line, maintains this response to gastrin in vitro and in vivo. We have reported that enprostil (a prostaglandin which reduces gastrin release) can reduce in vivo growth.

In this study SMS 201.995 (long acting somatostatin analogue which reduces serum gastrin concentration) was investigated. Nude mice received MKN45 xenografts and were allocated to control (n=10) (saline infusion) or one of two treatment groups (SMS 201.995 infusion by implanted osmotic mini pump for 0–7 at 25 ng/kg/day or 240 ng/kg/day). Tumour diameter was measured daily, blind of treatment group, for the 22 day experiment. Tumour growth was significantly slowed in both treatment groups, and remained depressed for some seven days after therapy before recovering (p<0.01 days 13–17). For example, at day 15 mean tumour diameter was 1.99 (0.73) in the control group, 1.35 (0.65) and 0.98 (0.23) in the low and high dose SMS groups respectively Mean post prandial serum gastrin at five days was 217 (66) in controls and 110 (32) and 47 (26) (p<0.02) in SMS treated groups. SMS 201.995 significantly reduces in vivo growth of MKN45, a human gastric cancer cell line. This may be related to its effect on serum gastrin concentrations.

Chronic enterogastric reflux (EGR) increases the gastrotoxicity of an acute bile acid challenge in the rat

P J VAN EDEEN, D ARMSTRONG, P TAYLOR, M MAGHSOUDLOO, G M MURPHY and R H DOWLING (Gastroenterology Unit, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals, London) Using the ex vivo rat
gastric chamber model, we found that 'virgin' stomachs responded to acute (10 min) challenges with bile acids and lysolicithin by loss of transmucosal potential difference (APD) and loss of superficial epithelial cells on scanning electron microscopy causing nucleic acid accumulation in chamber fluid (Δ[NA]). Chronic EGR, however, induces mucosal hyperplasia and the response of this 'adapted' stomach to the gastrotoxins is unknown. Therefore, in 13 controls (gastrectomy) and 11 rats with chronic EGR studied 16–20 weeks after gastrojejunostomy, we measured APD and Δ[NA] in response to a 10 min challenge with 5mM taurodeoxycholic acid at pH 6.0–7.5.

The median APD increased from 11.4 mV (semi-interquartile range SIR 2-8) in the controls to 13.7 mV (SIR 3.7) in the gastrojejunostomy group (p=0.048) while the median Δ[NA] increased from 2.0 (SIR 1-11) to 3.8 (SIR 1.14) μg/ml (p=0.032) (Mann-Whitney test).

Contrary to expectation, the gastric mucosal hyperplasia of chronic EGR enhances, rather than diminishes, the gastrotoxicity of an acute bile acid challenge.

Enhanced active glucose absorption by the jejunum in cystic fibrosis

P S Baxter, A J Wilson, N W Read (Departments of Paediatrics and Physiology, University of Sheffield, Sheffield) Steatorrhea is a feature of cystic fibrosis (CF), but it is not clear whether malabsorption of other nutrients is solely a consequence of pancreatic insufficiency or whether it also reflects a defect in the transport capacity of the enterocyte. In vivo perfusion studies have paradoxically shown enhanced absorption of glucose from the jejunum of CF patients. This could result from an increase in either the active or passive components of glucose transport. Active glucose absorption is a Na+ linked electrogenic process that increases transintestinal electrical activity. The rise in short circuit current (SCC) induced by luminal glucose (10 mM) was therefore measured in jejunal biopsies from control (22) and CF (11) patients using an Ussing chamber technique. The glucose-dependent increase in SCC was significantly greater (p<0.01) in CF biopsies (42±2.8–9 uA/cm²) than in control tissues (22±2.3+3 uA/cm²) Villus architecture was normal in both groups of tissues. Previous reports suggest the enhanced in vivo jejunal glucose absorption may reflect a decreased diffusion barrier overlying the mucosa however conflicting reports exist regarding the thickness of the unstirred layer in CF. These data show the enhanced glucose absorption is an active process and give no support to the contention that the absence of chloride channels in the apical membrane of the CF enterocyte impairs glucose absorption.

Abnormal jejunal potential difference records in cystic fibrosis

P S Baxter, A J Wilson, N W Read (Departments of Paediatrics and Physiology, University of Sheffield, Sheffield) Potential difference (PD) and pressure changes in the upper jejunum were recorded using an intraluminal catheter perfused with saline and a subcutaneous saline reference cannula in 17 healthy adult volunteers and in two patients with cystic fibrosis (CF).

In controls spike and wave like fluctuations in PD occurred during pressure changes and a stable PD was only seen in the absence of pressure changes. An intraluminal bolus of pilocarpine, 4 mg, caused the PD to become more negative by 4-0 (0.7) mV (mean(SE), range 0–75, n=13, p<0.001). Intraluminal prostaglandin E2 (PGE2), 0-1 mg, caused a similar change of 5-6 (0.5) mV (mean(SE), range 2.5–8.5, n=15, p<0.001). In the two CF patients, the variability of the PD during pressure changes was much reduced, resembling that seen during motor quiescence in controls. Spikes still occurred but no waves were seen. There were no significant PD responses to pilocarpine or PGF2.

In vitro, cholinergic and cAMP mediated secretagogues do not provoke a PD response in CF intestinal epithelium, reflecting absent chloride secretion. The lack of a PD response to secretagogues in vivo supports this. The absence of PD waves in association with pressure changes in CF patients supports the concept that such waves represent intestinal secretion related to muscle contraction.

Enzymic regulation of mucosal polyamines in normal rat intestine

T Rokkas, S Vaja, P Taylor, G M Murphy, R H Dowling (Gastroenterology Unit, Guy's Campus, UMDS of Guy's and St Thomas' Hospitals and Department of Surgery, Guy's Hospital, London) The synthesis of the polyamines putrescine, spermidine and spermine (which influence cell division and growth) is rate limited by ornithine decarboxylase (ODC) while putrescine degradation is controlled by diamine oxidase (DAO) but the relative importance of these ‘accelerator and brake’ enzymes is unknown and the possibility of feed back inhibition of ODC by putrescine, uncertain.

To study this, we measured jejunal (proximal 10 cm) and ileal (distal 10 cm) mucosal DAO and ODC activities and polyamine levels two hours after injecting either saline (controls; n=7) or a large (4000 U/kg BW) bolus of IV heparin to deplete intestinal mucosal DAO stores (n=6).

As expected, ileal mucosal DAO (μmol/g protein) was higher in ileum (26–9 (SEM 3–2)) than in jejunum (7–6 (0.5); p<0.001) but at both sites, heparin reduced mean DAO activity by 67% (p<0.001). As a result, putrescine levels (nmol/mg prot) increased from 0.98 (0.19) to 1.70 (0.17) in jejunum (p<0.02) and from 0.41 (0.07) to 1.64 (0.41) in ileum (p<0.01), but heparin-induced DAO depletion had no significant effect on spermidine and spermine levels.

The increased putrescine was associated with reduced ODC activity (pmol/h/mg prot) which fell from 180 (32) to 51 (22) (p<0.01) in jejunum and from 78 (13) to 38 (8) (p<0.05) in ileum. ODC activity correlating negatively with putrescine at both sites (r=0.86; p<0.001 and r=0.75; p<0.01, respectively) suggesting feed back inhibition (ODC always <100 above a putrescine threshold of ≥1.5).

These results suggest that: (i) in normal rats, DAO is more important than ODC in regulating mucosal putrescine levels, and (ii) putrescine exerts feed back inhibition of ODC.

Uptake and transfer of epidermal growth factor (EGF) by the small intestinal epithelium of the fetal rat

L T Weaver, P A Gonnella, G M Caponigro, W A Walker (Intrig G Neale) (Department of Pediatric Gastroenterology and Nutrition, Children's Hospital and Harvard Medical School, Boston, Mass USA) Epidermal growth factor correlates with maturation of fetal rat epithelium in vitro and vivo. Our aim was to determine if EGF is present in amniotic fluid and to study its absorption by fetal small intestine. Anaesthetised 20 day gestation rats underwent Caesarian section. Three fetuses were exteriorised, their abdomens opened and ligated loops of proximal and distal small intestine infused with 100 μg EGF. Infused segments were removed 30 min later, rinsed with PBS, fixed for EM, and tissue embedded in LR gold resin. Ultrathin sections were treated with rabbit antirat EGF antibody, the gold labelled goat antirabbit IgB before staining.
Epidermal growth factor was measured in amniotic fluid by radioimmunoassay. In proximal and distal small intestine EGF was membrane associated along the luminal surface and within apical endosomal compartments. Epidermal growth factor was detected free of the membrane in multivesicular bodies, in some basal vesicles and beyond the basolateral membrane. Concentration of EGF in amniotic fluid was 0.4 ng/ml. We demonstrated that EGF is transported across the epithelium of fetal rats. It is likely that amniotic fluid EGF plays a part in intestinal mucosal development, and may be active systemically after transplacental passage in utero.

Distribution of EGF and TGFα throughout the normal human gastrointestinal tract

S CARTLIDGE, J B ELDER, H GREGORY (Department of Postgraduate Medicine, University of Keele, Staffordshire and Department of Biochemistry, ICI Pharmaceuticals, Alderley Edge, Cheshire) The levels of EGF present in normal gastrointestinal mucosa are unknown. It is possible that this peptide plays a role in the maintenance and renewal of cells of the gut epithelium. A closely related peptide, TGFα, has hitherto been associated only with normal foetal and neonatal tissues, or with transformed cells. Epidermal growth factor receptors are widely distributed throughout the G-I tract mucosa. The aim of this study was to seek evidence for the presence of EGF or the related ligand TGFα in gut mucosa. We have extracted acid soluble proteins from normal human gastrointestinal mucosae freshly obtained from three healthy adult organ donors (two men, one woman) and from one juvenile (girl aged 7 years). Mucosal extracts from stomach, duodenum, jejunum, ileum, ascending colon, transverse colon, descending and sigmoid mucosa were subjected to protein estimation and specific radioimmunoassays for human EGF and TGFα. These assays can detect 25 pg peptide per tube. There was no cross reactivity at 20,000-fold addition in either assay.

In normal adults TGFα was detected in every sample. Levels were lowest in duodenal and jejunal mucosa (400 pg/g tissue). Stomach mucosa contained 2457 (484 pg/g; ileum (1290 (191); ascending colon (3040 (814)); transverse colon (2122 (781); descending colon (1033) and sigmoid colon (616 (51)). In contrast EGF levels were significantly low throughout the G-I tract mucosa (51–154 pg/g tissue, p<0.001). In the juvenile tissues no EGF was detected in any mucosal extract. TGFα levels were closely similar in gastric, duodenal and jejunal mucosa (mean 8200 pg/g tissue); 5042 pg/g in the ileum; ascending colon 3043, transverse colon 3685, descending colon 3530 and sigmoid colon 5119 pg/g. Validity of the RIA systems was further supported by the separation of extracted peptides using reverse phase chromatography. These results show for the first time the presence of TGFα throughout the normal adult and in far greater quantity in juvenile G-I tract mucosa.

A cell kinetic study on the effects of oestriadiol and oestrastim in mouse cell lines

J D HARRISON, S WATSON, J O ELLIS, D L MORRIS (Departments of Surgery and Pathology, Queen's Medical Centre, Nottingham) Gastric and colorectal carcinomas have been shown to be oestrogen receptor positive in up to 50% of cases; sex hormones may be a factor stimulating the growth of gastric malignancy. We have studied the effect of serial dilutions of oestradiol, the combined oestriadiol nitrogem mustard compound oestramustine (Estracyt, AB Leo) and a combination of the two compounds on the in vitro growth of two human gastric and five colorectal cell lines by 75Selenomethionine incorporation. Significant stimulation of the two gastric (both 24% greater than control) and two colorectal cell lines (20% and 34% greater than control) occurred at physiological concentrations of oestradiol (nanomolar). Oestramustine showed an inhibitory effect in all of the cell lines at 10 ng/ml, and a direct dose dependent inhibition was seen in two of the cell lines. The inhibitory effect of oestradiol at 2 μg/ml (15% and in one gastric and 24% in one colorectal line) was lost with increasing concentrations of oestradiol, suggesting that the effects of oestradiol may be linked to oestrogen receptors. We conclude that oestradiol stimulates gastric and colorectal cell lines and that oestramustine has an inhibitory effect which can be competitively blocked by oestradiol.

EGF and TGFα levels in a mouse model of adenocarcinoma of the colon

S CARTLIDGE, J B ELDER, J DOUBLE, M BIBBY (Department of Postgraduate Medicine, University of Keele, Staffordshire and Department of Clinical Oncology, University of Bradford) The hypothesis that the EGF-receptor pathway is involved in tumour growth is currently under investigation in our laboratory. TGFα has been described as an embryonic EGF and is reported to be expressed by tumour cells. Using a mouse model of transplantable colonic adenocarcinoma we have examined eight histologically distinct solid murine adenocarcinomas and control normal mouse colonic tissues for the presence of EGF and TGFα. The entire colon was removed from 20 male and 20 female 10 week old MRNI mice. The tissues from each sex were pooled and acid soluble proteins from each batch were extracted using the method of Roberts et al 1980. Solid tissues from each tumour line (minimum 3 g) were similarly extracted. Each extract was assayed for mEGF and TGFα activity using specific RIA systems. MEGF RIA had a sensitivity of 6 pg per tube and the TGFα RIA could detect 24 pg per tube. There was no cross reactivity between the assays. EGF was found in greater quantity in normal male mouse colonic extract (2-176 ng/g of tissue) than in female colonic extract (1-305 ng/g tissue). Even greater amounts of TGFα, previously thought to be an embryo and tumour specific peptide, were found in both normal male (3-768 ng/g) and normal female colon (1-589 ng/g). TGFα was present in all tumour lines but not in amounts greater than normal tissues. EGF levels were lower in general and in one case (T line 26) was not detected. Neither absolute values nor ratios of growth factors in the tumours, or between tumour and control tissues could be related to the degree of histologic differentiation. A negative correlation was found between the ratio: Tumour (TGFα)/Control Colon (TGFα) and tumour doubling time in days (r=-0.560, p<0.05), implying that the nearer (TGFα) is to normal mucosal (TGFα) the tumour doubling time shortens.

Intestinal permeability: osmolarity revisited

P SMETHURST, J S MENZIES, A J LEVI, I BURNASON (MRC Clinical Research Centre, Warford Road, Harrow, Middlesex) There is much controversy regarding the effect of test dose osmolarity on the permeation of radiotracer markers. Ten to 12 volunteers ingested 100 ml containing 3-O-methyl-D-glucose (3MG) 0-2 g, D-xylene (Dx) 0-5 g, L-Rhamnose (LRh) 1-0 g and 11CrEDTA 100 μCi to assess active and passive carrier mediated transport and trans- and para-cellular permeability respectively, as (A) baseline; (B) with absorbed osmotic fillers B1: glycerol 1400 mosm/l; B2: glycerol 2800...
mosm/l; B₂: urea 3500 mosm/l; (C) with 'non-absorbed' osmotic fillers; C₁: lactulose 300 mosm/l; C₂: lactulose 1400 mosm/l, with 5H urines.

The excretion of 3MG was unaffected. B₁₋₂ did not affect DX but C₂ decreased it significantly (37±9 (2-9)% to 19-2 (2-7)% M (SE)). B₁₋₂ did not affect LRh but C₁₋₂ decreased it significantly (21-0 (1-8)% to 10-6 (0-9)% and 5-7 (0-7)% respectively).

**EDTA** excretion was increased significantly by B₁₋₂ (0-72 (0-09)% to 1-69 (0-23)% and 4-9 (0-4)% but C₁₋₂ decreased it significantly to 0-45 (0-12)% and 0-29 (0-04)%.

**Osmolarity** ratios which reflect altered permeability confirmed increased permeability after B₁₋₂ and decreased after C₁. Increased lactulose toxicity (C₁ to C₂) increased significantly the **EDTA/LRh** ratio from 0-026 (0-007) to 0-052 (0-007).

The different permeation pathways differ in their response to test dose osmolarity. There are profound differences in baseline excretion values depending not only on osmolarity of the test solution but also on the nature of the osmotic filler.

**Detection of partial gastrointestinal (GI) obstruction by surface vibration analysis (SVA)**

P T Cullen, F C Campbell, B E Storey, A Cucchiari, L D Wingate (University Department of Surgery, Ninewells Hospital and Medical School, Dundee and GI Science Unit, The London Hospital) Gastrointestinal contraction 'clusters' with alternating quiescence occur in partial intestinal obstruction (PIO) but are only detected by invasive intraluminal manometry. Surface vibration analysis is a non-invasive test of GI activity patterns, which may be useful in PIO. In this study SVA recordings were taken: (1) In two volunteers with partial obstruction induced by intrajejunum balloon distension, and evaluated against simultaneous manometry. (2) In nine patients with suspected partial obstruction. Results were compared with those of 36 non-obstructed volunteers.

Part 1: manometry showed contraction 'clusters' with alternating quiescence, in jejunum proximal to the obstructing balloon. The bowel distal, was totally quiescent. The SVA response of alternating hyperactivity and quiescence corresponded exactly with proximal jejunal manometry. Part 2: partial obstruction was proved in seven patients and disproved in two (laparotomy). Surface vibration analysis after a test meal, showed an obstructive pattern of high amplitude peaks lasting *3-53 (0-1) mins alternating with quiescence lasting 4-6 (0-3) mins, in all patients with proven obstruction. The SVA response in volunteers and non-obstructed patients was sustained, with few individual peaks (6-2 (0-7) volunteers v 13-1 (1-8) obstructed p<0-01). Low amplitude (total SVA energy 195-4 (19) volunteers v 405-7 (52) obstructed p<0-01%). * median (range).

**ileal mucosal transport:** in vitro-validation of the 'mini-Using' Lauterbach chamber for the study of human intestinal ionic fluxes

W Kmiot, Valeri A Poxon, N J Birch, J P L Coleman, R J Davie, A W Paterson, M R B Kehgley (General Hospital, Birmingham and Wolverhampton Polytechnic, Wolver-hampton) The Lauterbach system consists of two isolated hemichambers linked by a 2-5 mm diameter port-hole in the centre of an otherwise impermeable perspex sheet. We have studied 135 human ileal specimens, orientated such that the mucosal and serosal surfaces were in their own separate hemichamber. Both surfaces were maintained in hyperoxygenated Krebs buffer solution, at 37°C. Repeatable, transmucosal potential differences (PD) were maintained for three hours 3-8 mV (0-8 mV=5-9 Vm). Glucose caused a significant, reproducible rise in PD (p<0-05) and ouabain/sodium fluoride, a significant fall in PD (p<0-05). Wet tissue weight remained unchanged throughout the study (NS), indicating no cell disruption and structural oedema. This was confirmed on histological examination. Complete port-hole occlusion by the preparation was demonstrated by transchamber polyethylene glycol (PEG) marker passage of less than 0-5%. Human ileal extracellular space values were comparable to those of the guinea pig model, using two labelled PEG markers of differing molecular weights: (1) **PEG** 900 14-42 (11-14-17-37)% *n=62; (2) **PEG** 4000 10-00 (6-41-14-82)% *n=70. These studies validate the Lauterbach system for study of human ileal mucosal transport.

5-HT actions on intestinal fluid and electrolyte transport

The British Society of Gastroenterology

E Beubler, G Burg, I M Coupar, P T Hardcastle, J Hardcastle, A J Kitching (introduced by R J Levin) (Sheffield University, University of Graz, Austria, and Victorian College of Pharmacy, Melbourne, Australia) 5-Hydroxytryptamine (5-HT)-induced changes in transintestinal electrical activity are used increasingly to characterise the 5-HT receptors that regulate intestinal ion transport. Such changes reflect 5-HT action on electrogenic ion transport (increased CI secretion), but fail to detect its influence of electroneutral NaCl absorption which makes an important contribution to net fluid movement. To determine whether the same receptor mediates these effects the actions of 5-HT antagonists on 5-HT-induced changes in transintestinal PD and fluid secretion were measured in vivo. Cisapride (5-HT₃ antagonist, 5×10⁻⁵M) and ketanserin (5-HT₂ antagonist, 5×10⁻⁵M) reduced the rise in PD induced by iv 5-HT, but ketanserin (5-HT₂ antagonist, 7×10⁻⁴M, 3×10⁻⁴M, 1×10⁻⁴M mol/kg iv) and BRL 43694 (5-HT₃ antagonist, 8×10⁻⁶M mol/kg iv) were without effect (p>0-05). Fluid transport determinations produced contrasting data. Under control conditions 5-HT (1×10⁻⁶M mol/min/kg SC, p<0-05), but was reduced by ketanserin (60)% inhibition at 7×10⁻⁶M mol/kg, 68% at 3×10⁻⁶M mol/kg, 90% at 1×10⁻⁶M mol/kg SC, p<0-01) and BRL 43694 (39%) at 2×10⁻⁶M mol/kg, p<0-05, abolished at 2×10⁻⁶M and 2×10⁻⁷M mol/kg SC, p<0-01). Different receptors mediate the actions of 5-HT on transintestinal PD and fluid movement. These intestinal receptors do not conform to the current classification of 5-HT receptor subtypes.

Specific 5-HT receptor antagonist (GR 38032) Slows colonic transit and reduces neuropotin (NT) response in man

N J Talley, S F Phillips, L J Miller, A K Haddad (Division of Gastroenterology, Mayo Clinic, Rochester, MN 55905, USA) GR 38032 (Glaxo) is a selective antagonist of 5-hydroxytryptamine (5-HT) type three receptors on enteric neurons. To determine if GR 38032 affects small intestinal and/or colonic transit, randomised, double blind placebo controlled crossover studies were performed. Using a radio-opaque marker technique, colonic transit was measured in 10 healthy volunteers (four men, six non-pregnant women) aged 23-70 on a standard 25 g fibre diet; 16 mg tys of
Inhibition of lipid peroxidation by sulphalazine and 5-aminosalicylic acid (5-ASA)

N A PUNCHARD, R M BERRY, R P H THOMPSON
(Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London)

The therapeutic actions of sulphalazine and its component 5-ASA in inflammatory bowel disease may be due to oxygen radical scavenging ability. The erythrocyte provides a cellular model for evaluating the effects of these compounds on non-enzymic lipid peroxidation.

Aliquots (5 ml) of 1/40 (v/v) suspension of packed, washed erythrocytes of known haemoglobin (Hb) concentration, in 1.0 mmol sodium azide, 15 mmol phosphate buffered 0.14 mol/l saline, from five human subjects were incubated for one hour at pH 7.4 with 1 ml of 0 (control), 10⁻², 10⁻¹, 10⁻⁰, or 10¹ mol/l sulphalazine or 5-ASA in 0.02 mol/l sodium hydroxide.

Lipid peroxidation, measured as malondialdehyde (MDA) production at 90 minutes, was initiated with 0.75 mmol/l t-butyl hydroperoxide.

Lipid peroxidation was significantly lower (p<0.001, paired t-test) inhibited by 10⁻¹ mol/l sulphalazine (0.32±0.10) mmol MDA/mg Hb; mean (SD) versus control incubations (0.80±0.15) mmol MDA/mg Hb). Whereas 5-ASA significantly inhibited (p<0.001) inhibited MDA production, even at 10⁻¹ mol/l (0.48±0.12) mmol MDA/mg Hb).

The ability of 5-ASA and sulphalazine dose dependently to inhibit lipid peroxidation in vitro may reflect inhibition of production of pro-inflammatory lipid peroxides in vivo. 5-ASA is more potent than sulphalazine. This effect may underly their therapeutic properties.

Effects of inert plastic particles on human colon function

J TOMLIN, N W READ (Sub-Department of Human Gastrointestinal Physiology and Nutrition, K Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield)

Part of the mechanism by which coarse wheat bran affects bowel function may involve mechanical stimulation of the mucosa by particle edges. The effect of ingesting 15 g/d inert plastic particles (<2 mm diameter) for 10 days on colon function was assessed in 12 volunteers. The amount of faeces excreted increased (1:35 v 1:06 kg/wk, p<0.05); daily stool mass rose by nearly three times the mass of plastic ingested (mean increase 40 g/d). Stool frequency increased from 6:9 to 8:3 stools per week (p<0.05) and whole gut transit time decreased from 54-2 to 38:2 h (p<0.05) compared with control periods without particles. Ease of defecation and the number of flatulent episodes were unchanged but stool consistency, assessed with standard photographs, was significantly softer. In comparison a supplement of 37.5 g/d wheat bran (calculated to provide 15 g/d indigestible residue to the caecum) increased stool mass (1:56 v 1:14 kg/wk, p<0.05), accelerated transit time from 53:0 to 42:3 h (p<0.05), but had no effect on other parameters. The comparable effect of plastic particles on transit time and stool output to coarse bran, suggests part of bran's action on the colon may be through mechanical stimulation of multimodal mucosal receptors.

Do oral preparations of peppermint oil affect colonic motility in patients with irritable bowel syndrome

N P J Cripps, J K Ramage, R J Leicester (Royal Naval Hospital, Haslar, Gosport, Hants)

Peppermint oil (PO) has been advocated for treatment of irritable bowel syndrome (IBS), but whilst local application in the colon has been observed to reduce motility, visually at colonoscopy and manometrically, the effects of oral preparations have not been studied. In a randomised, double blind crossover study, we studied the effect of enteric coated PO capsules on sigmoid motility, using perfused tubes placed via flexible sigmoidoscope at 20, 25 and 30 cm from the anus connected via a pressure transducer to a pen recorder. Ten patients with IBS were studied. After one week's dosing (1 capsule tid) with PO or placebo, fasting recordings were made for 30 minutes before and after a standard breakfast. The study was repeated one week later after crossover of treatment. Motility Index (MI=mean peak pressures x percentage duration of activity) was calculated for each period and results compared using paired t test. Although PO reduced MI pre and postprandially in 80% of patients overall, the difference between treatments was not statistically significant (mean MI preprandial, postprandial: placebo 191±3, 240; PO 150±5, 243; t=0.7, p=0.2, t=6.5, p=0.4). The lack of difference may be explained either by the heterogenous nature of IBS patients or PO is released too high in the small bowel to affect colonic motility.
Colonic motility in the irritable bowel syndrome

J M HAMDORF, D M INGRAM, R W SALLIE, N E HOFFMAN (INTRODUCED BY D J C SHEARMAN) (Department of Surgery, University of Western Australia, Gastroenterology/Liver Unit, Sir Charles Gairdner Hospital, Nedlands, Western Australia) Colonic intraluminal pressures were measured continuously for 24 hour periods at multiple sites in patients with the irritable bowel syndrome (IBS) defined as abdominal pain with alteration in bowel habit. An 8-lumen recording catheter was passed over a flexible guidewire introduced at colonoscopy under light sedation in subjects following bowel cleansing. Digitised data were filtered to remove movement artefact and corrected for baseline shift. Motility Index (M1), defined as the ‘area under the curve’ over five minute intervals, was calculated for each of right, transverse, descending, and sigmoid colon, and rectum during sleep, on waking, prandially and postprandially. Five patients (mean age=33.2 years) were compared with eight normal subjects (mean age=25.5 years). The only significant difference during sleep was in the right colon where activity in patients with IBS was significantly greater than in normals (p<0.01). The major abnormality seen in IBS was the marked increase in M1 in the postprandial period where the values were seen to be at least three times greater than normal (p<0.01). Abdominal pain reported by patients with IBS was seen to occur concurrently with synchronous pressure rises in adjacent segments in the colon.

The effect of hysterectomy on bowel function

T TAYLOR, A N SMITH, P M FULTON (Gastrointestinal Unit, Department of Surgery/Urology, Department of Community Medicine, University of Edinburgh) Hysterectomy is a common, relatively safe operation but long-term sequelae or bladder function have been recorded. Possible effects on bowel function have been less well studied. A retrospective case control study compared the present bowel habit of 91 women who had had a hysterectomy in the years 1976–1983 with 91 other women who had not. The bowel habit of the control group was comparable with that of the previous study by Connell et al (1965). Use of criteria for constipation and diarrhoea gave relatively close agreement with the subjects’ own perception of bowel habit. The posthysterectomy cases had less frequent bowel actions than controls (p<0.05) and considered themselves constipated more often. Although more cases than controls used laxatives and had hard motions, these differences did not reach statistical significance. Significantly more cases than controls, however, had consulted a doctor because of constipation. There was a highly significant correlation between altered bowel habit and altered urinary frequency after hysterectomy (p<0.01). The results support the hypothesis that hysterectomy increases the risk of constipation and that there may be a common mechanism causing both the bowel disturbance and the altered urinary function.

Prospective evaluation of Manning’s criteria for irritable bowel syndrome (IBS)

N J TALLEY, S F PHILLIPS, L J MELTON, A R ZINSMIEISTER (Division of Gastroenterology, Mayo Clinic, Digestive Diseases Core Center, Rochester, MN 55905, USA) Can the symptoms of IBS lead to a positive diagnosis, without using expensive tests? Whilst the six criteria of Manning (Br Med J 1978; ii: 653) are used widely, data on their validity are limited. To evaluate this, we studied 340 outpatients with a bowel disease questionnaire (BDQ), which objectively measured Manning’s criteria, abdominal pain, and bowel habits. The patients included 81 IBS, 35 non-ulcer dyspepsia, 89 organic GI disease and 135 healthy controls. Diagnoses were based on full and independent clinical evaluations, not on BDQ responses. Reliability was assessed by a test-retest procedure. Logistic regression was used to analyse the discrimination of Manning’s criteria alone, as against a composite 10 item IBS score, based on a priori grouping of questions.

Individual Manning criteria were all reliable. As the number of positive criteria increased, so did the probability of IBS (any three, probability IBS=50%, all six, probability IBS=80%). But, sensitivity and specificity for all six criteria were 27% and 87%, respectively. The composite IBS score discriminated IBS from other groups (p=0.01). Stools that were often loose and watery provided additional independent criteria for distinguishing among groups (p=0.002). Thus, symptoms can diagnose IBS positively, but Manning’s criteria are not highly sensitive.

Does postprandial increase in sigmoid colonic motility cause transit of colonic contents? A combined manometric and scintigraphic study

J ROGERS, H H TAY, J J MISIEWICZ, G WALKER (Department of Gastroenterology and Nutrition Central Middlesex Hospital, London) Nine normal subjects (mean age 22 yrs (0-5) (SD) with normal bowel habit were studied without bowel preparation. Transit was measured by quantitative dynamic scintigraphy of a 39 MBq semisolid bolus of 125I-Tc-DTPA labelled Regular (1 g in 5 ml H2O) instilled at 40 cm from the anus. Intracolonic pressures were measured with open-ended water perfused tubes at 50, 40, 30, and 15 cm from the anus, analysed electronically for pressure activity in mmHg/min (area under curve). After a 30 min basal period, a standard meal of 1040 Kcal was taken and records continued for 90 min. The meal stimulated a significant (p<0.02, manova) increase in pressure activity in all subjects. In five subjects there was no transit of the marker from the sigmoid colon over the 2 h period of study (97 (2.7) v 92-6 (6.2) mean (SD)% residual counts). In contrast there was significant (98.7 (0-9) v 44-9 (12.3) p<0.002, paired t-test) transit of the marker distally in three and proximal in one. The onset of transit coincided with a marked increase in pressure activity at 50 cm, proximal to the anus. The increase in colonic pressure activity in the sigmoid colon following a meal is predominantly non-propulsive. Transit of contents from the sigmoid is associated with increased pressure activity in the descending colon.

Anal cancer and the human papillomavirus

J H SCHOLEFIELD, J G PALMER, L V CRAWFORD, J M A NORTHERO, introduced by R J Nicholls (ICRF Colorectal Cancer Unit, St Mark’s Hospital, City Road, London and Imperial Cancer Research Fund Laboratories, Lincoln’s Inn Fields, London) Epidemiological evidence suggesting an association between anal squamous cell carcinoma and receptive anal intercourse, together with case reports of malignant change in condylomata, led us to hypothesise that there may be an aetiological association between anal SCC and the human papillomavirus.

We have collected fresh tissue from a prospective series of 41 cases of invasive anal squamous cell carcinomas, which we have examined for evidence of HPV DNA sequences using Southern blot analysis. This is the most sensitive and informative molecular biological technique available for the analysis of DNA sequences.
We have found evidence of HPV type 16 DNA in 23/41 invasive anal squamous cell carcinomas and evidence of HPV 18 DNA in two further cases. These results have close parallels with those found from similar studies of cervical carcinomas.

We have examined our series further using in situ hybridisation to demonstrate that the viral DNA is within the nuclei of the malignant epithelial cells.

The evidence from these studies supports the hypothesis that human papillomavirus may be an actiological factor in squamous cell carcinoma of the anus.

Functional results of colo-anal anastomosis with colonic reservoir and excision of anal mucosa for rectal carcinoma

F GUilleMOT, J LEROY, A CORtOT, J MUNDReY, R MARTI, P QUANdALLe, M D LAMBlIN, J D GIUEU (Clinique des Maladies de l’Appareil Digestif, Service de Chirurgie adulte Ouest, service d’exploration fonctionnelles neuro-chirurgicales, CHU Lille 59037, Lille, Cedex, and Clinique de Bully les Mines 62160, France) Although well described, coloanal anastomosis (CAA) with constitution of a colonic reservoir has been functionally poorly evaluated. The aim of this study was to assess ano-rectal continence after CAA and to elucidate the mechanism of incontinence in some patients with CAA.

Sixteen consecutive patients (65-2 yrs, eight men) operated on for rectal carcinoma were studied six months at least and as a mean 17-4 months (nine) after closure of temporary loop colostomy after collection of a J shaped reservoir of 8 cm with excision of anal mucosa from 5 mm under the dentate line up to the superior limit of the levators insertion on the ano-rectal junction. Patients and six controls (65-8 yrs) underwent: (1) anal manometry; (2) determination of maximum tolerable volume (MVT). Patients underwent measurement of colonic reservoir pressure during liquid continence test (60 ml/min of a saline solution for 25 min (LCT). Twelve of 16 patient (group 1) were continent and able to defecate spontaneously (bowel frequency=2.5/24 h); four of 16 were not continent (group 2). Colonic reservoir pressure before LCT was significantly higher in group 2 (30 (10-8) mmHg) than in group 1 (18.75 (9-1) mmHg); p<0.05. Reservoir contractions were recorded significantly more often in group 2 (four of four) than in group 1 (four of 12) during LCT: p<0.05. MTV was significantly lower in group 2 (165 (46-5) ml) (mean (SE)) than in controls (261 (50-8) ml).

Left-sided colonoscopy highlights the failure of haemocult to detect colorectal neoplasia

D P HOLEY, P DUNNe, T D RYAN, M CODD, P DERVAN, J CROWe, T O’CALLaGHAN, J R LENNON (Louth County Hospital, Dundalk and Mater Hospital, Dublin) The usefulness of haemocult as a screening test for colorectal neoplasia was evaluated by performing left sided colonoscopy on 90 asymptomatic subjects ≥44 years who were given three haemocult II envelopes for completion. Subjects with neoplasia at left sided colonoscopy underwent full colonoscopy and polypectomy or surgical excision. Those with positive haemocult and negative endoscopy had double contrast barium enema.

Of 880 (98%) returning four or more smears 75 (8.5%) were positive of whom three had carcinoma and 21 adenoma at left sided colonoscopy. Colonic investigation was negative in 48. Among haemocult negative subjects three had carcinoma and 141 (18%) adenoma (2 mm-5 cm).

Sensitivity of haemocult for carcinoma is 50% and for neoplasia 14%; specificity – 92% and 93% respectively; positive predictive value 4% and 34%; negative predictive value 99.6% and 82%; false negativity 50% and 86% and false positivity 96% and 66%.

To our knowledge this is the only study to evaluate haemocult in asymptomatic subjects by using left sided colonoscopy as the reference test. The failure of haemocult to detect 50% of malignant and 86% of benign neoplasms clearly demonstrates its limitations as a screening method.

Conventional versus extended pre-operative staging in rectal carcinoma

W P MORGAN, M BULL, R NAKIELNY, S A C DUNDAs, A MILFORD-WARD (Departments of Surgery, Radiology, Pathology and Immunology, Royal Hallamshire Hospital, Sheffield) Thirty two rectal carcinomas were staged preoperatively by clinical examination (CS), endorectal ultrasound (ELU), and computerised axial tomography (CT), and compared with the pathology of the operative specimen. Extranodal extension of the tumour was demonstrated by CS, ELU, and CT with a sensitivity of 59, 91, and 73; specificity of 100, 100, and 60; positive predictive value of 100, 100, and 80, and a negative predictive value of 53, 83, and 50%. Pararectal nodes with a diameter >1 cm were demonstrated by CS, ELU, and CT, with a sensitivity of 18, 64, and 82; specificity of 95, 90, and 90; and positive predictive value of 67, 78, and 82; negative predictive value of 69, 83, and 90%.

Other authors have previously reported that the presence and nature of tumour fixity can be distinguished preoperatively by serum levels of carcinoembryonic antigen (CEA), α, acid glycoprotein (AGP), and C reactive protein (CRP). In this study, there were no significant differences in the levels of CEA, AGP, and CRP in relation to Duke’s stage or tumour fixity (none, inflammatory or malignant). Patients with liver metasteses had significantly higher serum CEA levels.
rectal tumours. Both patients in the surveillance group were symptomatic at the time of review colonoscopy. There were no metachronous tumours.

In group A, 10 patients were found to have adenomatous polyps at the first post operative colonoscopy. Only one patient had a polyp at a second or subsequent colonoscopy.

These results imply that surveillance after curative surgery for CRC may, with safety, be restricted to a single colonoscopy to ensure a clean colon. These findings apply only to the early post operative years.

Hepatic perfusion index (HPI) in diagnosis and follow up of metastatic colorectal cancer

K C BALLANTYNE, R M CHARNLEY, G PYE, A C PERKINS, D R WHALLEY, M L WASTIE, J D HARDCastle (Departments of Surgery and Medical Physics, University Hospital, Nottingham) Previous work has suggested that up to 90% of patients with metastatic liver disease have a raised HPI and that dynamic liver imaging is of value in the identification of occult hepatic metastases.

We have evaluated this technique in 180 patients, 109 with primary colorectal cancer, 38 with suspected recurrent disease and 33 after curative resection of colorectal cancer, to determine its role in the detection and follow up of this disease. Serial imaging studies were performed in 21 patients with metastatic disease. Hepatic perfusion index was determined using peak of the left kidney time activity curve to define the division of arterial and portal blood flow.

Hepatic perfusion index was raised (>0.37) in 54/115 (47%) patients with no evidence of hepatic metastases, 17/27 (63%) patients with hepatic metastases at initial presentation, 21/25 (84%) with metastatic disease detected during follow up. Four of 12 (31%) of those with local recurrence and CT scan disease free livers had an elevated HPI. In 18/21 (86%) patients with metastatic liver disease serial imaging demonstrated a rising HPI with disease progression.

This study confirms the association of a raised HPI with hepatic metastases and suggests that a rising HPI on serial studies is associated with progression of disease.

Monoclonal antibodies to colorectal cancer

C Y YIU, L BAKER, M J O'HARE, C G CLARK (Department of Surgery, University College London and Institute of Cancer, Sutton, Surrey) For the immunoscintigraphy or targeting of colorectal cancer, monoclonals with a greater affinity for the tumour than normal tissues are required. Owing to tumour heterogeneity, any one monoclonal will only react with a proportion of colorectal cancers; a cocktail of monoclonals may be necessary for effective targeting. Antibodies with greater tumour specificity and reactivity are thus in demand. We have raised monoclonal antibodies to colorectal cancer using a crude membrane extract (CME) of tumours obtained from 13 patients. Balb C mice were immunised with CME and the spleen cells fused with the myeloma cell line NSO. A total of 10 fusions produced 893 hybridomas. Initial screening with an enzyme linked immunosorbant assay (ELISA) on CME showed that 245 were positive. Secondary screening with immunocytochemistry on frozen sections of colorectal cancer identified 67 reactive antibodies, five of which show membrane reactivity. One antibody UC-ICR 20-3 reacts with 11 of 13 (85%) different colorectal cancer sections. It has no reaction with connective tissue and a minimal reaction with normal colon and a few other epithelial cells. Flow cytometer analysis shows that it reacts with three colorectal cancer cell lines (LoVo, SW480, Colo 205) but not with blood cells or fibroblast. UC-ICR 20-3 is therefore suitable for the immunoscintigraphy or targeting of colorectal cancer.

Carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA) in colorectal cancers

B R DAVIDSON, V R SAMS, J STYLES, C G CLARK (Departments of Surgery and Pathology, University College London and Institute of Cancer Research, Sutton, Surrey) Carcinoembryonic antigen and EMA are tumour associated antigens which may be expressed by colorectal cancers. Their expression has not previously been compared in a consecutive series of colorectal cancers. The role of antibodies to CEA and EMA in localising occult metastatic deposits was also assessed. Adjacent sections of cancer, normal colon and lymph nodes from 34 consecutive patients undergoing excision of a colorectal cancer were examined by the indirect immunoperoxidase method using monoclonal antibodies to CEA and EMA in addition to conventional H&E staining.

Immunohistochemistry was carried out using standardised titres of both antibodies and incubation times. The percentage of tumour cells staining with each antibody was assessed on a four point scale.

All tumours expressed CEA whereas five of 34 (15%) did not express EMA. CEA stained >50% of tumour cells in 24 of 34 sections (71%) which was significantly greater than EMA (six of 34=18%) (p<0.01). CEA expression was greater in well differentiated tumours (p<0.05) whereas EMA expression was not significantly different. One hundred and sixty three lymph nodes were examined (median 6/ patient, range 2–11) on H&E with 31 nodal metastases being found in 13 patients. Immunohistochemistry of nodal deposits was negative in three sections with CEA and in two with EMA. Occult metastatic tumour not visualised on routine H&E staining was located with anti-CEA in one patient but not with anti-EMA.

Effects of cytochalasin B and colchicine on colonic restitution

P H ROWE, C HANLEY, R M CASON (Department of Surgery, Guy's Hospital, UMDS, St Thomas, London) Restitution is restoration of the continuity of the surface epithelium by cell migration. It has been previously reported to occur in colonic mucosa in vitro. We investigated the effects of colchicine, a potent inhibitor of DNA synthesis and cytochalasin B, an inhibitor of cell migration on the process of restitution in colonic mucosa.

Using chambered bull frog colonic mucosa (n=10) exposed to molar NaCl in the luminal chamber exhibited an immediate fall in potential difference (PD) and a fall in resistance (R). Tissues removed (n=5) after NaCl exposure exhibited severe mucosal injury with denudation of the basal lamina. After 10 minute NaCl exposure and replacement of NaCl with standard luminal solution, when tissues were allowed to recover for four hours, there was histological reconstitution of the surface epithelium and the PD and R returned to values, not significantly different from the PD and R in controls. Tissues (n=7) pretreated with colchicine (10–5 M) for 90 minutes, treated with NaCl and four hour incubation in the chambers also exhibited electrical and histological recovery. Tissues (n=5) pretreated with cytochalasin B (10–4 M) exhibited no evidence of recovery. In conclusion, cytochalasin B but not colchicine inhibits the process of restitution in amphibian colonic mucosa after injury by molar NaCl. This supports our hypothesis that restitution of the colonic mucosa involves epithelial cell migration and not rapid cell division.
Restitution occurs in colonic mucosa in vitro after bile salt injury

Q Zhang, C Hanley, R C Mason, P H Rowe, J McColl (Department of Surgery, Guy's Hospital, UMDS, St Thomas Street, London) Restitution is restoration of the continuity of the surface epithelium by epithelial cell migration and has been previously reported to occur in colonic mucosa in vitro after injury by hyperosmolar NaCl.

We investigated whether restitution in colonic mucosa occurs following injury by bile salts. Using chambered bull frog colonic mucosa exposed to 10 mM sodium deoxycholate (DOCA) in the luminal chamber, exhibited an immediate fall in potential difference (PD) from 83 (16) (mean (SE)) to 8.0 (4) mV and fall in resistance (R) from 200 (7) to 60 (20) ohm cm². Tissues removed (n=6) following DOCA exposure exhibited severe mucosal injury with denudation of the basal lamina. After 10 minute DOCA exposure and replacement of DOCA with standard luminal solution, when tissues (n=11) were allowed to recover for four hours, there was histological reconstitution of the surface epithelium and the PD and R returned to values, not significantly different from the PD and R in controls (n=10).

We conclude restitution occurs in colonic mucosa in vitro after bile salt injury. Restitution is therefore an important repair process and probably occurs after a variety of injurious agents.

A protective effect of sulindac against 1,2 dimethylhydrazine (DMH)-induced colonic tumours in mice

M Moorghen, P Incé, Karen J Finney, D R Appleton, J P Sunter, A J Watson (University Departments of Pathology and Medical Statistics, University of Newcastle upon Tyne) Sulindac, a non-steroidal anti-inflammatory drug is alleged to cause the disappearance of tumours in cases of human adenomatosis coli. We used the DMH model of colonic carcinogenesis using Balb/c mice in a controlled study to investigate the effects of sulindac on carcinogenesis and on established tumours. In one cohort of animals sulindac was administered for up to 11 weeks after the initial period of tumour induction. In a separate cohort sulindac and DMH were administered concurrently for a period of up to 24 weeks in order to assess any possible effect on tumour development.

Sulindac failed to cause the regression of established colonic tumours, whereas when administered concurrently with DMH, it caused a reduction in both the number of mice with tumours and the number of macroscopic tumours and microadenomas per animal.

Whilst we have failed to reproduce the phenomenon of tumour regression in this experimental model, we have demonstrated a protective effect with regard to the development of new tumours. The fact that impaired development of new tumours was paralleled by a reduction in the incidence and number of microadenomas suggests that sulindac exerts its effect at a stage in the tumorigenesis process before microadenoma formation.

Natural killer cell activity of peripheral blood, mucosa, and tumour infiltrating mononuclear cells in patients with colorectal cancer

M N Aparicio-Páges, H W Verspaget, A S Peña, C B H W Lamers (Department of Gastroenterology and Hepatology, University Hospital Leiden, The Netherlands) Natural killer (NK) cell activity has been reported to be decreased in peripheral blood mononuclear cells of cancer patients. We have studied the NK cell activity not only from the peripheral blood, but also from the intestinal mucosa and the tumour of patients with colorectal carcinomas.

Peripheral blood mononuclear cells from patients and controls (both n=15) were isolated by Ficoll/Hypaque density gradient centrifugation. Mononuclear cells from intestinal mucosa and tumour (n=12) were isolated by a multistep isolation procedure using DTT-EDTA-Collagenase incubations and density gradient centrifugation. Natural killer cell activity was determined by an 18-h chromium-51 release assay at effector:target cell ratio of 50:1 (blood) and 500:1 (intestine and tumour). The targets used were the erythromyeloid K-562 cell line, and two human colon carcinoma cell lines CaCo-2 and HT-29. The results are expressed in % cytotoxicity.

Peripheral blood mononuclear cells from the patients showed a similar NK cell activity, compared with the controls, against all three targets (K-562, 52 (11) v 58 (2), CaCo-2 225 (4) v 28 (5), and HT-29 13 (5) v 12 (2), respectively). Tumour infiltrating mononuclear cells had a significantly (p<0.01) lower NK activity compared with the normal intestinal mucosa mononuclear cells (K-562 14 (2) v 33 (7) and CaCo-2 12 (2) v 34 (6) respectively).

The present study shows no defect in peripheral blood NK cell activity in patients with colorectal cancer. In contrast, however, colorectal tumours have a decreased NK cell activity compared with normal intestinal mucosa. These observations are indicative of a deficient immune surveillance at the tumour level in colorectal cancer.

Application of plasminogen activator measurements to endoscopic biopsies as markers of gastrointestinal malignancy

P A F de Bruijn, H W Verspaget, G Griffioen, J H Verheyen, G Doouewaard, C B H W Lamers (Department of Gastroenterology and Hepatology, University Hospital and Gauubius Institute TNO, Leiden, The Netherlands) In resection specimens of colorectal adenocarcinomas, the concentration of urokinase-type plasminogen activator (u-PA) is markedly increased when compared with the normal parent mucosa, while on the contrary, the tissue-type plasminogen activator (t-PA) shows a decrease in malignant colonic tissues.

In this study, assays for u-PA and t-PA, antigens as well as activity, were analysed on their efficacy to distinguish between endoscopic biopsies from normal and malignant tissues. For reference, u-PA and t-PA were also investigated in the ultimate resection specimens of the same patients (n=14), which were all proven to have a carcinoma. The results were compared with the histology of adjacent biopsies as well.

In the tumour biopsies, a significant (p<0.001) and more than six-fold increase of u-PA antigen (12-6 (2-0) v 2-1 (0-4) ng/mg protein) was found when compared with the normal tissue biopsies. Combined with the t-PA antigen level (3-1 (0-5) v 3-8 (0-8)) which was equal or lower than in the normal mucosa, the ratio of u-PA/t-PA antigen in the biopsies was found to be a good (p<0.001) discriminating parameter for malignancy (ratio >2-2) with a sensitivity of 86% and a specificity of 100%. In the resection specimens, these figures were better 100%. Among the biopsies, only two false negatives out of fourteen cases were found, similar as to the histological evaluation. Discrimination between normal and tumour tissue based upon u-PA and t-PA activities was less efficient than by the respective antigens.

Determination of plasminogen activators can effectively be applied to endoscopical colonic biopsies. Assays for u-PA and t-PA antigen in endoscopical biopsies may contribute to the detection of malignancies in the colon.
Familial aggregation of tumours of the large bowel

M PONZ DE LEON, R SASSATELLI, C SACCHETTI, G ZANGHIERI, A SCALMATI, L RONCUCCI (Istituto di Patologia Medica, Università di Modena, via del Pozzo 71, 41100 Modena, Italy) Genealogical trees of 389 patients with colorectal cancer registered in 1984–86 and of 389 controls were analysed with the objectives: (a) to determine whether there was an increased frequency of cancer among first degree relatives, (b) to identify kindreds with hereditary colorectal cancer (Lynch syndrome). Eighty nine cases of colorectal cancer were observed among first degree relatives of patients and 19 among control relatives (cumulative incidence ration 4·48, p<0·001). In 182 patients there were one or more cases of cancer (of all sites) among relatives; similarly, in 68 patients (18 controls) there were one or more relatives affected by colorectal cancer. In patients without or with only one neoplasm in their family members tumours were mostly located in the left colon; however, cancer of the right colon (a feature of Lynch syndrome) was frequently observed in patients with two or more cancers of all organs among relatives and even more often in patients with two or more colorectal cancers in their families. In conclusions, our findings suggest that a genetic susceptibility to colorectal cancer may exist in approximately 15–20% of the registered patients. Moreover, in a further subgroup of about 5% of all cases the marked excess of colorectal cancer among relatives (two or more) and the frequent location of tumours in the right colon strongly support the diagnosis of Lynch syndrome.

Ileal reservoir inflammation (Pouchitis) after restorative proctocolectomy ileal reservoir

P A FARRANDS, N A SHEPHERD, R J NICHOLLS (St Mark’s Hospital, City Road, London) Inflammation of the reservoir is a recognised complication of restorative proctocolectomy with ileal reservoir. Ninety patients treated between 1979 and 1987 were followed at three to six monthly intervals for a mean of 4·2 years (range 0·9–9 years). Function and endoscopic findings were recorded and inflammation in biopsies from the reservoir was graded histologically on a scale 0–6. Pouchitis was defined by clinical, endoscopic, and histologic criteria as previously described. Frequency of defecation was correlated with both endoscopic and histologic severity of inflammation (r=0·72, p<0·01 and r=0·49, p<0·01). Fourteen patients (15%) developed pouchitis. The time of onset ranged from 0 to 36 months from closure of the temporary ileostomy. Inflammation fluctuated over weeks to months from mild (grade 0–2) to severe (grade 5–6). All 14 cases of pouchitis occurred in patients with total colitis (n=68) significantly more frequently than in those with left sided colitis (n=15) (p<0·05 Fishers exact test). No patient with polyposis (n=7) developed pouchitis. Extent of colitis appears to be a marker for pouchitis.

What is the role of vascular pressure in high anal pressure in patients with haemorrhoids?

WEI MING SUN, N W READ, T C DONELLY, A G JOHNSON (Department of Surgery and Sub-Department of Human Gastrointestinal Physiology and Nutrition, University of Sheffield) Multisport anal manometry and anal sphincter electromyography were conducted in 26 male patients (aged 31–77 years) with non-prolapsing haemorrhoids and eight matched controls. Fifty per cent patients complained of a feeling of obstructed defecation. The basal pressures were significantly higher in patients than in normals (66 (2) v 43 (7) cmH2O, mean (SE); p<0·05), but there was no significant difference in maximum squeeze pressures (280 (13) v 257 (20) cmH2O). During rectal distension, 92% of patients showed no relaxation in the most caudal channel, even when relaxation occurred in the inner anal channels, the internal anal sphincter electrical oscillations were abolished and the external sphincter EMG was not increased above pre-distension values. Residual anal pressures during balloon distension were significantly higher in patients than in normals (51 (1) v 34 (4) cmH2O; p<0·01). When subjects increased their intra-abdominal pressures to inflate a balloon, the rectal pressure was significantly higher in patients than in normals (132 (10) v 94 (7) cmH2O; p<0·05). Pressures in the anal cushions (30 (2) cmH2O) were measured in 10 patients; they were much higher than normal capillary or venous pressure, and showed respiratory oscillation, and pressure increases during coughing (64 (7)) and straining (61 (6)). Pressures after straining were higher than before straining (39 (3) v 30 (2) cmH2O; p<0·05). This study suggests that the abnormally high anal pressures in the anal canal in patients with haemorrhoids may be related to an increased vascular pressure in the anal cushions.

The British Society of Gastroenterology

Spontaneous anal relaxation – a cause of faecal incontinence?

WEI MING SUN, D D KERRIGAN, N W READ, T C DONELLY (Sub-Department of Human Gastrointestinal Physiology and Nutrition, University of Sheffield) Multisport anal manometry and external anal sphincter (EAS) electromyography in 25 of 140 patients with faecal incontinence and six of 35 age and sex matched healthy controls during a 20–30 min period of rest, showed periods of spontaneous anal relaxation lasting >15 sec and reducing pressure in the outermost anal channels by >20 cm water. The patients exhibited more episodes of relaxation than the controls (4·0 (0·6) v 2·2 (0·2) per subject; mean (SE); p<0·05) and the pressure fell to lower values (19 (1) v 42 (5) cmH2O; p<0·01), but the duration of relaxation was not significantly different (47 (5) v 40 (5) seconds; p>0·05). Fifty per cent and 68% of the episodes of spontaneous relaxation in normal subjects and patients respectively were associated with simultaneous rectal contractions. Eighty three per cent of episodes in normal subjects were associated with compensatory increases in electrical activity of the EAS, and leakage did not occur. Only 31% of patients showed increased EAS activity (p<0·05) and leakage only occurred in those patients who did not show this response. When internal sphincter slow waves were apparent on the EMG records, these were abolished or attenuated during spontaneous relaxation. The rectal volumes required to elicit anal relaxation (10 (0) v 28 (7) ml; p<0·05), to induce sustained relaxation (60 (8) v 82 (5) ml; p<0·05), and to cause a desire to defaecation (36 (4) v 63 (9) ml; p<0·05) were all lower in incontinent patients who showed spontaneous relaxation compared with those who did not. In conclusion spontaneous relaxation of the internal sphincter may be a cause of incontinence in patients with a sensitive rectum.

Chronic constipation is associated with evidence of impaired urethrovaginal and sacral reflex function

D D KERRIGAN, W M SUN, T C DONELLY, N W READ (Department of Surgery/Sub-Department of Human GI Physiology, K Floor, Royal Hallamshire Hospital, Sheffield) Sixteen chronically constipated female patients (aged 20–66 yrs) underwent combined multisport anorectal manometry with external anal sphincter (EAS) EMG, video-urodynamic assessment and neurophysiological studies of evoked pelvic spinal
reflexes. For the latter, the dorsal nerve of the clitoris was stimulated electrically and the latency of the evoked reflex activity in the external anal and urethral sphincters was measured using concentric needle and surface electrodes. Resting and squeeze anal pressures and the threshold rectal distension required to cause internal anal sphincter relaxation were similar in constipated patients and healthy female controls. Constipated women, however, required a higher volume to elicit a desire to defecate (p=0.001) and 73% failed to relax their EAS when attempting to expel a simulated stool. Fifty six per cent of the constipated women displayed urodynamic abnormalities (increased bladder capacity, obstructed voiding and stress incontinence). Complete absence of clitoro-urethral evoked sacral reflexes was found in 75% of constipated subjects (compared with 20% of healthy controls, p<0.02). It was notable that each of the five patients who had related the onset of their constipation to hysterectomy had absent sacral reflexes and impaired urodynamics.

An electromyographically derived (anismus) index in pelvic floor outlet obstruction during defaecation straining

B M KAWIMBE, N R BINNIE, A N SMITH
(University Department of Surgery/ Urology, Western General Hospital, Edinburgh) Obstructive defaecation due to failure of relaxation of the pelvic floor muscles during straining, or anismus, may be associated with abdominal pain, excessive straining, constipation and pathological changes such as pelvic neuropathy, faecal incontinence, megacolon and rectal prolapse.

An anismus index of the pelvic floor muscles recorded non-invasively relates the anal sphincter EMG activity during straining to the anal sphincter EMG activity during voluntary squeezing. EMG activity during straining – EMG activity at rest/EMG activity during squeezing – EMG activity at rest×100.

The anismus index (normals 0% or less) was calculated for patients (n=60) with distal bowel problems. The correlation between the mean anismus index and associated conditions was as follows – perineal descent 33-8%, pelvic/perineal pain 59%, faecal incontinence 64-7%, megacolon 76-1%, intractable constipation 80-8%, rectal prolapse 86-7%, pelvic neuropathy 108-6%, and ‘occlusive’ defaecation straining 114%.

Using this index it is possible to predict the extent of pathological changes and suggest management. Mild anismus (<25%) produced minimal complaints; moderate (25–50%) responds to conservative measures (suppositories, dilator). Severe anismus (>50%) was associated with secondary pathological changes, most of which required a pelvic floor repair or subtotal colectomy.

Predictive value of computed tomography (CT) scanning of the gall bladder in determining gall stone type

S RAJAGOPAL, P BILLS, A KEIGHTLEY, G M MURPHY, R H DOWLING (Gastroenterology Unit, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals, London) Non-surgical treatment of gall bladder stones is confined to cholesterol-rich stones and although 80–85% of radiolucent (plain radiograph+OOG) stones are cholesterol rich, the remaining 15–20% are not, often do not dissolve and are sometimes CT-dense. To study this further, we used a Philips Tomoscan 350 to measure stone attenuation in preoperative patients (Hounsfild units: HU) and correlated this subsequently with analysis (chemical, atomic absorption, infra-red spectroscopy, electron probe and scanning EM) of stones obtained at surgery.

There were significant linear correlations between HU score and (i) stone total calcium (CaTOT: r=0.853; p<0.001) and (ii) calcium carbonate content (CaCO3: r=0.826; p<0.005) but not with (iii) cholesterol content (r=0.278; NS). Although stone CaTOT correlated significantly with CaCO3 (r=0.84; p<0.001) and most CT-dense stones were CaCO3-rich, some CT-dense stones contained little or no CaCO3. Stones with >3% CaTOT by weight (n=12) invariably had >90 HU: only two of 15 with <3% CaTOT had >90 HU. Stones with <60 HU (n=10) were invariably cholesterol-rich and had <1-5% CaTOT: those with >110 HU (n=8) always had >4% CaTOT, with overlap in the intermediate group (60–110 HU).

Computed tomography scanning has high sensitivity and specificity in predicting gall stone type: CT-dense stones are mainly CaCO3-rich.

Gall bladder wall thickening in chronic liver disease – a new sign of portal hypertension?

S H SAVERYMUTTU, A E A JOSEPH, J D MAXWELL (St George’s Hospital, London) A thickened gall bladder wall is often seen on ultrasound in alcoholic cirrhosis. Hypoalbuminaemia is thought to be the cause as there is a strong association between bowel wall thickening and low serum albumin. The stomach is also frequently thickened in cirrhosis, however, but in this situation – the recently described congestive gastropathy – portal hypertension is the cause. To determine the role of portal hypertension in producing gall bladder wall thickening we studied 37 consecutive stable cirrhotics. Ultrasound assessment of the gall bladder wall was made after an overnight fast using a Technical auto-sensor. Wall thickness >4 mm or greater was considered abnormal. Twenty six patients had a thickened gall bladder wall and all had evidence of portal hypertension. Hypoalbuminaemia was not an important factor since it was only present in five cases. These results suggest that portal hypertension, not hypoalbuminaemia is the dominant factor in causing gall bladder wall thickening in cirrhosis. Ultrasound demonstration of gall bladder wall thickening in chronic liver disease should suggest the presence of portal hypertension.

Optimising wavelengths for common duct laser lithotripsy

A MURRAY, R BASY, P D FAIRCLOUGH, R F M WOOD (St Bartholomew’s Hospital, London) Laser energy has been shown to have the potential to fragment gall stones in the common bile duct, but the optimal parameters in terms of efficiency of fragmentation and safety have yet to be defined. We report in vitro studies of gall stone fragmentation to determine these parameters. From 10 patients with multiple stones, 55 gall stones with a mean weight of 1.1 g and a mean maximal diameter of 12 mm were randomised into six groups. One stone from each patient was analysed for bile pigment, cholesterol and inorganic salt content. Each group was subjected to laser energy from a Pulsed Dye laser at a wavelength of 440, 480, 504, 560, 590, or 635 nm. The energy was conveyed by a 0-4 mm flexible optical fibre held in direct contact with the stone held under saline. Pulse energy was increased until gross fragmentation occurred. There was no direct correlation between fragmentation energy and stone weight or chemical composition. Fragmentation was most efficient at 440 nm. The energy required was significantly greater at all the longer wavelengths (p<0.01). Furthermore at short wavelengths
bile acts maximally as an absorber of stray laser light, thus minimising risk to the duct. These effects are consequent upon the absorption peak of bilirubin at 450 nm. Our results suggest that the Pulsed Dye laser at short wavelengths is likely to be optimal for gall stone lithotripsy.

Efficacy and cost of extracorporeal shock wave lithotripsy (ESWL) for cholelithiasis

T D Ryan, J R Lennon, J P Crowe (Hepato-Biliary Unit, Mater Misericordiae Hospital, Dublin) Gall stones can be successfully treated by ESWL using the Siemens Lithostar. Whether it represents a reasonable alternative to surgery has yet to be determined.

Twenty one patients (mean age 43 years) with stones in a functioning gall bladder, have been treated by ESWL. There were 10 solitary (1–3 cm in diameter) and 11 multiple (2–10 in number) stones. In three patients the stones had a calcified rim and three a calcified centre. Gall bladder opacification to allow stone localisation was achieved with oral iopanoic acid. Nine patients had one treatment session and 12 had two. A mean of 8000 (2000–14000) shock waves were delivered per patient. Stone fragmentation was achieved in 14 patients (66%) but five had fragments 5 mm and one patient developed pancreatitis because of fragment impaction and required urgent cholecystectomy and exploration of the common duct. To date eight patients have been reviewed at six weeks, two had complete gall bladder clearance of fragments. Of the seven failures three underwent cholecystectomy and three cholecystolithotomy.

Because of the significant failure rate, the in-hospital costs of gall stone management by ESWL were 24% greater than that of a surgical approach.

This audit reveals that substantial improvements have yet to be achieved before ESWL can be accepted as a treatment option for cholelithiasis.

Up and down the bile duct: improved success for endoscopic stenting of malignant biliary obstruction using the combined percutaneous-endoscopic approach

A Polydorou, J F Dowset, D Vaira, S R Cairns, J Croker, P B Cotton, R R Mason, R C G Russell, A R W Hatfield (Departments of Gastroenterology, Radiology, and Surgery, The Middlesex and London Hospitals, London) During the three year period ending June 1988, 94 patients with malignant biliary obstruction had attempted combined percutaneous-endoscopic endoprosthesis insertion (CP) after failed endoscopy alone insertion (ERCP). All neoplasms were not amenable to attempted curative resection. Only one stent was placed unless evidence of sepsis in undrained segments developed. Strictures were divided into common bile duct (low) and hepatic duct ( hilar) groups. The latter were subdivided into types I, II, or III (after bismuth). Success was defined as a fall in bilirubin >30% and loss of pruritus.

There were 59 low, eight type I, 12 type II, and 15 type III strictures. The mean age was 71 years and the mean bilirubin 370 μmol/l. PTBD was successful in 90 patients (96%). CP was successful in 76 patients (81%). For low, type I, type II, and type III strictures, the success rates were 80%, 100%, 83%, and 73% respectively, i.e., total (ERCP+PTBD+CP) procedural morbidity was 27, 2, 11, and 10 events respectively or 46%, 25%, 92%, and 67% respectively, and the 30 day mortalities were 22%, 13%, 42%, and 13% respectively. The mean survivals of deceased patients (70) were 2-5, 7-4, 1-2, and 7-3 mths respectively. Only four of the deaths within 30 days of CP were directly procedure related and 44% of complications were related to the initial ERCP. Five hilar stricture patients (14%) needed a further CP to deal with septic undrained segments. Endoprostheses has been required on 20 occasions with ERCP successful in 16 and repeat CP in four.

The combined procedure improves the success rate of endoscopic stenting but increases procedural morbidity and is associated with considerable disease related early mortality.

Late results of endoscopic biliary duct clearance in patients considered unfit for surgery

C J H Ingoldby, J El-Saad, R I Hall, M E Denyer (Departments of Medicine and Surgery, St James’s University Hospital and Seacroft Hospital, Leeds) Endoscopic clearance of bile duct stones is frequently performed in patients with gall bladders in situ. The need for subsequent cholecystectomy is disputed. We have examined the long-term outcome of endoscopic biliary clearance in a larger series than previously reported.

Endoscopic sphincterotomy was performed on 186 patients with common bile duct stones and gall bladders pararenal, who were considered unfit for surgery. One hundred and seventy one patients were jaundiced and 18 also had clinical cholangitis. The mean age of treated patients was 79-7 years (range 27–92) and only 13 were aged less than 60. Sphincterotomy was successful in 185 (99%) and complete clearance in 172 (92-5%). Early complications occurred in nine patients (4-8%) of whom three died (1-6%). The patients have been followed for a mean of 32 months (range 6–72 months). Eighteen patients have required subsequent cholecystectomy (9-6%), with six major complications, but no deaths. There have been 27 unrelated deaths and 156 patients remain alive and symptom free.

Endoscopic treatment alone is safe and effective in the majority of frail and elderly patients and can reduce the need for surgery in this high risk group.

ENDOSCOPY POSTERS

Is routine sedation appropriate for upper gastrointestinal endoscopy (UGE)?

P A Cann, D D Kerrigan (Departments of Gastroenterology and Surgery (J Floor), Royal Hallamshire Hospital, Sheffield) One hundred and twenty consecutive out-patients (76 men) undergoing their first UGE were randomised to receive xylocaine spray plus 10 mg diazepam, or spray alone. Upper gastrointestinal endoscopy was performed by either an experienced or a relatively inexperienced endoscopist, making four subgroups of 30 patients. Patients completed postal questionnaires; endoscopists rated patients’ reaction to the spray and UGE.

Four questionnaires were not returned, four patients allocated spray alone required sedation, and one allocated sedation declined it. Patients in both groups reported similar tolerance for each endoscopist. When asked if sedation would be preferred at any subsequent UGE, 29% of non-sedated patients would prefer to receive diazepam (v 88% of the sedated group, p<0.001). Reasons for declining sedation were: interference with subsequent activities (52%), not remembering diagnosis/advice (27%), and fear of needle/impaired consciousness (21%). Tolerance without sedation was better in men (p=0.025) and in patients >50 yrs (p=0.01). Reaction to xylocaine spray did not predict UGE tolerance.

Despite endoscopists’ impression that ease of UGE was similar in each group, sedated patients reported excellent tolerance more frequently than non-sedated.
Reversal of midazolam sedation for gastroscopy by flumazenil

R C PEARSON, P MORRIS, P F MCCLOY, K D BARDHAN (Manchester Royal Infirmary, Oxford Road, Manchester and District General Hospital, Moorgate Road, Rotherham) Flumazenil, a benzodiazepine antagonist, was used to reverse midazolam induced sedation in a double blind placebo controlled study in patients undergoing gastroscopy. Assessments were made up to one hour after reversal and again 18-24 hours later. Eighty patients in two centres received midazolam 5 mg iv before gastroscopy. After endoscopy half (n=40) received flumazenil (0-5 mg iv) and the others (n=40) placebo. Significantly more patients were fully conscious in the flumazenil group at five minutes (77-5% v 27-5%; p<0.001) and 30 minutes (80% v 42-5%; p<0.001) after reversal, but not at 60 minutes. Times to complete Trieger (dot joining) tests were significantly faster in the flumazenil group at 5, 30, and 60 minutes. Recall of the endoscopy after sedation was the same in each group (30% and 25% p=0.62), but significantly more of the flumazenil treated group remembered transfer to recovery area (95% v 56%, p<0.001). A two line rhyme recited 60 minutes postreversal was recalled accurately the next day by similar numbers (60% and 55-5%). There was no evidence of reseadation after flumazenil. The only adverse event was severe pain up the arm during injection of flumazenil in one patient.

Flumazenil safely and effectively reverses midazolam induced sedation but not amnesia for gastroscopy.

Endoscopic sphincterotomy: how safe and successful in the 1980s?

D Vaira, L M D'Anna, J Dowsett, S R Cairns, A Polydorou, S Williams, A Hatfield, P R Salmond (Department of Gastroenterology, The Middlesex Hospital, London) Recent studies suggest that endoscopic sphincterotomy may not be as safe as previously stated. There is, however, no recent large single centre study where prophylactic antibiotics are used routinely and where a policy of nasobiliary or stent placement for failed duct clearance exists. Since November 1983, sphincterotomy was the treatment intention in 1007 consecutive patients at our centre, results were prospectively entered into a computer program.

Full immediate and medium term follow up (mean 23-7 months; range 2-58 months) has so far been obtained for 667 patients. Indication was choledocholithiasis — 555 (gall bladder in situ 384), dilated bile duct without cholangiographic confirmation of stone 112. Sphincterotomy was achieved after successful cholangiography at the first attempt in 530 (79-4%), at the second in 89 (13-3%), and at the third in 26 (3-9%). Six patients of the latter group had a combined procedure. The final sphincterotomy success rate was thus 96-6%. Sphincterotomy failed in 22 cases — 18 with failed and four with successful cholangiography. Duct clearance was obtained in 82-6% of cases, 15-5% had pigtail stents inserted and 2-8% had surgery. The early (<one month) post-procedural complication rate was S/bleed-
Successful endoscopic management of post-operative bile leak

S R CAIRNS, A HEAGERTY, J DOWSETT, D Vaira, A POLYDOROU, A HATFIELD (Department of Gastroenterology, The Middlesex Hospital, London) Sixteen patients (M/F 4/12) mean age 61 years were referred for endoscopic management of postoperative biliary leakage persisting for between three and 52 weeks after surgery. Presenting features were bililucutaneous fistula in nine, perihepatic abscess in four, and persistent T-tube drainage in three patients. Six patients were jaundiced at the time of referral. Endoscopic retrograde cholangiography (ERC) demonstrated site and cause of biliary leakage in all patients. The cause of biliary leakage was retained common duct stones (five cases), benign biliary stricture (five cases), and malignant biliary obstruction (six cases). Treatment was endoscopic sphincterotomy in six, endoscopic placement of a 10 French polyethylene stent in nine, and 6-5 French polyethylene stents in one patient. There were no complications of sphincterotomy or stent placement. Bile leakage ceased in all patients with resolution of jaundice and sepsis. Patients with stones cleared from the duct remain well up to 34 months (mean 19) after endoscopic therapy. Stents were removed in patients with benign strictures after between two and nine months with resolution of the stricture in all but one case. Three patients stented for malignant biliary obstruction died after mean five months. Retrograde cholangiography is highly effective in determining the site and cause of postoperative biliary leakage. Endoscopic therapy can provide immediate and in some cases, definitive treatment.

Safety of sodium picosulphate/magnesium citrate mixture (Picolax) in the bowel preparation of patients with inflammatory bowel disease (IBD)

A J G MCDONAGH, P SINGH, W J PILBROW, G R YOUNGS (Departments of Gastroenterology and Radiology, Chester Royal Infirmary, Chester) The adverse effects of Picolax are milder than those of earlier agents such as sennosides and, in a survey of consultant members of the North of England Gastroenterology Society, we found that 89% of respondents routinely use Picolax to prepare the colon for radiology or endoscopy. Ninety two per cent of these clinicians still reduce or omit the laxative in patients with known or suspected IBD. For some patients poor colonic cleansing means repeated tests.

Our own experience suggested that it was not necessary to reduce the dose of Picolax in IBD patients and, to confirm this, we studied the adverse effects in patients undergoing colonic investigation. All received full dose Picolax and 55 out of a total of 267 examinations were in IBD subjects.

Picolax precipitated or exacerbated abdominal pain in a smaller proportion of IBD patients than in other diagnostic groups (p<0.01). Inflammatory bowel disease patients also had less increase in stool frequency (p<0.001) and gave a lower score for nuisance resulting from Picolax (p<0.05) than those with diverticular disease or the irritable bowel syndrome. There was no evidence of disease exacerbation. We conclude that Picolax bowel preparation can be safely used in full dosage in patients with inflammatory bowel disease.

A new light delivery system for the treatment of obstructing gastrointestinal neoplasms

J T ALLARDICE, A C ROWLAND, C P SWAIN, M F GRAHN, N S WILLIAMS (The London Hospital Laser Centre, Surgical and Gastroenterology Units, The London Hospital, Whitechapel, London) Laser treatment of GI neoplasms is severely hampered by the inability to deliver a predetermined energy density to constrictions. We have therefore designed and constructed a new light delivery system (LDS) which overcomes this problem.

Our system uses a polytetrafluoroethylene diffuser, mounted on an optical fibre to scatter laser light cylindrically. A perspex window encloses the system in a modified Eder-Puestow dilator. A specially developed computerised densitometry method shows that longitudinal and circumferential fluxes provided by the LDS are uniform, optical density 2±0.5 units. Stricture dilatation equates target and LDS surface areas and provides fluxes in the order of 200 mW/cm². A central guidewire channel allows accurate endoscopic and radiological placement. Stainless steel caps define a closed system ensuring that all light is absorbed by tumour target. Interchangeable sizes (10–15 mm diam and 2–7 cm length) suit stricture parameters, the system is durable and easily cleaned.

Patients with obstructing oesophageal or rectal malignancies treated with photodynamic therapy improved by at least one grade when assessed by quantitative barium examinations and symptomatic improve-
ment. The closed system concept has for the first time enabled accurate dosimetry to the entire stricture length and ensures that a predetermined light energy dose is absorbed by tumour.

Endoscopic evaluation of human colonic blood flow in health and inflammatory bowel disease

D E LOFT, C J SHORROCK, S A RILEY, W D W REES (Department of Gastroenterology, Hope Hospital, Eccles Old Road, Salford) Alteration in blood flow may play a pathogenic role in colonic mucosal disease. Using the technique of laser doppler flowmetry (LDF) we have measured colonic mucosal blood flow (CMBF) during colonscopic in 17 healthy subjects and six patients with inflammatory bowel disease.

Colonic mucosal blood flow was measured using a Peri flux PF2 LDF with endoscopic probe passed down an Olympus CF-L3R colonoscope. Blood flow was measured at various sites (rectum, sigmoid, descending, transverse) in the colon of eight subjects prepared with a phosphate enema and nine prepared with X prep and 500 ml of 10% Mannitol. Rectal blood flow was measured in six patients with inflammatory bowel disease; five with ulcerative colitis and one with Crohn’s colitis.

In the normal subjects there was no significant regional variation in CMBF (means (SE): rectum=22.7 (3.5); sigmoid 20.8 (2.6); descending colon 21.9 (5.1); transverse colon 22.0 (5.0) arbitrary units). Coefficient of variation was <10%. Blood preparations used did not influence CMBF (22.8 (5.9), n=8 and 22.5 (4.5), n=9). Rectal blood flow was significantly increased in six patients with inflammatory bowel disease (53.8 (8.4), p<0.002, 2 tailed Mann Whitney U test).

The technique of laser doppler flowmetry may be used to assess colonic blood flow in man. Preliminary observations suggest that blood flow is significantly increased in patients with inflammatory bowel disease.

Screening for colonic cancer in patients with Barrett’s oesophagus

D A F ROBERTSON, C L SMITH (Department of Medicine II, Southampton General Hospital, Tremona Road, Southampton) An association between Barrett’s oesophagus and the development of colonic neoplasia has been described (Sontag, Lancet 1985) but not confirmed. We have prospectively screened 28 patients with Barrett’s oesophagus by colonoscopy and compared results with 56 age and sex matched controls, presenting with symptoms suggestive of irritable bowel syndrome. Barrett’s oesophagus was defined as histologically confirmed columnar epithelium at least 3 cm above the superior margin of a manometrically defined lower oesophageal sphincter. Eleven of 28 patients were identified only after a follow up gastroscopy and biopsy. No patient had symptoms suggestive of colonic neoplasia.

No patients had oesophageal tumours or high grade dysplasia. Six patients with Barrett’s oesophagus had colonic tumours (21%) (one Duke’s B carcinoma, one Duke’s A carcinoma, two multiple adenomatous polyps, two solitary adenomatous polyps) compared with one control (2%) (solitary adenomatous polyp) (p<0.01%).

We conclude that (1) This study confirms the high prevalence of colonic neoplasia in Barrett’s oesophagus. The yield from screening colonoscopy in Barrett’s oesophagus is higher than in other groups at ‘high risk’ from colonic neoplasia such as long standing inflammatory bowel disease. (2) Barrett’s oesophagus may be more common than appears at a first endoscopy. (3) Colonoscopy is more important than gastroscopy in screening for cancer in Barrett’s oesophagus.

Acute stress affects oesophageal function

D A F ROBERTSON, K NAYLOR, R C S AYRES, C L SMITH (Department of Medicine II, Southampton General Hospital, Tremona Road, Southampton) Stress can affect gastrointestinal function but the mechanisms involved in the stress response are not clear. Abnormal oesophageal motility may be responsible for some symptoms in the irritable bowel syndrome. We have studied the effect of three different stressful stimuli – hyperventilation, dichotic hearing and the forearm cold pressor test on oesophageal function in healthy volunteers (n=15, mean age 22 years). Persistsis in the lower oesophagus was measured in response to swallows of 4 ml cold water using a triple lumen capillary perfusion catheter with ports 5 cm apart, the lowest being 5 cm above the lower oesophageal sphincter, under control conditions and during each stressful stimulus.

Hyperventilation produced marked tachycardia but no demonstrable change in oesophageal function. Dichotic hearing produced no change in pulse or blood pressure but a marked increase in the frequency of non-peristaltic waves (10.5% to 26.7%, p<0.001) and of the amplitude of peristaltic waves (70.9 mmHg to 88.7 mmHg, p<0.01).

The cold pressor test produced systolic and diastolic hypertension and increased amplitude of peristalsis (85.6 mmHg, p<0.01), and increased frequency of non-peristaltic contractions (34.7%, p<0.01).

Stressful stimuli can markedly affect oesophageal functions in normal subjects.
During the cold pressor test this is associated with sympathetic overactivity, but not during dichotic hearing challenge.

Comparison of indomethacin and fenbufen on morphology and blood flow in human gastric mucosa

C J SHORROCK, W D W REES (Department of Gastroenterology, Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford) Thirty four healthy volunteers were gastroscoped before, one, seven, and 28 days after treatment with indomethacin 50 mg tds or the NSAID drug fenbufen 450 mg bd. Mucosal integrity was scored (0 (normal) to 4 (severe damage)) and gastric mucosal blood flow measured using a laser doppler technique.

With indomethacin, all had mucosal damage at day 1 (scores: 1-7 (0-2), n=24). Damage persisted at day 7 (score: 0-96 (0-2) with two subjects developing discrete ulcers. Virtually all damage had resolved at 28 days (n=18). Fundal and antral mucosal blood flows were reduced at day 1 (arbitrary units: 64 (4) v 52 (4) post indomethacin in fundus, n=12, p<0.01; 40 (3) v 31 (4) post indomethacin in antrum, n=12, p<0.05). At 28 days values had returned to baseline.

With fenbufen, there was mild damage at day 1 (score: 0-2 (0-14), n=10), significantly less than with indomethacin (p<0.0001). Damage was more marked at day 7 (score: 0-6 (0-3), n=9). At 28 days all damage had resolved. Fundal and antral blood flows were unchanged at day 1 but at day 7 fundal flow had fallen, corresponding to the greater damage (62 (3) v 50 (3), n=9, p<0.05). Mucosal recovery was associated with return of blood flow to normal.

In conclusion, gastric mucosal function is disrupted by indomethacin and to a lesser extent by the prodrug, fenbufen. The mucosa adapts to continued damage by both agents.

Longterm palliation of malignant dysphagia - laser v intubation

L A LOIZOU, D GRIGG, C ROBERTSON, M ATKINSON, S G BOWN (National Medical Laser Centre, University College Hospital, London and Queen's Medical Centre, Nottingham) The short term efficacy of laser palliation of malignant dysphagia is well documented; few groups, however, have analysed the follow up in sufficient detail to give a true comparison with endoscopic intubation. We prospectively compared 45 patients with carcinomas of the oesophagus and gastric cardia treated with endoscopic Nd:YAG laser therapy at UCH with 12 patients treated by endoscopic intubation in Nottingham; the two groups were comparable for mean age, tumour position and length, and proportion of squamous cell and adenocarcinomas. Dysphagia was graded on a scale of 0-4 (0=normal swallowing, 4=dysphagia for liquids). Mean dysphagia grade (DG) pre-treatment was 3 (SD=1) in both groups. Dysphagia was initially improved by at least 1 grade in 75% of laser treated cases and 83% of intubated patients (NS). Successful overall long term palliation of dysphagia was achieved in 59% of laser treated patients and 83% of intubated patients (NS); the mean DG over the remainder of the patients lives (mean survival 18 weeks) was 1-6 (SD=0.5) for both groups (p<0.05 compared with pre-treatment DG for both groups). Laser treated patients however, required an average of 4-7 procedures compared with 1-2 for intubated patients (p<0.05). Twenty per cent of laser treated and 27% of intubated patients could eat most or all solids (NS). Treatment induced perforation occurred in 17% of patients undergoing intubation but in only 2% of laser treated patients.

The longterm quality of palliation is very similar with both endoscopic techniques but laser treatment requires more frequent endoscopy. Laser therapy should be considered as complementary to endoscopic intubation particularly for recanalising tumour overgrowth of tubes and strictures initially impassable with a guide wire. Laser treatment alone can be used when oesophageal endoprostheses are poorly tolerated.

Does an early diagnosis of hepatocellular carcinoma (HCC) improve survival in cirrhotic patients?

F FARINATI, M ZAGOLIN, M CHIARAMONTE, A FLOREANI, S FAGIUOLI, R NACCARATO (Department of Gastroenterology, Institute of Internal Medicine, University of Padova, Italy) In the attempt to improve the severe prognosis of HCC we carefully followed up a group of 315 consecutive cirrhotic patients with fetoprotein (FP) determination and ultrasound (US) every six months; 199 men (mean age 54, range 17-81 yrs, 62 HBsAg+ve, 72 alcoholics, eight with haemochromatosis, 29 with PBC, and 135 with cryptogenic cirrhosis) entered the study. Two hundred and eighty six were in the A or B and 29 in the C risk group according to Child. Forty patients (13%) dropped out of the study and 12 died from liver failure but in no one HCC was demonstrated at autopsy. Mean follow up is presently 17 months. Twenty six cases of HCC have been diagnosed and incidence, on the bases of mean follow-up, is 6-7% per year, FP levels were below 100 ng/ml in 13 patients (50%), and 25 ng/ml in five (19%). Twenty nine other patients with FP ranging from 25 to 100 ng/ml and negative US are being screened for HCC. Ultrasound was diagnostic in 26/26 patients. False positives at US were relatively low (2.5%). Seven cases of HCC were diagnosed in HBsAg+ve (7-9% per year), four in alcoholic cirrhosis (3-7% per year), three in haemochromatosis (25%), one in PBC (2-3%), 11 in cryptogenic cirrhosis (5-7%). Only 12 cases of HCC are included in this study. Survival periods in the three operated patients are six, 10 and 32 months respectively. Mean survival in non-operated HCC patients is 4-8 months (range 1-15). In conclusion, US seems to be more useful than FP in screening for HCC. Even FP values 100 ng/ml must be regarded as diagnostic; in cirrhosis an incidence of HCC higher than 6% per year is to be expected, particularly in haemochromatosis and HBsAg+ve patients; finally, although the survival rate is encouraging for operated patients, even a careful follow-up does not seem to improve the resectability rate.

Liver membrane phosphorylation by hepatic growth factors

A C SELDEN, D A VESEY, H J F HODGSON (Department of Medicine, Royal Post-graduate Medical School, London) Partial hepatectomy in man and rats induces a high molecular weight growth factor in serum, hepatotropin, capable of stimulating hepatocyte proliferation in culture. To characterise the early membrane events initiated by hepatotropin, we incubated rat liver membranes with purified preparations of rat hepatotropin for 15–30 minutes, at 0°C before the addition of 3H-ATP, terminating phosphorylation after 1 min–2 h, and analysing the phosphorylated membrane proteins by SDS-PAGE and autoradiography. Changes were compared with the effects of the hepatic mitogen EGF. Hepatotropin did not phosphorylate the EGF receptor, visible in 5% SDS-PAGE at MW 170 kD, but enhanced phosphorylation of a 17KD band visualised in 15% PAGE. Quantitative analysis by digitising autoradiography confirmed significant phos-
phorylation. Epidermal growth factor caused the expected phosphorylation at 170 kD, but did not alter phosphorylation of the 17 kD protein. Further characterisation of this protein, phosphorylated by hepatotropin, should elucidate the mechanism of hepatic regeneration after partial hepatectomy.

Malignant obstructive jaundice: what is the best management? A prospective randomised trial of surgery vs endoscopic stenting

J F DOWSETT, R C G RUSSELL, A R W HATFIELD, P B COTTON, A G SPEER, J HOUGHTON, T LENNON, L STANESBY, K MACRAE, R AHERN (The Departments of Gastroenterology and Surgery, The Middlesex and London Hospitals, London and The Cancer Research Campaign Trials Centre) During a two and a half year period to June 1988, 103 patients with obstructive jaundice (bilirubin >100 µmol/l) caused by primary unresectable low common duct malignancy (pancreas, ampulla) and no contraindications to surgery were randomly assigned to surgical bypass or endoscopic stent insertion. Fifty two were allocated surgery and 51 stenting. All had normal duodenums and no previous endoscopic nor surgical intervention. There were no significant differences in age, sex, nor risk factors between the two groups. Two surgical and one stenting patient were not treated because of rapid clinical deterioration after randomisation.

Surgical bypass was successful in 47/52 (90%) and stenting in 47/51 (92%) [NS]. The three surgical failures were stented (two successful, one failed) and the three stenting failures had surgery (all successful). There were 44 surgical complications in 21 patients (seven major) and 15 stenting complications in 14 patients (three major) [p<0.01]. The 30 day mortality of surgery was 13% and of stenting 8% [NS]. Twenty eight surgical and 30 stenting patients are dead. The mean survival was 3-5 months for surgery and 5-0 months for stenting (alive: mean 5-5 months for surgery and 4-5 months for stenting). Average hospital stay was 15 days for surgery and 11 days for stenting [NS]. Two stented patients have required gastroenterostomy. Malignancy was biopsy proven in 63% of surgical patients and 76% of stenting patients. Stents have been changed on 14 occasions (10 patients).

Endoscopic stenting for malignant low biliary obstruction has a significantly lower procedural complication rate than surgical bypass. No significant difference has been shown, however, in terms of success, 30 day mortality, in hospital stay nor survival.

Selection, organisation, and follow up of children on home parenteral nutrition (HPN)

P STAPLEFORD, W M BISSET, P J MILLA (Hospital for Sick Children, Great Ormond Street, London) Some children require PN for prolonged periods of time. Recent advances have made the use of HPN in such children possible. We present experience of five children (age 14 months to 15 years) who suffered from chronic intestinal pseudo-obstruction (three), congenital enteroatresia (one), and short gut syndrome (one). They were all developmentally normal, from a stable family and had at least 20% residual absorptive function. All children received a single bag amino acid/glucose/electrolyte solution ± a lipid emulsion, which supplied between 40-80% of their nutrient requirements. The nutrients are prescribed by the GP on a FP10, the district health authority supply the infusion pumps and disposables and the nutrients are delivered by a commercial home care company. We have followed up these children for two to 18 months (av 10-4) at monthly intervals. All are growing and developing normally. Catheter related complications include one line infection (patient receiving additives to PN) and two blocked lines due to fat sludging where lipid was added to single bag of nutrients. Non-catheter related complications were equally few, three patients developed subclinical selenium deficiency and one thiamine deficiency. Oral supplementation of vitamins and trace elements successfully reversed the deficiencies. Our experience suggests that parenteral nutrition can successfully be carried out at home in children in the UK, that additives should be given orally whenever possible, that lipid should not be used in a single bag system and that unusual deficiency states may occur. We recommend that a multidisciplinary approach on a regional basis should be used.

Crypt cell production rate (CCPR) and surface membrane characteristics of transplanted human fetal small intestine

L T WEAVER, R B HENDRED, A QUARONI, J FOLKMAN, W A WALKER (INTRO G NEALE) (Departments of Gastroenterology and Surgery, Childrens Hospital, Boston, Mass and Division of Biological Sciences, Cornell University, NY, USA) Fetal human gut is inaccessible to direct study in vivo. We transplanted small intestine from nine fetuses of 18 to 20 week gestation (obtained with permission after therapeutic abortion) subcutaneously into athymic nu/nu mice. Mucosal morphology and CCPR were measured by microdissection, and metaphase arrest after administration of colchicine to host mice 35-150 g post-transplant. Enterocyte surface characteristics were studied with a panel of immuno-fluorescent monoclonal antibodies to human microvillus membrane antigens.

Mean crypt depth of transplanted tissue was 240 µm. Crypt cell production rate was 4.4 cells/crypt/h and net villus influx 12-2 cells/villus/h. Crypt cell production rate of athymic mice was 15-5 cell/crypt/h, comparable with balb/c mice. Untransplanted tissue expressed sucrase, peptidase and aminopeptidase. Transplanted tissue expressed these antigens plus maltsase and lactase within 130 days. Immunoprecipitation of proteins from brush border isolated from fetal intestinal membranes confirmed these findings.

Human fetal small intestine regenerates after subcutaneous transplant to athymic mice, exhibits epithelial cell turnover and maturation of expression of a range of surface antigens. The model represents a means to study the ontogeny of the prenatal human gastrointestinal tract.

Indomethacin induced increased small intestinal permeability: the role of prostaglandins

J BARNASON, P SMETHURST, G C FENN, C E LEE, I MENZIES, A J LEVI (MRC Clinical Research Centre, Searle Pharmaceuticals and St Thomas's Hospital, London) Increased intestinal permeability is thought to be an important initiating factor in the development of NSAID induced small intestinal inflammation but the role of prostaglandins is uncertain.

Twelve volunteers ingested a 100 ml test solution containing 3-O-M-glucose (3 MG, 0.2 g), D-xylene (DX, 0.5 g), L-rhamnose (LRh, 1.0 g) and "EDTA (100 µCi) followed by five hour urines to assess active and passive carrier mediated transport and trans- and paracellular permeability respectively. Each was assessed as (A) baseline; (b) following 200 µg misoprostol (-16, -12, -8½, -4, -1½, -½); (C) indomethacin 75 and 50 mg (-8, -1 h); (D) B+C combined.

Baseline urine excretion (mean (SE)) of 3 MG, DX, LRh, and "EDTA was 45-8
(3.2%), 31.5 (2.0%), 10.2 (0.6%), and 0.75 (0.07%) respectively. B, C, and D had no significant effects of 3 MG, DX, LRh. B had no effect on "EDTA (0.66 (0.08)%). C increased the excretion significantly (1.96 (0.31)%, p < 0.001) with 11 of 12 above the normal range. Excretion of "EDTA following D was 1.16 (0.17)% which was significantly different from A and C. These changes were mirrored by changes in "EDTA/LRh ratios which reflect alterations in intestinal permeability.

These studies suggest that indomethacin induced increased intestinal permeability is mediated by reduced mucosal prostaglandins. Coadministration of misoprostol with NSAID’s may in the long term prevent the frequency and severity of small intestinal inflammation due to NSAID.

Evidence for an increased driving force for active glucose transport across the jejunal brush border membrane (BBM) in chronic diabetes

E S DEBNAM, H Y EBERHAIM (Department of Physiology, Royal Free Hospital School of Medicine, Rowland Hill Street, London) Although studies in man and experimental animals have reported a stimulation of intestinal glucose uptake in diabetes mellitus, the mechanisms involved remain unclear. Here we describe the effects of diabetes on BBM potential difference (Vm) in intact tissue and glucose uptake by BBM vesicles. Rats were injected with streptozotocin (60 mg/kg, iv) and were glycosuric and hyperglycaemic when used four to six weeks later. Microelectrode studies using tissue bathed in gassed bicarbonate saline revealed a hyperpolarisation of Vm in jejunal (control, -47.2 (1.0) mV (42); diabetic, -57.4 (1.5) mV (54), p < 0.001) but not ileal tissue (control, -40.2 (1.5) mV (30); diabetic -40.2 (1.6) mV (25)). Ion substitution studies during these experiments implied a reduced Na permeability in jejunal, but not ileal BBM in diabetes. Brush border membrane vesicles were prepared from jejunal mucosa and "H-D-glucose (1 mM) uptake, expressed per mg protein, measured in the presence of a 100 mM NaSCN gradient. The peak: equilibrium ratio was unaffected by diabetes (control, 4.4 (0.6) (10); diabetes, 4.5 (0.5) (nine) but initial uptake (6 sec) was increased by 51% in this condition (p < 0.05).

We conclude that the more rapid glucose movement across the BBM is a consequence of an enhanced driving force for Na-glucose cotransport.

Colonic inflammation and HLA/DR Ag expression in the colon of children with idiopathic protracted diarrhoea (IPD) and autoimmune enteropathy

S HILL, R MIRAKIAN, G R BOTTAZZO, P J MILLA (The Middlesex Hospital and Hospital For Sick Children, London) Some children with IPD, circulating enterocyte antibodies (Ec Ab), and enteropathy also have a colitis. We have examined the colon endoscopically in 17 such patients. Multiple biopsies were studied histologically and by immunocytochemistry for HLA Class II expression by the colonocytes and compared with histologically normal colon from control subjects. Seven patients had cytoplasmic Ec Ab, seven patients brush border Ec Abs, and three patients both. In three of seven patients who only had cytoplasmic Ec Abs no colitis was present. The remaining 14 patients had evidence of a colitis characterised by inflammatory infiltrate of lymphocytes and plasma cells and an absence of epithelial granulomas, crypt dysplasia, or goblet cell changes. Class II (DR complex) expression was absent in both surface and crypt colonocytes of control biopsies. In 14 patients with colitis, the DR expression of DR molecules was seen in crypt and surface colonocytes together with DR+ve cells in the lamina propria. In the three patients without colitis, DR expression was absent. Our data show that in over 80% of children with IPD and an autoimmune enteropathy that inflammatory changes occur in the colon. We suggest that analogous to similar phenomena in the glands of patients with classical autoimmune disease that DR+ve colonocytes would be able to act as antigen presenting cells, by passing macrophage requirements and could lead to autoimmune disease.

Anti-neutrophil nuclear antibody in inflammatory bowel disease and primary sclerosing cholangitis

J A SNOOK, R W CHAPMAN, K FLEMING, D P REWELL (Departments of Gastroenterology and Pathology, John Radcliffe Hospital, Oxford) Some patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) have circulating autoantibodies to an antigen in the portal tracts of obstructed human liver. In this study we have demonstrated with an immunoperoxidase/PAAP double-labelling technique that the antigen is specifically located within the nuclei of tissue neutrophils. The serum titre of anti-neutrophil nuclear antibody (ANNA) has been determined using isolated peripheral blood neutrophils. In the PSC group (n = 32) ANNA was present in 84% with a median titre of 1 in 1000. In the group with IBD alone (n = 76) ANNA was present in 86% with a median titre of 1 in 100. In contrast, only 12% of controls (n = 41) were ANNA positive and none had a titre of more than 1 in 10. In the IBD group, titres were significantly higher in patients with recently active disease. In the PSC group, high titre ANNA correlated with raised plasma concentrations of aspartate transaminase (p < 0.01), alkaline phosphatase (p < 0.01) and total immunoglobulin (p < 0.01). Binding of ANNA to intact blood neutrophils in vivo could not be demonstrated and neutropaenia was not a feature. The results provide further evidence of involvement of autoimmune mechanisms in IBD and PSC.

Surveillance in extensive ulcerative colitis improves prognosis without always preventing cancer

D M MELVILLE, J E LENNARD-JONES, B C MORSON, J K RITCHIE, C B WILLIAMS (St Mark’s Hospital, City Road, London) Over 22 years, 401 patients with extensive ulcerative colitis entered a surveillance programme with the aim of detecting precancer or carcinoma at a curable stage. Of 344 patients who remained with the programme, 12 were operated upon at stage of high grade dysplasia but 17 had a carcinoma (Duke’s A 9, B 3, C 4, disseminated 1). Excluding nine patients who emigrated, five carcinomas developed in 48 patients who left the programme (Duke’s A 1, B 1, C 1, disseminated 2) at intervals of four to six years. The cumulative risk of carcinoma among all patients was 3% (CI 0–13) at five years, 5% (CI 0–18) at 20 years, and 9% (CI 0–32) at 25 years. There were two deaths from carcinoma among patients within the programme and three among those who left it. The main reasons why surgery was not performed before development of carcinoma were dysplasia and undetected carcinoma (eight), carcinoma without preceding high grade dysplasia (six), and failure of patient compliance (six). The limitations of dysplasia as a marker of precancer and patient compliance make it unlikely that any surveillance programme will achieve complete prevention of carcinoma in ulcerative colitis. The crude 5 year survival rate in this series up to 1983, after operation for carcinoma was 84%. However, and 12 patients were operated upon at a stage of precancer.
The presence of sialomucin at the resection margin identifies patients at risk of local recurrence of colorectal cancer

P M DAWSON, H C REES, N A HABIB, T G ALLEN-MERSH, C B WOOD (Departments of Surgery and Histopathology, Charing Cross and Westminster Medical School and the Royal Postgraduate Medical School, London) We have previously shown that a sialomucin band extending for >3 cm from a colorectal cancer is significantly associated with tumour penetration into adjacent structures. This study has assessed whether the presence of sialomucin in the surgical resection margin might predict those patients at risk of local recurrence.

Sialomucin at the resection margin was estimated by the high iron diamine–alcian blue stain in 358 patients undergoing 'curative' excision of primary colorectal carcinoma. Patients were scrutinised for local recurrence during a median follow up of 24 months from operation by clinical examination and sigmoidoscopy, and where appropriate, ultrasound, CT scan, or colonoscopy.

Sialomucin was detected at one or other colonic resection margin in 106 patients (29-6%). Local recurrence occurred significantly ($\chi^2=14.19, \text{p}<0.001$) more often in the sialomucin group (32-0%) than among patients in whom sialomucin was absent from the resection margin (18-6%). Multivariate analysis (Cox models) suggested that sialomucin at the resection margin was the strongest predictor of local recurrence coming above Duke's stage and length of distal margin of excision from tumour.

Sialomucin at the resection margin is 70% accurate as a predictor of local recurrence and could be used in determining the need for adjuvant treatment.

Does oral tripotassium dicitrato bismuthate (TDB) provide a depot preparation of bismuth?

C J GAVEY, M-L SZETO, C NWOKOLO, R F POUNDER (Academic Department of Medicine, Royal Free Hospital School of Medicine, London) The mechanism of delayed ulcer relapse after healing with tripotassium dicitrato bismuthate is unclear, as bismuth alone often fails to sterilise the gastric mucosa. This study measured plasma bismuth concentration and 24 h urinary bismuth excretion before, during, and after six weeks of treatment with DeNol tab 2 bd in nine patients (24–66 years, with normal hepatorenal function).

The median plasma bismuth concentration before treatment (2 ng/ml) rose significantly during treatment at three and six weeks to 12 and 17 ng/ml respectively ($\text{p}<0.01$). At three, six, nine, and 12 weeks after treatment there were non-significant changes of median plasma bismuth (5, 4, 2, and 4 ng/ml), compared with before treatment. The median 24 h urine bismuth excretion before treatment (2.9 $\mu$g/24 h) rose significantly during treatment at three and six weeks to 698.4 and 1012.2 $\mu$g/24 h respectively ($\text{p}<0.01$). At three, six, nine, and 12 weeks after treatment there was a persisting significant rise of bismuth excretion (110.0, 30.4, 11.6, and 9.5 $\mu$g/24 h respectively, $\text{p}<0.01$).

Bismuth is absorbed during acute treatment with DeNoltabs, causing an 8.5-fold rise of plasma bismuth concentration and a 349-fold rise of 24 h urinary bismuth excretion. Sequestration of bismuth in the body for at least 12 weeks could party explain the persisting action of the compound.

Carbohydrate deficient (de-sialylated) transferrin – a specific test for detecting alcohol abuse

A KAPHUR, G WILD, D R TRIGER (Departments of Medicine and Immunology, Royal Hallamshire Hospital, Sheffield) We have investigated the clinical value of carbohydrate deficient transferrin (CDT) as an indicator of alcohol abuse. Carbohydrate deficient transferrin was measured by isoelectric focussing on agarose gel in 84 patients with alcohol related liver damage and in 57 controls. In 15 alcoholics admitting to at least 80 g alcohol daily for more than three weeks, CDT was detectable in 13, being absent in two subjects consuming 80–100 g daily. Serial samples in nine patients withdrawing from alcohol under hospital supervision showed disappearance of the protein after three to 17 days. Carbohydrate deficient transferrin was detected in 8/63 outpatient alcoholics claiming to have stopped drinking; in 0/31 patients with non alcoholic liver disease; and 0/26 controls with non-hepatic disorders. Sensitivity and specificity of CDT in detecting alcohol abuse was 86% and 100%, considerably superior to $\gamma$GT (93% and 38%) and MCV (71% and 74%). Carbohydrate deficient transferrin related to alcohol abuse rather than to alcoholic liver damage.

We conclude that CDT is highly sensitive and specific for detecting alcohol consumption in excess of 80 g daily for at least three weeks. After alcohol cessation it is detectable for much longer than urine or blood alcohol. Its superiority to conventional laboratory markers suggests that it may be useful in clinical practice.

Randomised double-blind placebo controlled study of somatostatin for control of variceal bleeding

A K BURROUGHS, P A MCCORMICK, D SPRENGERS, M HUGHES, F D'HEYGERE, N MCINTYRE (Academic Departments of Medicine and Clinical Epidemiology, Royal Free Hospital and School of Medicine, London) Use of vasoactive drugs for variceal bleeding is controversial. Somatostatin (250 $\mu$g bolus; 220 $\mu$g h infusion) versus placebo bolus/infusion, was assessed double-blind for control of bleeding and prevention of early rebleeding from varices over five days. Therapy failure occurred when (i) blood/plasma 6 units transfused over six hours at any time within first 24 h or (ii) between 18 h and five days: haematemesis, or melaena with either change in vital signs or 2 g/dl haemoglobin drop. Sclerosis or transection followed. There were 198 variceal bleeding episodes in trial period. Exclusions, 22 (prior failure); 19 (previous randomisation 30 days); 16 (no haemodynamic change); 21 (others).

Randomised 120 episodes (92 patients): ST (61), Pugh ABC grade (15, 26, 20); placebo (59), grades (14, 24, 21). Failure was significantly different: placebo 35 (59%) v ST 22 (36%), $p=0.033$ (log rank test on curves of failure time). In ST patients less blood/plasma transfused ($p<0.004$). No differences in complications or 30 day mortality per episode. Cox's model was used to assess clinical, endoscopic and time factor variables – for example, interval-admission to start of infusion, influencing trial failure. Only Pugh's score and trial group were significant. Somatostatin reduced the risk of failure to control bleeding by 41% (95% CI, 66% reduction to 0-1% increase $p=0.0503$), regardless of liver disease severity. Somatostatin is more effective than placebo and is safe in acute variceal bleeding.

Vasoactive intestinal peptide (VIP) stimulation of natural killer cell activity against a human colon carcinoma cell line

E A F VAN TOL, H W VERSPEGET, A S APEÑA, J B M J JANSEN, M N APARICIO-PAGÉS, C B H W LAMERS (Department of Gastroenterology and Hepatology, University Hospital, Leiden, The Netherlands) Neuropeptides are directly involved in certain aspects of
regulation of both the cellular and the humoral immune response. In the present study the effect of different concentrations of vasoactive intestinal peptide (10^{-3}\text{--}10^{-8} \text{M VIP}) on spontaneous cell mediated cytotoxicity of peripheral blood mononuclear cells (PBMC) against two tumour cell lines, colon CaCo-2 and erythroleukemia K-562, was evaluated by using the 51Cr-release assay. The mechanism of VIP modulating cytotoxicity was studied by NK-cell deprecation experiments with anti CD16 and complement lysis, and effector or target cell preincubation.

Vasoactive intestinal peptide significantly (0.05<p<0.01) stimulated the NK-cell activity against CaCo-2 in both four hour (10^{-8}\text{--}10^{-4} \text{M VIP}) and 18 h (10^{-5}\text{--}10^{-1} \text{M VIP}) assays whereas hardly any effect was seen against K-562 cells (only 10^{-6} \text{M VIP}, 18 h). Depletion of CD16+ cells from PBMC almost completely inhibited cytotoxicity against both cell lines in both four hours, over 94%, and 18 h, over 74%, assay periods. Vasoactive intestinal peptide incubations did not affect the residual cytotoxic response against both target cell lines. Moreover, VIP preincubation studies revealed that the actual stimulation of the cytotoxic response is dependent on the influence of the neuropeptide on both effector and target cells simultaneously.

Vasoactive intestinal peptide stimulates the cytotoxicity against colon tumour cells through specific activation of CD16+ NK-cells. Tumour cell lysis might be facilitated by simultaneous binding of VIP to both effector and target cells. Hormonal regulation of the immunesurveillance could thus be of relevance in the development of colorectal tumours.

**Laser lithotripsy of large bile duct stones under direct vision via peroral choledochoscopy**

P B Cotton, R A Kozarek (Duke University Medical Center, Durham, North Carolina and Mason Clinic, Seattle, Washington, USA) We have attempted lithotripsy of duct stones under direct vision at endoscopy with the Candela flash lamp excited dye laser in seven patients, who had failed standard endoscopic approaches (including mechanical lithotripsy). All were high risk for surgery, aged 64 to 80 years. Two had failed external shockwave lithotripsy, and one had had three unsuccessful percutaneous procedures. In that case the laser energy was applied through a percutaneous miniscopic. In the remainder, an Olympus prototype mother and baby system was used (mother channel 5-5 mm, baby scope 4-5 mm, channel 1-7 mm). A nasobiliary tube was used for flushing during lithotripsy. Energies of 30--60 mJ were used usually at 10 Hz, with 20--2029 pulses via a 200 u core radioopaque fibre. Stones were fragmented in all patients, but the duct could be cleared in only four (including three of the last four). Significant technical improvements are being made to improve focusing. There were no complications. Two of the failures underwent successful surgery; the third died in liver failure with hepatoma and portal hypertension. Tunable dye laser lithotripsy is a complex technique, but effective, and deserves further evaluation.