The British Society of Gastroenterology

The Spring Meeting of the British Society of Gastroenterology was held from 25–27 April 1984 at the University of Salford under the presidency of Dr R B McConnell. The scientific programme included 116 spoken communications and 46 poster communications selected by the programme committee. The abstracts are given below. Further details of the meeting appear on p. 540.

LIVER
T1–14

T1 Establishment of a cell-line (PLC/NUT/1) containing integrated hepatitis B virus (HBV) DNA from a hormone associated human primary liver cell cancer
N J CURTIN, P G INCE, K L GAUNT, M J F FOWLER, O F W JAMES, AND M F BASSENDINE (Departments of Medicine and Pathology, University of Newcastle upon Tyne and Cell Biology Laboratory, Royal Free Hospital School of Medicine, London) A continuous human cell line has been established from the primary hepatocellular carcinoma (PLC) of a British woman. The patient had no serological markers of HBV infection (HBsAg, HBeAb, and HBsAb ELISA-Abott all -ve X2). She had received long term sex hormone treatment for endometriosis. The tumour was alphafoetoprotein (AFP) secreting and arose in a non-cirrhotic liver.

The cell line, designated PLC/NUT/1, grows as an adhering monolayer: the cells are of epithelial type and secrete alphafoetoprotein. Karyotyping has shown a chromosome mode of 63: 71% falling within the range 51–67. There are eight identifiable chromosomal markers confirming a clonal origin. Despite negative serum markers, HBV DNA was shown to be integrated into the cellular DNA of PLC/NUT/1 by nucleic acid hybridisation using a cloned HBV (32P) DNA probe. Digestion with a restriction endonuclease enzyme, Hind III, which does not cut HBV DNA, yielded only one major and two minor fragments (larger than hepatitis B virus DNA) containing HBV DNA sequences. This suggests that there are at most only three integration sites of HBV DNA in these cells unlike the PLC/PRF/5 (Alexander) cell line in which there are 8+. When PLC/NUT/1 is hetero-transplanted subcutaneously into male athymic mice, tumours develop at the site of inoculation. These are primary liver cancer similar in morphology to the original tumour and immunoperoxidase staining is positive for HBsAg and AFP. These results suggest involvement of HBV in this hormone associated PLC. The paucity of sites of integration of HBV DNA into the DNA of this human PLC cell line will facilitate study of the oncogenicity of HBV.

T2 Antiviral therapy for chronic hepatitis B virus (HBV) infection: treatment outcome and influence of pretreatment factors
D M NOVICK, A S F LOK, P KARAYANNIS, M J F FOWLER, J MONARDINO, S SHERLOCK, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital, Pond Street, Hampstead, London) A randomised trial of adenine arabinoside monophosphate (ARA-AMP) versus lyphmo-blastoid interferon (IFN) in the treatment of chronic HBV infection is in progress. ARA-AMP was given at a dosage of 10 mg/kg/day for five days and then 5 mg/kg/day im 12 hourly for a total of four or eight weeks. Interferon was given at 10 MU/m2/day intra-muscularly daily for five days and then thrice weekly for a total of 12 weeks. All 45 patients were HBV carriers with raised transaminase concentrations for more than six months. All were hepatitis B e antigen (HBeAg) and HBV-DNA positive, and all had biopsy-proven chronic liver disease. Fifteen, 14 and 16 patients received ARA-AMP (four or eight weeks) or IFN, respectively. To date, a persistent loss of HBV-DNA has been observed in five patients treated with IFN and three with ARA-AMP (four weeks). All five responders to IFN lost HBeAg and two lost HBsAg; two responders to ARA-AMP lost HBeAg and one lost HBsAg. Interferon was better tolerated than ARA-AMP, which caused neurotoxicity or myalgia in 11 of 29 patients. Because only a minority of patients respond to antiviral therapy, we reviewed the clinical features of 38 male HBeAg-positive HBV carriers in this and previous antiviral trials who had been followed for one year or longer. The aim was to identify pretreatment factors predicting a favourable response. defined as loss of HBeAg and HBV-DNA. Only two of 19 (11%) homosexual men responded, compared with 10 of 19 (53%) heterosexual men (p<0.02). Both homosexual responders had received IFN. None of 13 homosexual men, but eight of 16 heterosexual men, responded to ARA-AMP or ARA-A (p<0.01). Responders had higher transaminase concentrations than non-responders but were otherwise similar.

Interferon may be more effective and better tolerated than ARA-AMP. Homosexual men respond less frequently to antiviral therapy, especially ARA-AMP, than do heterosexual men.

T3 Significance of the delta antigen in acute hepatitis B
D A KELLY, D CARROLL, A G SHATTOCK, B M MORGAN E O’CONNOR, AND D G WEIR (Department of Medicine, Trinity College, Dublin and Department of Medical Microbiology, University College, Dublin) During a recent hepatitis B epidemic in parents and drug abusers, 29% of patients were found to have associated delta antigenaemia. We have followed up 30 delta positive drug abusers in order to ascertain: (i) the clinical course of their liver disease; (ii) the extent of transmission of both hepatitis B surface antigen (HBsAg) and the delta antigen (δAg) to close contacts.

All patients presented with acute hepatitis B. Using an ELISA assay to estimate the δAg and anti-δAg.
patients were positive for δAg and 10 had anti-delta (anti-δ) on initial testing. The clinical course was uneventful in 25/30 patients. 5/30 patients had a prolonged illness with cholestasis, none of the patients developed fulminant hepatitis. All patients cleared both HBsAg and δAg, and there has been no progression, as yet, to chronic liver disease.

A total of 53 family contacts were traced. 50 contacts had no evidence of positive markers for either hepatitis B or delta infection. Three family contacts had antiHBs, one of these was positive for anti-delta. Many patients denied or refused to name sexual contacts and only eight were traced. Five out of eight of these contacts had positive hepatitis B markers (3-HBsAg; 2-anti-HBs) and two of these had δAg; one had anti-delta. All three also admitted to parenteral drug abuse whereas the two patients with negative delta markers were not drug addicts.

It is concluded that in this group of patients the combination of acute hepatitis B and simultaneous delta infection has not had an adverse effect on their liver disease, and while there was a low rate of transmission of HBsAg to family and sexual contacts, transmission of δAg was confined to parenteral drug abusers.

T4 Genetic factors in the response to hepatitis B virus? A study in 34 sets of siblings

M CHIARAMONTE, A FLOREANI, C SCANDOLA, M G PORNARO, M G BERLANDA, AND R NACCARATO (Department of Internal Medicine (Division of Gastroenterology) and Blood Bank University of Padova, Italy) The aim of this study was to investigate the respective roles of the following factors in the familial clustering of HBsAg carriers: consanguinity, sex, age at the infection and vertical transmission. To that, we studied 34 kindreds (total sibs n=98) and 52 spouses of HBsAg carriers. We correlated the response to HBV infection with sex, age, infection in parents and sequence of sibs in the family (assuming that the different responses to HBV might be due to the different ages of sibs at the entry of the infection into the family).

The overall prevalence of HBV infection was 79% in spouses, 97% in adult sibs and 70% in child sibs, while HBsAg+ve/ HBV+ve rate was 14% in spouses, 76% in adult sibs and 81% in child sibs. In 14 kindreds, all the sibings were HBsAg+ve: in five, all the infected sibs were HBsAg+ve: while in 15, anti-HBs+ve subjects were present along with HBsAg carriers. Parents (either the mother or the father) were HBsAg+ve in 64% of the first group, in 75% of the second group and in 38% of the third group families. In three families of the third group, both parents were HBV-ve, while the parents from the other families had antiHBV antibodies. No relationship was found between the response to HBV and age, sex, or sequence of the sibs in the family.

The subjects negative for HBV were then vaccinated (HEVAC-B, Pasteur). The antiHBs titres in both vaccinated subjects and in spontaneously antiHBs producers were similar in spouses and siblings.

In summary, being that the risk of HBV infection is similar for spouses and siblings, the blood relatives have a high risk of remaining HBsAg+ve. This trend is not strictly correlated to the vertical transmission. We conclude that these results are consistent with the existence of a genetic predisposition to the failure of HBsAg clearance, which, however, seems not to involve the antiHBs production. This genetic factor is independent from, and possibly stronger than, age and sex.

T5 Pancreatitis in fulminant hepatic failure

R J EDE, K MOORE, W MARSHALL, AND R WILLIAMS (Liver Unit and Department of Chemical Pathology, King's College Hospital, London) Acute pancreatitis is a recognised complication of acute viral hepatitis and has also been reported in association with fulminant hepatic failure (FHF). We now report a prospective study of 36 patients admitted to this unit with fulminant hepatic failure, all of whom were examined for serum enzyme evidence of pancreatic injury.

Serum lipase and total serum amylase were measured (Boehringer and Phadebas respectively) and pancreatic iso-amylase activity was determined by electrophoretic fractionation on cellulose acetate using a modification of the method of Legaz and Kenny. Electrophoresis was performed at 4°C for 90 minutes with a constant current of 0.5 mA/cm and isoenzymes, stained by Phadebas reagent, were quantitated as a percentage of total amylase activity.

Total amylase activity was increased (>300 IU/l) in 24 of the 36 patients and in 11 patients activity was greater than 10 000 IU/l. Isoenzyme electrophoresis performed in the 29 patients with total amylase activity >200 IU/l revealed a distinct P1 band, indicative of acute pancreatitis, in 22 cases. In four of the patients with total amylase >1000 IU/l the P1 isoenzyme was absent and the increased activity was attributable mainly to an increase in the salivary S3 isoenzyme of uncertain aetiology. Serum lipase activity was raised (>400 IU/l) in 31 patients (86%) and was increased in all but one of the patients with detectable P1 isoenzyme. The high frequency of pancreatic enzyme abnormalities found in this study suggests that acute pancreatitis may be more common than previously suspected in fulminant hepatic failure.

T6 Evaluation of terfenadine compared with other drugs in the treatment of biliary pruritus

H J KENNEDY, J S DUNCAN, AND D R TRIGER (Department of Medicine, Royal Hallamshire Hospital, Sheffield) Pruritus is a troublesome symptom of chronic obstructive liver disease. Antihistamines and cholestyramine are widely used but both cause adverse side effects. We have compared terfenadine (a new H1 specific antihistamine reported to be free of sedative effect) with cholestyramine, chlormpheniramne, and placebo in a single blind randomised crossover trial in 10 patients with long standing pruritus secondary to chronic liver disease.

Objective assessment was made by psychometric testing and electroencephalography. In addition, the patients kept a daily record of pruritus and of side effects. Each drug was taken for a two week period in random order.

Cholestyramine (up to 12 g daily) and terfenadine (60 mg twice daily) both had significant antipruritic activity when compared with placebo (Wilcoxon's rank sum test p<0-05). Substantial benefit was often found with one or other of these drugs rather than both. Chlormpheniramne (up to 4 mg tds) was ineffective and caused side effects in three patients. Cholestyramine caused gastrointestinal symptoms in five patients. Terfenadine was well tolerated and did not produce any clinical or electroencephalographic deterioration. We conclude that terfenadine is of value in the management of some patients with biliary pruritus. There may be a place for concurrent use of terfenadine and cholestyramine in some individuals.
T7
Primary biliary cirrhosis (PBC): a new prognostic index

J L SHAFER, R BENNETT, W JONES J D K BROWN, AND M M MARSH (Departments of Medicine, Radiology and Medical Physics, Hope Hospital and University of Manchester, School of Medicine, Salford) Primary biliary cirrhosis usually runs a prolonged asymptomatic course. The onset of liver failure and decompensation is preceded by progressive rises in bilirubin concentrations. Our aim in this study was to predict impending hepatic dysfunction by prospectively analysing E-HIDA kinetics in primary biliary cirrhosis. The test, which was repeated annually over three years, was carried out on 11 patients (9F/2M; age range 47–75 years) who each received 14 Mq 99Tc99m-E-HIDA. Plasma decay curves, based on 16 consecutive venous samples over 24 hours, were used to determine (i) the interval for plasma radioactivity to reach 5% of the injected dose (t½) and (ii) the total area under the concentration-time curve (AUC). Total urinary radioactivity was measured over 24 hours. Hepatic uptake of tracer was monitored at minute intervals after intravenous injection for two hours with a computerised γ-camera. From these observations the rates of liver uptake and clearance of tracer were determined. The above data were then subjected to a principal components analysis from which a radioactive index (RAI) was derived. Values for RAI (range 13–277) showed a highly significant correlation with plasma bilirubin (r=0.83; p=0.001). In three of four patients who died from liver failure during the course of the study, the RAI exceeded 100 12–18 months before the accelerated rise in plasma bilirubin was noted. Serial measurements of RAI in the remaining seven patients have remained unchanged, and treatment of five of these latter subjects with D-penicillamine neither appeared to alter plasma bilirubin concentrations, or RAI. Thus, the RAI is (i) a reproducible index of liver function in PBC, and (ii) appears to be much more sensitive than plasma bilirubin concentrations in predicting the onset of terminal liver failure.

T8
‘Plugged’ percutaneous liver biopsy. A safe method for patients with impaired blood coagulation

S A RILEY, W R ELLIS, D J LINTOTT, H C IRVING, A T R AXON, AND M S LOSOWSKY (St James’s University Hospital, and the General Infirmary, Leeds) Tissue diagnosis is often desirable in patients with severe liver disease, but percutaneous liver biopsy is usually avoided in those patients whose prothrombin time is prolonged by three seconds or more or whose platelet count is less than 80×10⁹/l. Alternative methods, such as transvenous biopsy, are not always satisfactory. We use a simple modification of the percutaneous method, in which, under ultrasound or fluoroscopic control, the needle track is plugged with gel-foam on withdrawal. Either a modified ‘Tru-cut’ needle is used in which the outer sheath can be left in the liver on removal of obturator plus specimen, or a ‘Medicut’ (18G) sheath is placed over the biopsy needle beforehand and passed into the liver before withdrawal of needle and sample. The procedure requires breath holding for about 15 seconds and has been used in 18 patients with disturbed coagulation. Biopsies were between 0.4 and 2.2 cm in length, in 17 cases were adequate for diagnosis, and contributed information with potential to influence management. One patient, already moribund with severe, rapidly progressive liver disease, could not cooperate and bled significantly from the biopsy site, dying subsequently. No detectable bleeding occurred in the other patients whose haemoglobin levels did not fall after the procedure.

We conclude that plugged biopsy is useful, safe, and easily performed, but patient cooperation is essential.

T9
Cirrhosis in young adults: might transplantation alter the outcome?

J J KEATING, R D JOHNSON, P J JOHNSON, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital, London) Results relating to survival after liver transplantation vary between centres and are likely to depend both on the nature and stage of the liver disease. The decision as to when the operation should be performed requires a knowledge of the natural history of such patient groups. We have, therefore, performed a retrospective analysis of the clinical course and survival of 75 young adults (aged 15–30 years) presenting for the first time with cirrhosis between 1970 and 1983 (median follow up period, 4.5 years). The aetiology of the cirrhosis was autoimmune chronic active hepatitis (38), cryptogenic (16), Wilson’s disease (9) and other varieties (11).

Only one death has occurred in the 37 patients with well compensated liver disease (33 Child’s grade A and 4 Child’s grade B) whereas of the 38 patients with decompensated liver disease (Child’s grade C) 22 (88%) of the 25 treated conservatively have died. In contrast seven (54%) of the 13 Child’s grade C patients undergoing liver transplantation are alive and well. Comparison of survival in the two groups by life table analysis (log-rank test) showed that the transplanted group survived significantly longer (p<0.05), 50% survival being 50 and 15 months respectively.

T10
Unexpected effect of vitamin K on factor VIII in liver disease

D A KELLY, S MIKAMI, E G D TUDDENHAM, AND J A SUMMERFIELD (Department of Medicine and Haemophilia Centre, Royal Free Hospital School of Medicine, London) Factors V and VIII are now thought to be synthesised in the liver and inactivated by protein C, a recently discovered vitamin K dependent protease, which is also synthesised in the liver. In order to ascertain the effect of liver disease on these glycoproteins we estimated factor V using a bioassay; factor VIIIIC using both bioassay (VIIIIC) and immunoassay (VIII:CAg): and protein C antigen using radioimmunoassay, in 35 patients before and after parenteral vitamin K 10 mg. Using the prothrombin ratio and its response to vitamin K as an index, 22 patients were considered to be vitamin K replete (13 had parenchymal liver disease and nine had primary biliary cirrhosis on maintenance vitamin K). Thirteen patients with extrahepatic cholestasis were vitamin K deficient. The plasma concentration of VIII:CAg was raised in both groups (vitamin K replete – 2.7±0.4 units/ml; vitamin K deficient – 4.2±0.1 units/ml, mean ± SEM, normal range 0.5–2.0 units/ml) while VIIIIC was minimally raised in the vitamin K deficient group only (2.5±0.2 units/ml). There was a significant fall in the plasma concentrations of both VIIIIC (38%) and VIII:CAg (36%) following vitamin K (p<0.001). Factor V levels were low in the vitamin K replete group (0.54±0.1 units/ml, mean ± SEM, normal
range 0·5–1·5 units/ml) and twice that level in the vitamin K deficient group (1·2±0·1 units/ml, p<0·001). Protein C levels were low in both groups (0·7±0·1 mean ± SEM, normal range 0·74–1·39 units/ml). There was no significant change in either factor V or protein C antigen levels following vitamin K. The data suggest (i) that the raised factor VIII: Cag levels and, (ii) the reduction in both ViliC and VIII: Cag following vitamin K in liver disease were not mediated by protein C; (iii) that protein C has little effect on circulating levels of Factors V and VIII in vivo.

**T11 Effects of A β2-blocker (ICI 118, 551) on the hepatic haemodynamics**

S A JENKINS, J JOHNSON, P DEVITT, J N BAXTER, AND R SHIELDS (Department of Surgery, Royal Liver Hospital, Liverpool) Although propranolol may be effective in lowering portal pressure, β2-blockade sometimes makes resuscitation difficult should the patient experience severe variceal haemorrhage. This study was therefore carried out to investigate the effect of varying rates of an exclusive β2-blocker (ICI 118, 551) infusion on hepatic haemodynamics in the rat.

Male Wistar rats received a 20 minute infusion at either 0, 1·25, 2·5, 5·0, 10·0 or 20·0 μg/min/kg bw β2-blocker. Portal pressure, portal venous flow, arterial blood pressure and pulse were recorded continuously throughout the experiment. Liver blood flow was measured by the clearance of xenon-133 before and after the infusion of β2-blocker.

Infusions of 0, 1·25, 2·5 and 5·0 μg/min/kg bw β2-blocker had no significant effect on hepatic haemodynamics. After an infusion of 10 μg/min/kg bw β2-blocker, there were significant reductions in portal pressure (6·6±0·9 to 3·7±0·8 mm Hg) portal venous flow (34·6±1·8 to 26±2·3 ml/min) and liver blood flow (37·6±4·1 to 25±8±2·6), without significant reduction in pulse or arterial blood pressure (Student’s t test). Greater reductions in portal pressure and liver blood flow were obtained after an infusion of 20 μg/min/kg bw β2-blocker.

The results suggest that an exclusive β2-blocker (ICI 118, 551) can modify hepatic haemodynamics without a cardiac effect and may be of value in the treatment of portal hypertension.

**T12 Role of free oxygen radicals in rat models of hepatic injury**

M J P ARTHUR, I BENTLEY, A R TANNER, AND RALPH WRIGHT (Department of Medicine, Southampton General Hospital, Southampton). Free oxygen radicals promote injury in a variety of tissues, but there is limited evidence of their role in the pathogenesis of liver damage. We have studied the role of free oxygen radicals in rat models of mild and severe hepatic injury produced by intravenous C Parvum administration with or without the subsequent administration of intravenous endotoxin. The effect of superoxide dismutase (SOD) and allopurinol (Allo) in preventing such injury was studied. On day 1, 100 male Wistar rats received C Parvum. On Day 6, 50 rats received endotoxin and 50 received normal saline. They were then subdivided into groups of 10 and treated as follows: controls, normal saline intra-venous; experimental groups, superoxide dismutase 5000 u/kg intravenous; allopurinol 100 mg/kg po for three days +50 mg/kg intravenous; combined SOD and Allo as above; heat inactivated SOD (HI-SOD). Assessment included mortality, serum alanine aminotransaminase (ALT) and isocitrate dehydrogenase (ICDH) concentrations at the time of death or when killed on day 7.

In the severe hepatic injury model, mortality was decreased in the SOD (0/10, p<0·005), Allo (2/10) and combined SOD/Allo groups (2/10) compared with control (6/10) and HI-SOD groups (7/10). Furthermore, there was a significant reduction in serum ALT concentrations (Mean ± SD IU/l) in the SOD (132±128, p<0·01) and combined SOD/Allo groups (448±88, p<0·05) compared with controls (778±783), whereas ALT concentrations in the HI-SOD group were not significantly different. Similar changes were found for serum ICDH levels. In addition, the same trends in ALT and ICDH concentrations were observed in the mild hepatic injury model. These results indicate that free oxygen radicals may play an important role in the pathogenesis of hepatic injury.

**T13 Impaired platelet function and prolonged bleeding time in chronic alcoholics**

W J JENKINS, D P MIKHAILIDIS, M A BARRADAS, J U JEREMY, AND P DANDONA (Departments of Medicine and Chemical Pathology, Royal Free Hospital, London) High concentrations of ethanol are known to impair platelet aggregation and the release of thromboxane A2 (TXA2) acutely in volunteers. Impaired platelet function and a prolonged bleeding time secondary to alcohol abuse may contribute to the increased incidence of upper GI haemorrhage in chronic alcoholics.

Seventeen consecutive patients with alcoholic liver disease of varying severity were studied after admission for alcohol withdrawal. Bleeding times were measured by the Simple II modification of the template method. Platelet aggregation was induced in platelet rich plasma by adding either adrenaline 5 μmol/l, ADP 10 μmol/l or collagen 1 mg/l and TXA2 generation was measured by radioimmunoassay of TXB2. Eight patients with the longest bleeding times were studied serially after one and two weeks abstinence.

The mean bleeding time in chronic alcoholics on admission (10·5, range 4·5–26·5 minutes) was significantly prolonged (controls mean=5·6, range 2·5–9·5 minutes) (p<0·05). Prolongation of the bleeding time correlated significantly with impaired platelet aggregation induced in vitro by ADP, adrenaline, or collagen (p<0·05) and reduced TXA2 generation/106 platelets (p<0·05). Serial studies showed that these abnormalities of platelet function persisted after alcohol withdrawal but corrected together with the bleeding time after two weeks abstinence.

Chronic alcohol abuse is associated with impaired platelet function and prolonged bleeding times, which persist for up to two weeks after alcohol withdrawal. This may predispose to upper GI haemorrhage.

**T14 Chronic liver disease in abusers of alcohol and parenteral drugs: a report of 204 consecutive biopsy-proven cases**

D M NOVICK, R J STENGER, A M GELB, J MOST, S R YANCOVITZ, AND M J KREEK (INTRODUCED BY H C THOMAS) (Departments of Medicine and Pathology, Beth Israel Medical Center, and Mount Sinai School of Medicine, and The Rockefeller University, New York, New York, USA). Abusers of parenteral heroin or cocaine frequently develop chronic active hepatitis (CAH), chronic persistent hepatitis (CPH), or non-specific reactive hepatitis (NSRH) as a result of persistent virus infections or adulterants of the drugs. Alcohol abuse (AA) may occur before or after parenteral drug abuse.
(PDA), but little has been published on liver diseases in patients with both AA and PDA. In a hospital for addictive diseases, we evaluated 204 consecutive patients who underwent liver biopsy because chronic liver disease was suspected. Patients thought to have acute viral hepatitis were not biopsied. The addictive diseases consisted of alcohol alone in 23, parenteral drug abuse alone in 34, and both alcohol abuse and parenteral drug abuse in 147. Cirrhosis was found in seven patients (30%) with AA alone, three (9%) with parenteral drug abuse alone, and 76 (52%) with both (p<0.001). Chronic active hepatitis was found in one (4%) with alcohol abuse, 15 (44%) with parenteral drug abuse, and 17 (12%) with both (p<0.001). For other diagnoses, no differences in addictive diseases were found. Twenty six of the 204 patients had alcoholic hepatitis, 23 had fatty infiltration, 10 had chronic persistent hepatitis, nine had non-specific reactive hepatitis, one had hepatocellular carcinoma, and 16 had other diagnoses. Evidence of decompensated liver disease was more common in patients with both AA and PDA. The 147 combined abusers included 39 with AA and PDA at the time of liver biopsy and 96 with AA who had stopped PDA. Cirrhosis was found in 10 (26%) of the former group and 58 (60%) of the latter (p<0.005). We conclude that abuse of both alcohol and parenteral drugs is associated with a more severe chronic liver disease than that seen with either AA or PDA alone.

with bile salts, rendered isotonic, and separately infused at 5 ml· min⁻¹ for 30 minutes via an ileal port situated 175 cm from the mouth of 13 healthy volunteers. Throughout the study a fat free nutrient solution was infused at 3 ml· min⁻¹ just beyond the duodenojejunal flexure and jejunal intraluminal pressures were recorded through water perfused ports opening 15, 25, and 35 cm further distally. Jejunal motility was strikingly inhibited by ileal oleic acid (n=6), percentage duration of activity being only 6±2 (mean ± SEM) of the first 30 minutes after oleic acid infusion compared with 41±2 during the control hour (n=13, p<0.01). Pressure activity then recovered rapidly to 31±71%, one and a half hours after completing the oleic acid infusion (NS vs control). After ileal triolein infusion jejunal inhibition was slower in onset, percentage activity falling to 26±4 and 20±6 (p<0.01, n=13), 30 and 60 minutes after completing the infusion. Recovery was more gradual, reaching control values (38±11) only after two hours. Ileal MCTs produced significant jejunal inhibition (n=6, p<0.01) intermediate in magnitude and time course between oleic acid and triolein, while ileal glycerol had no significant effect (n=6, p>0.10). These findings indicate that receptors for the ileal brake reflex are more responsive to free fatty acids than to intact triglyceride, suggesting that intraluminal lipolysis is essential if the ileal brake is to be activated by malabsorbed fat in man.

without steatorrhoea (p<0.01) and 91±9 minutes for 12 healthy controls (p<0.01). Slow transit was not associated with delayed gastric emptying as assessed by gamma-camera in 10 of the coeliac patients but was associated with various indices of jejunal injury including impaired release of the upper ‘gut’ hormones cholecystokinin, gastric inhibitory polypeptide, and insulin (r=0.38, 0.35, and 0.40, all p<0.05, n=31). Slow transit was also associated with the raised fasting levels, delayed postprandial rise, and reduced integrated incremental postprandial response of plasma cholecystokinin (all p<0.05, n=14), results consistent with delayed gall bladder emptying as previously described in coeliacs. Of all the variables assessed, however, the best predictor of delayed transit was the 24 hour faecal fat excretion (r=0.52, n=26, p<0.01). Our findings support the hypothesis that jejunal injury and impaired pancreatic biliary secretions are associated with delayed transit because, by impairing fat absorption and increasing ileal fat load, they activate the ileal brake, thereby slowing small bowel transit.

**T17**

**Ileocolonic junction – phasic and tonic specialisation at a gastrointestinal sphincter**

E M M Quigley, S F Phillips, B Cranley, B M Taylor, and J Dent (The Gastroenterology Unit, Mayo Clinic and Foundation, Rochester, MN, USA) The ileocolonic junctional region contains a zone of sustained tone, the ileocolonic sphincter (ICS) and also shows unique patterns of phasic motor activity. Our aim was to delineate the topographic distribution of these motor patterns. Studies of fasting ileocolonic motor activity were performed for a total of 90 hours in seven conscious dogs using multiple closely spaced perfused catheters (five dogs) and extraluminal strain gauge transducers (two dogs). Pull-through pressure measurements at the ileocolonic junction were then carried out at laparotomy in each dog and areas of sustained tone marked under direct visual and radiograph control. After removal of the bowel the anatomical features of these high pressure zones were defined by light microscopy.

Unique phasic patterns were recorded from a 35 cm segment incorporating the ileocolonic sphincter, 30 cm distal ileum, and 5 cm proximal colon; discrete bursts of rhythmic activity progressively replaced
irregular phase II type activity as the ICS was approached while at a mean interval of 115 minutes distinctive, high amplitude propulsive waves swept through the segment. In contrast, sustained tonic pressures (10–70 cm H$_2$O) were recorded only from a 1–2 cm zone at the ileocolonic junction. Rises of tonic pressure related to phasic bursts were greater here (55.5±5.1 cm H$_2$O) than in distal ileum (12.8±2) or proximal colon (19.5±6.7) and episodes of tonic relaxation were confined to this zone. Pull-through studies similarly identified a narrow (mean length 2 cm) high pressure zone (mean amplitude 34 cm H$_2$O) which corresponded to the anatomical ICS. Thus motor specialisation is evident at two levels in this region; tonic responses being confined to the anatomical sphincter while unique phasic patterns identify a more extensive functionally distinct segment.

T18

Demonstration of receptors for prostaglandin $E_2$ on rat small intestinal epithelial cells

G Smith, G Warhurst, and I A Turnberg

(Department of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford) Prostaglandins, produced in the small intestine by subepithelial tissues and degraded by the epithelium, may have a role in control of intestinal secretion. We report here studies performed to examine the possibility that prostaglandins act by a receptor mediated mechanism. Plasma membrane fractions from rat small intestine epithelial cells showed a small but significant specific binding of $^3$H PGE$_2$ (total binding 22.23±2.2, non-specific 19.85±1.77 and specific binding 2.38±0.48 fmol/mg protein, p<0.02, paired t test).

Biochemical studies support the conclusion that a receptor mediated mechanism activates epithelial adenylate cyclase. Solubilisation of plasma membrane adenylate cyclase with Lubrol PX markedly inhibited prostaglandin $E_2$ stimulated activity of the cyclase. This procedure separates the receptor moiety of adenylate cyclase from the catalytic unit. Similar results were obtained with VIP stimulated activity. Non-receptor mediated stimulation, with $\gamma$GTP, forskolin or fluoride which directly activate the nucleotide binding or catalytic units, however, was unaffected by solubilisation.

In addition VIP and PGE$_2$ stimulation of adenylate cyclase required GTP which non-receptor mediated stimulation by fluoride did not. These data support a model in which subepithelially produced prostaglandins stimulate epithelial secretion by a receptor mediated activation of adenylate cyclase. The studies have implications for secretory diarrhoeal diseases in which locally produced prostaglandins may be an important mediator.

T19

Intestinal permeability in patients with longstanding psychiatric disease

N C Wood, A M J Shapiro, S Khan, P Quirke, K McGuigan, I Hamilton, R S H Mindham, J Rothwell, and A T AXON

(The Gastroenterology Unit, The Professorial Department of Psychiatry, and Professorial Department of Pathology, The General Infirmary, Leeds) The cellubiose/mannitol test which is based on the differential absorption of two different sized molecules is a reliable screening test for coeliac disease and is also abnormal in other conditions characterised by abnormalities in intestinal permeability such as Crohn’s disease and dermatitis herpetiformis. Previous studies have suggested an increased incidence of coeliac disease in schizophrenia and is also abnormal in other conditions characterised by abnormalities in intestinal permeability such as Crohn’s disease and dermatitis herpetiformis. Previous studies have suggested an increased incidence of coeliac disease in schizophrenia and is also abnormal in other conditions characterised by abnormalities in intestinal permeability such as Crohn’s disease and dermatitis herpetiformis. Previous studies have suggested an increased incidence of coeliac disease in schizophrenia and is also abnormal in other conditions characterised by abnormalities in intestinal permeability such as Crohn’s disease and dermatitis herpetiformis. Previous studies have suggested an increased incidence of coeliac disease in schizophrenia and is also abnormal in other conditions characterised by abnormalities in intestinal permeability such as Crohn’s disease and dermatitis herpetiformis.

The studies have implications for secretory diarrhoeal diseases in which locally produced prostaglandins may be an important mediator.

T20

Screening for small intestinal mucosal damage using the lactulose-L-rhamnose sugar permeability test

I A Santana, M B Talbot, B K Sharma, and R E Pounder

(Academic Department of Medicine, Royal Free Hospital School of Medicine, London) It is often difficult to identify the minority of patients with organic disease from the majority with functional disorders. In a prospective study, patients presenting with diarrhoea have been screened for small intestinal mucosal damage using a sugar permeability test.

The test, using lactulose and L-rhamnose as probe molecules, can detect untreated villous atrophy or Crohn’s disease. It is non-invasive and is performed at home: the fasting patient swallows 4.7 g lactulose, 1 g L-rhamnose, and 12 ml glycerol made up to 100 ml with water. Urine is collected for the next five hours, and the concentration of the probe sugars in the urine measured using thin layer chromatography.

Seventy seven consecutive new outpatients with diarrhoea were fully investigated: nine were found to have ulcerative colitis, 10 Crohn’s disease, six villous atrophy, and 52 were thought to have a functional disorder. All the patients who presented with either Crohn’s disease or villous atrophy had an abnormal sugar test: there were no false negative results. Forty nine of the 52 patients with a functional disorder had a normal test. Two of nine patients with ulcerative colitis had an abnormal sugar test, but no other evidence of small intestinal disease.

The lactulose-L-rhamnose sugar permeability test is a simple, safe, and a non-invasive screening procedure for small intestinal mucosal damage.

T21

Non-invasive assessment of the superior mesenteric artery blood flow in man

M I Qamar, A E Read, R Skipmore, J M Evans, and P N T Wells

(University Department of Medicine, Bristol Royal Infirmary Department of Medical Physics, Bristol General Hospital, Bristol) Methods
available for the assessment of superior mesenteric artery blood flow (SMABF) are invasive and difficult to perform. In the present study transcutaneous Doppler ultrasound was used to estimate SMABF. A duplex scanner, which consists of a real-time imaging system associated with a Doppler ultrasound flowmeter, was used to study the SMABF in 46 healthy subjects. By processing the Doppler shift signals of the superior mesenteric artery the instantaneous average velocity of the blood flow over the cardiac cycle was calculated. Both the diameter of the vessel and the angle between the vessel and Doppler beam were measured from the real time image. The mean (±SEM) resting SMABF was 561±32 ml/min. There was no difference in flow between the sexes or in different age groups. In the second group of 15 healthy volunteers the SMABF was measured before and after a mixed meal (683 kcal) for two hours. The blood flow increased within five minutes of the end of the meal by 61% and more than doubled within 15 minutes. The potential application of the method in the diagnosis of chronic intestinal ischaemia will be discussed.

T22 Peptide chain length of protein hydrolysates influences jejunal nitrogen absorption

R G REES, G K GRIMBLE, P P KEOHANE, B E HIGGINS, M WEST, R C SPILLER, AND D B A SILK (Departments of Gastroenterology and Nutrition and Chemical Pathology, Central Middlesex Hospital, London) The nature of the enzymic digestion and the nature of the product composition influence the absorption characteristics of partial enzymic hydrolysates of dietary protein. The present study was carried out to investigate the influence of peptide chain length on absorption.

Three highly purified, low MW, ovalbumin hydrolysates of similar amino acid composition were prepared and none contained significant amounts of peptides of greater than five amino acid residues. The short chain preparations (OH1 and OH2) contained only 16% and 29% of their amino acid content as peptides containing three to five residues, whereas a medium chain preparation (OH3) contained 68% of amino acids in this chain length range.

An in vivo jejunal perfusion technique was used in normal human subjects to compare absorption of nitrogen from the three hydrolysates. Isotonic test solutions, containing 30 or 100 mmol/l αNH₄I were infused in random order in two sets of experiments.

Nitrogen absorption occurred significantly faster from both short chain preparations (OH1 and OH2) than from the medium chain preparation (OH3) at 30 mmol/l (p<0.02) as well as at 100 mmol/l (p<0.05).

These data are the first demonstration, in man, that subtle increases in peptide chain length slow the rate of absorption from partial enzymic hydrolysates of dietary protein. Furthermore, optimum absorption occurs from preparations containing a predominance of di- and tripeptides.

T23 Fasting and postprandial ileal function in adapted ileostomates and normal subjects

S D LADAS, P E T ISAACS, G M MURPHY, Y QUERESHI, AND G F SLADEN (Gastroenterology Unit, Guy’s Hospital, London) The reduction from the estimated daily flow through the normal ileum of 1.5–2.5 l/day to the 0.5–0.8 l/day output of a well adapted ileostomy could be because of increased electrolyte absorption in response to salt depletion or to a reduction of postprandial flow secondary to delayed transit and increased mucosal contact time.

We compared the output of 11 well adapted ileostomies (after ulcerative colitis) with the ileal flow measured by intestinal perfusion in five normal subjects, fasting and in response to a liquid meal. The oro-ileo-ileal transit of the meal marker (phenol red) was the same in the two groups, but ileostomy output was less than normal ileal flow, both fasting (16.3±10.9 vs 62.4±11.5 ml/h, p<0.001) and postprandially (35.4±27 vs 96.1±20.2 ml/h, p<0.0001). K concentration was higher in ileostomy fluid (p<0.05) than in normal ileal content but Na concentrations did not differ. In fresh samples, osmolality was higher in ileostomy fluid than in ileal fluid both fasting (353±63 vs 287±55 mOsm/kg, p<0.05) and postprandially (347±47 vs 283±7 mOsm/kg, p<0.02) but the mean pH was alkaline in both ileostomy fluid (7.4–7.5, fasting – postprandial) and normal ileal content (7.4–7.8). Previously reported acid pH of ileostomy fluid was probably because of fermentation of the samples.

The reduction of both the fasting and postprandial ileal flow and the increased luminal potassium concentration in the absence of changes in transit time suggest that adaptation to ileostomy is primarily a response to chronic salt depletion rather than an altered response of the ileostomate intestine to meals.

T24 HLA-DR typing in coeliac disease and dermatitis herpetiformis: evidence for further genetic heterogeneity

A ELLIS, C J TAYLOR, M DILLON-REMNY, S LEWIS-JONES, J C WOODROW, R B McCONNEL, AND C H VICKERS (Gastroenterology Unit, Broadgreen Hospital, Department of Child Health and Tropical Child Health, Alder Hey Children’s Hospital, Department of Medicine and Department of Dermatology, University of Liverpool, Liverpool) We have previously shown that adult coeliac disease (ACD) differs genetically from juvenile coeliac disease (JCD). Both forms of the disease have a significantly increased frequency of HLA-DR3 compared with controls but in addition juvenile coeliaics have an increased frequency of HLA-DR7 and a decreased frequency of HLA-DR2 compared with both controls and adult coeliacs. Dermatitis herpetiformis (DH) is also strongly associated with HLA-DR3. A large proportion of patients with this condition have a gluten sensitive enteropathy which is frequently not discovered until after the skin disease presents, usually after the age of 20. Thus patients with DH should have HLA-DR frequencies similar to adult coeliacs. Thirty seven patients with DH, 63 patients with JCD (less than 20 years), and 46 patients with ACD (greater than 20 years) have been HLA-DR typed. All three conditions have a significantly increased frequency of HLA-DR3 (100, 89.1, and 88.9% respectively) compared with controls (26.2%). Whereas, however, HLA-DR2 is reduced in JCD (4.8%) it is normal in ACD (26.1%) and DH (29.7%) (controls 28.6%) and HLA-DR7 is increased in JCD (57.1%), normal in ACD (26.1%), and reduced in DH (10.8%) (controls 29.2%). Thus HLA-DR typing indicates further genetic heterogeneity among patients with gluten sensitive enteropathies.

T25 Coeliac disease and dermatitis herpetiformis: antibody classes to wheat gliadin

P J CICLATIRA, H J ELLIS, P D HOWDLE, R M
The British Society of Gastroenterology

T26

α-Gliadin antibodies in childhood coeliac disease – a screening test

JACINTA KELLY, C O’FARRELLY, C O’MAHONY, A THOMPSON, J P REES, C FEGHIERY, AND D G WEIR (Departments of Immunology and Clinical Medicine, Trinity College, St James’s Hospital, and The National Children’s Hospital, Dublin) The diagnosis of coeliac disease is established by the demonstration of a typical histological lesion with reversal of this lesion after gluten withdrawal. We have previously reported that the measurement of α-gliadin antibodies (AGAs) is a useful screening test in adults. The purpose of this study was to determine whether this screening test could be applied to a paediatric population.

AGA of IgG class was initially measured in 54 control children, whose ages ranged from 15 months to 15 years. A gradual increase in AGA levels was observed and paralleled the increase in the subject’s age. AGA levels were then measured in 43 children undergoing jejunal biopsy. Ten had jejunal mucosal changes consistent with coeliac disease and all except one had raised AGA (IgG class) levels. Of 38 patients with normal biopsies, 32 had normal antibody levels and this included all previously diagnosed coeliac patients (seven) who were observing a gluten free diet. Measurements of AGAs in this population was therefore found to have a specificity of 82% and a sensitivity of 90%.

These results show that measurement of AGAs is of value in screening a paediatric population for coeliac disease and may be used to measure dietary compliance.

T27

Evidence that intestinal histiocytic lymphoma is immunologically distinct from coeliac disease

CLIONA O’FARRELLY, C O’MAHONY, S O’BRIAIN, C FEGHIERY, AND D G WEIR (Departments of Immunology and Clinical Medicine, Trinity College, Dublin, Ireland) The characteristic histological feature of both coeliac disease and intestinal lymphoma is partial villous atrophy (PVA) of the small intestinal mucosa. In coeliac disease the mucosal lesion usually responds to dietary exclusion of gluten. A small percentage of adult coeliac patients, however, fail to improve.

From a total of 200 patients with PVA initially diagnosed as having coeliac disease and treated with a gluten free diet, eight failed to respond either clinically or histologically. Four patients were subsequently shown to have intestinal histiocytic lymphoma and four, by definition, had non-responsive adult coeliac disease. The latter four patients had maintained a strict gluten free diet for nine to 12 months. At the commencement of dietary therapy, all four patients showed raised α-gliadin antibody levels using an enzyme linked immunosorbent assay. (Previous investigations showed that this test is 82% sensitive and 87% specific for coeliac disease.) The α-gliadin antibody levels returned to normal within six months of gluten withdrawal (in a similar manner to those coeliac patients who respond satisfactorily to dietary restriction).

The four patients who were ultimately diagnosed as having intestinal histiocytic lymphoma had normal α-gliadin antibody levels throughout the period of observation.

These findings suggest that the α-gliadin antibody levels in patients with PVA may be of prognostic significance and may help in distinguishing those patients with non-responsive coeliac disease from those with underlying intestinal histiocytic lymphoma.

T28

Mucosal lymphocyte response to gluten challenge in coeliac disease (CD)

R J LEIGH AND M N MARSH (Department of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford) It has been held that the epithelium in untreated CD is ‘infiltrated’ with lymphocytes, a view that has not been substantiated by recent morphometric analyses. As a peptic-tryptic digest of gluten (Frazier’s Fraction 3 or FF3) is known to damage coeliac mucosa we set out to determine whether oral challenge with small graded doses of FF3 causes lymphocyte infiltration and whether this effect is dose dependent.

Treated CD patients, and volunteers, were challenged orally with either FF3 (100, 500, 1000, 1500 mg) or 500 mg of control protein B-lactoglobulin (LG). One micrometre toluidine blue stained epon sections of biopsies obtained before, and 12, 36, 60, and 84 hours after each challenge, were analysed morphometrically: (1) the absolute number (N) of EL overlying a constant test area of 105 μm2 of muscularis mucosae was determined for each biopsy; (2) the mean nuclear diameter (MND), per cent immunoblasts (MND >6 μm) and per cent mitotic index (per cent M1/3000 EL), as indicators of lymphocyte ‘activation’ were determined; (3) the ratio of EL penetrating basement membrane to N – that is, flux ratio (FR) – gave some estimate of EL turnover across the epithelial basement membrane; (4) cryostat sections (5 μm) were reacted with anti-T lymphocyte monoclonal antibodies for qualitative analysis of EL.

A progressive dose related increase in N
(per cent increment over control biopsy) occurred in CD mucosa at 12 hours with FF3 (500 mg, p<0.01; 1000 mg, p<0.05; 1500 mg, p<0.005), waning by 36 hours. The 12 hour infiltrate comprised ‘suppressor’ phenotype (T8’) small lymphocytes. There was no evidence of lymphocyte ‘activation’, and FR did not change. Crohn’s disease mucosa did not respond to LG, nor controls to either immunogen.

Oral challenge with FF3 causes dose dependent, time related infiltration of CD epithelium by ‘suppressor’ lymphocytes.

ENDOSCOPY
T29–33

T29 Prospective multicentre study of British sphincterotomy: initial results and complications
R A FROST (FOR THE BRITISH COLLABORATIVE STUDY OF ERCP) (The Middlesex Hospital, London) Since 1981, endoscopists from 13 British centres have collaborated in a prospective study of patients presenting for ERCP. A computer sheet was designed which contained 430 numbered pieces of information concerning presenting features, investigations, procedures, and final conclusions.

Two hundred and sixty seven patients have now been entered on the database of a main frame computer. Seven hundred and twenty one patients have come to sphincterotomy, with a total of 822 procedures, including 91 precuts and 60 extensions of sphincterotomy. There have been 20 sphincterotomies of tumour and five pancreatic sphincterotomies.

Six hundred and four patients with common bile duct stones presented for sphincterotomy. Cannulation was achieved in 97% and sphincterotomy was successful in 97% of those cannulated. After sphincterotomy the duct was shown to be clear of stones in 85%. The overall success rate for sphincterotomy and duct clearance was therefore 80%.

Of the 721 sphincterotomy patients, 11% developed a complication, the overall mortality being 1%. The three most common complications were haemorrhage, cholangitis, and pancreatitis, all with an incidence of 3%. The incidence of retroperitoneal perforation was 1%, there being no deaths in this group. Surgical treatment was required for 40% of bleed, 14% of cholangitis, 11% of perforation, and 5% of pancreatitis.

T30 Successes, failures and complications of endoscopic sphincterotomy
L LEASE, D L CARR-LOCKE, AND J NEOPTOLEMO (Gastroenterology Unit, Leicester Royal Infirmary, Leicester) During a six year period, 2011 ERCPs and 394 endoscopic sphincterotomies (ES) were performed in one centre by one endoscopist. Indications for ES were common duct stones (319), papillary stenosis (37), ampullary tumours (24), endoprosthesis (eight), sump syndrome (four), and biliary dilatation (two).

Successful ES was accomplished in 95.4% overall and successful clearance of stones achieved in 93.4%. Both figures improving with experience. A nasobiliary catheter was used in 19 patients, eight with successful mono-octanoin dissolution therapy.

Failure of ES and/or CBD. clearance occurred in 21 patients with common duct stones (6–6%). 18 later undergoing surgical bile duct exploration, two of whom died postoperatively. Reasons for failure were inaccessibility of the papilla – for example, duodenal diverticulum – inability to perform ES or achieve an adequate incision, large stones and a narrow bile duct below a stone.

Complications occurred in 40 patients (10%): haemorrhage (19), acute pancreatitis (eight), cholangitis (six), impacted basket (three), retroperitoneal perforation (three), and gall stone ileus (one). Emergency surgery was required in 15 patients: six for haemorrhage, one for pseudocyst, three for retained stones and cholangitis, two for impacted baskets, two for retroperitoneal perforation, and one for gall stone ileus. Overall mortality within one month of ES was 12/394 (3%) of which three were directly related to ES (0.8% of total, 7.5% of complications). The complication rate was higher after ES for papillary stenosis.

Endoscopic sphincterotomy is a highly successful technique for treating papillary and biliary disease but awareness of the possibility and frequency of complications is essential to instigate appropriate treatment when these occur.

T31 Value of precut papillotomy at ERCP and endoscopic sphincterotomy
D F MARTIN AND D E F TWEEDLE (Departments of Radiology and Surgery, University Hospital of South Manchester, Manchester) In 196 patients undergoing retrograde examination of the bile ducts a cholangiogram was obtained with ease in 166 (85%). In 10 patients in whom biliary pathology treatable endoscopically was suspected a precut papillotomy allowed cholangiography in nine (total success 89%). Pancreatitis occurred in four patients, one of whom had precut. Retroperitoneal leakage of contrast was seen in one precut patient. All patients with complications recovered. Of 94 patients requiring endoscopic sphincterotomy (ES), 90 with bile duct stones, this was easily achieved in 74 (78%). In the other 20 patients precut papillotomy allowed full sphincterotomy in 17, giving an overall success rate for ES of 97%. In the 90 patients with bile duct stones there were removed or passed spontaneously in 82 (91%). Complications occurred in seven of the 94 ES patients, one of whom died. Of the 20 precut patients, one developed cholangitis and one pancreatitis but both recovered. It is concluded that precut papillotomy is helpful in achieving a cholangiogram in selected patients and in performing sphincterotomy where deep cannulation of the bile ducts is not possible. There are no particular complications of the procedure.

T32 Management and outcome of endoscopic perforations of the pharynx and oesophagus
K R HINE AND M ATKINSON (University Hospital, Queen’s Medical Centre, Nottingham) In recent years the increasing use of therapeutic endoscopy has led to an increase in instrumental perforations of the oesophagus and pharynx. The management of such perforations is still a matter of debate.

We have treated 28 endoscopic perforations of neoplasms of the oesophagus or gastric cardia and in addition have dealt with eight pharyngeal perforations sustained during endoscopy. The perforation was recognised endoscopically in 18, by the immediate development of surgical emphysema of the neck in three and by radiology (including contrast radiology) in the remaining 15. Ten of those detected only by radiology were asymptomatic.

All patients were treated conservatively
using broad spectrum antibiotics, avoiding any oral intake of food or fluid and feeding the patient either parenterally or through a fine bore feeding tube.

Seven of the 36 patients died as a result of the perforation (all oesophageal) and this included four in whom the tear extended into the pleural cavity.

Instrumental tears differ from spontaneous and foreign body perforations of the oesophagus as, when recognised early, extravasation of food or barium into the mediastinum can be prevented. With early recognition, appropriate conservative treatment results in an 80% survival rate from the tear often allowing several months of comfortable life before the patient succumbs to the neoplasm itself.

T33
Selection of patients for upper gastrointestinal endoscopy without sedation

S D LADAS AND S A RAPIS (Gastroenterology Unit, 2d Propaedeutic Medical Unit of the Athens National University, Evangelismos Hospital, Athens, Greece) Sedation for upper gastrointestinal endoscopy occasionally produces serious side effects, adversely affects the ability of the patient to work or drive a car, and causes delays in a busy endoscopy unit. Assessment of the patient’s response to digital examination of the pharynx (finger-throat test) predicts which patients will tolerate gastroscopy without sedation.

Of 100 consecutive patients (age 18–87 years) 84 were tolerant to pharyngeal examination (positive finger-throat test) and had gastroscopy without sedation. The toleration of gastroscopy was excellent in 36, satisfactory in 24, and poor in only four. There was no significant difference in the ages of the patients with excellent toleration (n=36) 55.6±16.9 (mean ± SD) years old, satisfactory toleration (n=24) 53.4±11.7 years, and endoscopy after sedation (n=16) 55.9±16.0 years. p=0.9. Fourteen patients were offered a follow up examination, none refused, and their toleration of endoscopy was the same as in the first examination.

As the predictive value of a positive test is 0.95, it is concluded that the finger-throat test can accurately predict which patient will tolerate gastroscopy without sedation with a standard forward viewing endoscope.

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T34
Non-invasive endoscopic measurement of oesophageal variceal pressure: effect of drugs and sclerotherapy

J DAWSON (Department of Medicine, Queen Elizabeth Hospital, Birmingham) Propranolol and sclerotherapy have become established therapies in the management of bleeding oesophageal varices. A number of problems remain, however, notably the potential toxicity of β-blockers in liver disease and the postulated adverse effects of partial sclerotherapy on pressure within residual varices. Hitherto, studies have been impeded by the invasive techniques necessary to measure portal pressure. We have evaluated a pneumatic pressure gauge which can be attached to a standard endoscope and measure non-invasively the pressure directly from a varix.

This ‘variceal pressure’ was validated by showing a close correlation with splenic pulp pressure (r=0.97) in diverse liver diseases and with hepatic venous wedge pressure (r=0.92) in cirrhotics. Furthermore, predicted changes in variceal pressure were observed after propranolol therapy and bolus somatostatin.

The gauge can be applied to screen drugs for efficacy in lowering portal pressure. Intraduodenal isosorbide dinitrate in doses causing a profound fall in arterial pressure produced no change in variceal pressure in eight cirrhotics. This drug is thus valueless as a therapeutic alternative to propranolol. Studies in patients after partial sclerotherapy showed no pressure rise in residual patent varices. The gauge also readily differentiated patent varices from visually similar fibrous tags. Prospective studies in progress will, from a single procedure, give definitive information on the relative risks posed by variceal size, appearance, and pressure in predicting a future bleed.

T35
Origin of chronic right upper quadrant pain

J G KINGHAM AND A M DAWSON (Department of Gastroenterology, St Bartholomew’s Hospital, London EC1) Despite evidence from several authorities that chronic right upper quadrant (RUQ) pain with fat intolerance rarely originates from the biliary tract, the myth of chronic cholecystitis persists. The cause of such pain is ill defined but our preliminary observations suggested that it could arise from the gut. We have studied 16 consecutive patients referred for investigation of severe chronic RUQ pain. The majority (12) were women. Symptoms had been present for two to 23 years. All had undergone repeated investigations of the pancreaticobiliary, gastrointestinal, urinary, and even gynaecological systems without a satisfactory diagnosis and 20 abdominal operations had been performed on 10 patients in unsuccessful attempts to cure their pain. The aim of this study was to reproduce the patient’s customary pain by balloon distension of the alimentary tract at various sites along its entire length.

The oesophagus and small intestine were approached by mouth with a weighted latex balloon (40 ml) on a fine tube. The colonic balloon (250 ml) was introduced alongside a standard colonoscope. In 15 of 16 patients their customary pain was completely and reproducibly mimicked by insufflation of the balloon in at least one site. The pain always subsided with deflation of the balloon and returned with reflation. The trigger sites were ileum (10), jejunum (10), right colon (seven), and duodenum (five). In nine more than one trigger site was found. Close questioning revealed features of the irritable bowel syndrome in the majority (10) and depression in many (eight) though the symptoms were not spontaneously volunteered. Reproduction of pain has provided a convincing demonstration to this difficult group of patients that they have a sensitive gut.

T36
Does bowel rest have any role in the treatment of acute colitis?

P B MCINTYRE, J POWELL-TUCK, S R WOOD, J E LENNARD-JONES, E LEBREBOURS, P HECHETS-WEILER, J P GALMICHE, AND R COLIN (St Mark’s Hospital, London, and Hospital Charles Nicolle, Rouen Cedex, France) To test the efficacy of ‘bowel rest’ a group of patients with severe acute non-infective colitis starting treatment with intravenous prednisolone were randomised to continue oral food or not. An adequate nutritional state was maintained in those who took no nourishment by mouth by the intravenous route. The two groups were comparable in terms of age, sex, disease extent, and weight loss during the present attack. Of
operative the 27 patients who received no nutrients by mouth, 11 required urgent surgical treatment during that admission (one postoperative death), and of the 20 patients who continued to eat, five required urgent surgical treatment (two postoperative deaths). Daily stool weights (mean ± SEM) tended to be less with ‘bowel rest’ than oral food after seven days, 253±45.6 g compared with 312±59.4 g, and after 14 days, 229±64.3 g compared with 309±69.7 g. The final diagnoses based upon pathological criteria were ulcerative colitis (27), indeterminate colitis (four), and Crohn’s colitis (16). Among the patients with ulcerative colitis, five of 12 who continued to eat needed urgent surgery compared with nine of 15 who took no food. Of the four patients with indeterminate colitis, one continued to eat; of the three who had ‘bowel rest’ two required urgent surgery. Among the 16 patients with Crohn’s disease none required urgent surgical treatment. Within the first 14 days, all nine treated with ‘bowel rest’ but only five of seven who continued to eat, improved. During a follow up of five to 60 months, three patients who responded to medical treatment later required elective surgery. There is no evidence that ‘bowel rest’ was effective in acute ulcerative or indeterminate colitis. In this trial Crohn’s colitis needed urgent surgical treatment less often than acute ulcerative (p<0.01) or indeterminate colitis (p<0.05) but the reason for this is unclear.

T38 Is childhood coeliac disease declining?

R F A LOGAN, ANNE FERGUSON, S COLE, L J H ARTHUR, G K H HOLMES, M J S LANGMAN, AND R E MCONNELL (University Hospital, Nottingham; Western General Hospital, Edinburgh; Common Services Agency, Edinburgh; Derby Royal Infirmary, Broadgreen Hospital, Liverpool) To investigate reports of a decline in the incidence of childhood coeliac disease we have used data from (1) a hospital based register of coeliacics in Edinburgh, (2) records of 1·1 million local authority school entry medical examinations in Scotland 1967-81, (3) hospital records in Derby, and (4) Coeliac Society membership records 1970-81. All four sources show a marked decline in numbers of childhood coeliacs born since 1976. In Edinburgh and Lothian the prevalence of coeliac disease at age <2 years fell from 73 to 38/100 000 for births in 1970-75 and 1976-1980 respectively and from 101 to 45/100 000 for children of all ages born in these periods. The prevalence of coeliac disease reported at Scottish local authority school entry medical examinations having averaged 69 and 62/100 000 in children born in the 1960s and 1970-75 respectively, had fallen to 19/100 000 in children born in 1976 (peak of 84/100 000 for 1972 births). Hospital records in Derby show a 50% decline in numbers diagnosed since 1976 and Coeliac Society membership records from eight regions of England and Wales show a decline from 25 to 13 coeliacs aged <2 years at diagnosis for birth years 1970-76 and 1977-80.

These data show that in births since 1976 throughout Great Britain there has been an approximate halving of the number of children who have developed coeliac disease. The geographic extent and the size of the decline suggest that neither local factors, such as epidemic infections, nor small increases in frequency and duration of breast feeding are sufficient explanations. The decline does coincide with the removal of gluten from some widely used baby foods. Whether this represents prevention, postponement, or only decline in severity of coeliac disease in unknown.

T37 Oesophagitis lowers the angina threshold

H ALBAN DAVIES, Z DANZIGER, AND E RUSH (Department of Medicine, Ipswich Hospital, Suffolk) Heberden observed that angina was often aggravated by eating. We have investigated whether experimental oesophagitis affected the exercise tolerance of five patients with ischaemic heart disease. They all had positive exercise tests (ST segment depression >1·5 mm) and four had significant coronary artery stenosis shown angiographically. Subjects walked on a treadmill while the oesophagus was perfused with saline or 0·1 N HCl. Each subject performed four tests in sequence and two solutions of each type were perfused in a ‘blind’ order. The distance to the angina point was 261 m (±294) with the saline and 134 m (±58) with the acid perfusion tests. At equivalent distances during the acid and saline walks the cardiac work, indicated by the rate-pressure product, was similar (13 726±2116; 14 668±2658, respectively). ST segment depression was 0·8 mm (±0·27) during acid and 1·15 mm (±0·45) during the saline walks. No patient had pain during a preliminary perfusion period of 20 minutes before each walk.

Acid oesophageal perfusion lowered the angina threshold in four out of five patients, although the mechanism is unclear. This may have clinical relevance as the treatment of myocardial ischaemia includes nifedipine and nitrates, drugs which are known to decrease the lower oesophageal sphincter pressure and may induce oesophagitis. Mean values ± SD.

T39 Endoscopic retrograde cholangiopancreatography (ERCP) in pancreatitis with continuing pain

P A WINSTANLEY, A P MANNING, D J LINTOTT, AND A R AXON (The General Infirmary, Leeds) The role of ERCP in the diagnosis of chronic pancreatitis is established but its value in those already known to have pancreatitis and with continuing abdominal pain has not been evaluated. We therefore studied the ERCPs of patients known by other criteria to have pancreatitis and with recurring or persistent abdominal pain. Radiographs were examined by two experienced observers: terminology and grading of chronic pancreatitis followed the Cambridge Classification 1983; clinical data were obtained from Unit records and case note review. One hundred and seventy one patients fulfilled the entry criteria; 35 ERCPs were unavailable and 20 designated as technically inadequate. Of the remaining 116 (66 men, 50 women; mean age 46 years, range 9-80 years), 82 had recurrent and 34 persistent pain diagnosed as pancreatitis. Radiological changes of chronic pancreatitis were graded mild in 13, moderate in 24, and marked in 38; 69 had diffuse and six had localised changes. Forty ERPs were normal or equivocal; one patient who fulfilled the entry criteria had pancreatic carcinoma. Twenty six ERPs showed lesions which were potentially surgically remediable: three had changes localised to the tail, six had one or more large cavities and 17 had main pancreatic duct obstruction/stricture, in five cases with a large cavity. ERC, performed in 73 patients, showed gall stones in 14, of whom seven had common bile duct (CBD) stones; in 12 the stones had not been diagnosed before ERCP. In all, 38 patients (33%) were shown to have pancreatic or biliary lesions theoretically amenable to conservative surgery. We conclude, therefore, that all patients diagnosed by other criteria as having pancreatitis and continuing to have pain should undergo ERCP.
Long term mortality after vagotomy and drainage

P C H Watt, C C Patterson, AND T L Kennedy (Departments of Surgery and Medical Statistics, The Queen’s University of Belfast) Long term survival after gastrectomy is known to be reduced due mainly to smoking related disease. The significance of postgastrectomy cancer is controversial. Little is known of the long term survival after vagotomy and drainage (V+D).

We examined the mortality in 735 patients (576 men, 159 women) who had vagotomy and drainage procedures for duodenal ulcer in one hospital between 1957 and 1967 and compared it with expected age and sex specific mortality rates from the Registrar General’s reports for Northern Ireland. On 1 September 1982, 430 were still alive. 281 were dead, and 24 were lost to follow up. The expected number of deaths in the group was only 184 (p<0.0001).

Cause specific death rates were examined using death certificate information. Lung cancer was the cause of death in 46 patients but was expected in only 13, giving an observed to expected ratio of 3.5 (p<0.0001). Deaths from all smoking related diseases were 1.4 times more common in the V+D patients than expected (p<0.0001). Gastric cancer was the cause of death in 16 patients and was expected in only five, giving an observed to expected ratio of 3.3 (p<0.0001).

It was concluded that after V+D there is marked increase in mortality due to both smoking related diseases and gastric cancer.

Diarrhoea in acquired immune deficiency syndrome (AIDS)

C Bories, M Salmeron, Y Le Charpentier, B Messing, A Galan, J C Ramraud, AND R Modigliani (Gastroenterology and Pathology Department, Hopital Saint-Lazare, Saint-Denis, Paris Cedex 10, France) Chronic diarrhoea is frequent in AIDS but has been poorly investigated as yet. We report here four male AIDS patients who underwent complete digestive investigations. All patients had at least three opportunistic infections, a profound cellular immune deficiency, and a low OKT4/OKT8 lymphocyte ratio (<0.08; n=2-3). Diarrhoea was a presenting symptom in all subjects; in three of them it was watery (daily stool outputs exceeding frequently 11 and not influenced by fasting). Xylose and vitamin B12 were frankly malabsorbed in all cases; steatorrhoea (17 and 24 g/24 h) was found in the two patients who could ingest significant amounts of fat; faecal l-antitrypsin clearance was increased (45 to 112 ml/24 h; N<15) in three subjects. Search for pathogens in stools, jejunal fluid, and gut biopsy specimens (optical and electron microscopy) showed Cryptosporidium (C) in two cases, Isospora belli (IB) in one case, and in the last case Microsporidians (M) (genus still undescribed) and Giardia; Candida albicans was present in three patients; otherwise there was partial villous atrophy and slight inflammatory infiltrate of the duodenojejunal mucosa. In one case with C, the slow marker intestinal perfusion technique showed a profuse fluid secretion in the duodenum and proximal jejunum, with water and ion reabsorption.
in the more distal small intestine and the colon. All patients needed prolonged total parenteral nutrition. C and M could not be eradicated despite multiple drug trials. *Isospora belli* was transiently cured by sulphadiazine-pyrimethamine; CA and G were eradicated without change in diarrhoea. Only one patient is presently at home; two still need TPN and one died after six months of TPN.

F4

**Colonic crypt cell production rate is faster in the relapse, compared with the remission phase, of ulcerative colitis**

A ALLAN, T ROSSER, J B BRISTOL, AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol)

Existing studies of colonic epithelial cell kinetics in patients with ulcerative colitis rely on static methods and give discrepant results. We report the measurement of crypt cell production rate (CCPR) using stathmokinetic methods in rectal biopsy specimens maintained in organ culture. Rectal biopsy specimens were obtained from patients with ulcerative colitis and from patients with a normal rectum.

Organ culture of biopsies was carried out for 16 hours followed by a further three hours over vincristine containing medium. Electron microscopy revealed good preservation of histological architecture during culture. Vincristine arrested dividing cells in metaphase and after crypt microdissection these metaphase figures were counted to derive the CCPR.

Linear accumulation of metaphase figures by cultured biopsies was observed, p<0-001. Optimal doses of vincristine to induce metaphase arrest in normal and colitic mucosa were established. Mucosa from colitic patients in histological relapse showed a faster CCPR (14.2±2SE, 0.78 cells/h, n=8) than mucosa from colitic patients in remission (CCPR 9.78±SE 0.48 cells/h, n=14, p<0-01). The CCPR of colitic patients in remission was not significantly faster than the CCPR of patients with histologically normal mucosa (CCPR 8.52±SE 0.36, n=14, p<0-1). These findings are at variance with previous results founded on static methods.

F5

**Audit of a stomatherapy service**

R P PHILPWS, W K PRINGE, AND M R B KEIGHLEY (Department of Surgery, General Hospital, Birmingham) We have analysed the activities of a stomatherapy service in one hospital over three years (1980 to 1982). The service is used by six general surgeons, but only two specialise in inflammatory bowel disease.

Two hundred and seventy-six colostomies were constructed, 72% of patients had malignant disease, 17% were performed as emergency operations, and 51% were temporary stomas. Only 45% of the colostomy patients were counselled before operation. In surviving patients (243, 88%), 11% received no regular follow up. Complications were recorded in 60 surviving patients (25%): skin excoriation 8%, leakage 7%, sepsis 8%, hernia 5%, prolapse 2%, retraction 2%, stenosis 1%, infarction 1%, and bleeding 1%. Only 25 of these patients (10%), however, required surgical refashioning.

One hundred and eighty-four ileostomies were constructed, 52% of the patients had ulcerative colitis and 41% had Crohn’s disease. 13% were performed as emergency operations and only 11% were temporary. 83% of ileostomy patients received preoperative counselling. There were nine hospital deaths (5%) and 98% of the surviving patients (n=175) have attended for follow up. Complications occurred in 99 surviving patients (51%): skin excoriation 27%, flux 17%, sepsis 10%, leakage 9%, retraction 9%, hernia 4%, bleeding 4%, prolapse 3%, and stenosis 10%. Only 32 of these patients (18%), however, required surgical refashioning.

This audit indicates that far too few patients having colostomy are properly counselled before operation and that complications occur in at least half of all patients having ileostomy.

F6

**Is continuous sulphasalazine (SASP) necessary in patients with ulcerative colitis (UC)?**

R J DICKINSON, A KING, D G D WIGHT, G NEALE, AND J O HUNTER (Departments of Medical Gastroenterology and Pathology, Addenbrooke’s Hospital, Cambridge) Sulphasalazine is probably effective in patients with ulcerative colitis (UC) because it is anti-inflammatory. Sulphasalazine taken continuously therefore would maintain remission by lowering ‘background’ inflammation or by inhibiting minor relapse. The latter might also be achieved by ‘on demand’ SASP taken at the first symptoms of relapse. This hypothesis has been tested in a prospective trial. Patients with UC in remission who had been taking continuous SASP for at least six months were followed closely in a hospital clinic. By random allocation group 1 patients took SASP 2 g/day continuously and group 2 patients took SASP 3 g/day at the first symptoms of relapse. No other therapy was given. Rectal biopsies were taken at 0, four, eight, and 12 months and if relapse occurred (symptoms persisting for over one week). Rectal biopsies were scored ‘blind’ on a 0–9 point scale. The trial was completed at relapse or after 12 months. Twenty eight patients completed the trial. Of the 10 patients in group 1, three relapsed. Of the 18 patients in group 2, seven relapsed, five took SASP at some time during the trial but did not relapse, and six remained well off therapy. The mean rectal biopsy inflation score was 1.3 (n=28) at the start of the trial. The mean score at four months, eight months, and 12 months in those maintaining remission in groups 1 and 2 were 0–8 and 2–1 (NS), 0–6 and 2–8 (NS), and 2–0 and 1–6 (NS). The mean score in patients who relapsed was 6–2 (p<0.01). Persistent inflammation was not significantly greater in patients not on continuous SASP and ‘on demand’ SASP may be as effective as continuous therapy in the maintenance of remission in ulcerative colitis.

F7

**Postoperative bleeding and Latamoxef prophylaxis in surgery for colorectal and inflammatory bowel disease**

P J FABRICIUS, D L MORRIS, G OZUNER, B SCAMMEL, R N ALLAN, AND M R B KEIGHLEY (Gastroenterology Unit, General Hospital, Birmingham) Latamoxef is a broad spectrum antibiotic particularly suitable for surgical prophylaxis which we have now used in 177 patients, though latterly we suspected that it might be associated with an increased incidence of postoperative bleeding.

Of 102 patients undergoing surgery for colorectal disease there were 10 cases of serious postoperative bleeding. These patients received two doses of Latamoxef (2 g) with or without Metronidazole. There were only five episodes of bleeding after 286 comparable operations performed in the preceding three years when other antibiotics were used (p<0.01). Serial prothrombin times were measured in 16 of the 102 patients and of these seven had pro-
longed prothrombin times in excess of five seconds compared with preoperative levels.

Of 52 patients undergoing surgery for inflammatory bowel disease six cases of serious postoperative bleeding were observed. All patients received Latamoxef for five days (6 g/day) with three doses of Metronidazole (500 mg intravenously) over 24 hours. We observed only one bleeding episode in the preceding 25 consecutive operations when other antibiotics were used. Eleven of the 52 patients had serial prothrombin times of whom eight had prothrombin times at least five seconds longer than preoperative values.

Recently 25 surgical patients with colorectal disease were given two doses of Latamoxef (2 g) together with vitamin K 10 mg intravenously. Despite this serious bleeding was observed in four patients and prolonged prothrombin times in two.

We conclude that Latamoxef causes serious postoperative bleeding in some patients which cannot always be prevented by the addition of vitamin K.

F8 Rectal function after pelvic irradiation

J S Varma and A N Smith (University Department of Surgery, Western General Hospital, Edinburgh) Radiotherapy is being increasingly applied to malignant disease of the prostate, bladder, and cervix. Varying degrees of damage to the rectum are accompanied by symptoms such as frequency, urgency, and faecal incontinence.

Rectal function has been compared in controls and in symptomatic men (n=10) who had received external beam radiotherapy for prostatic carcinoma two to five years previously. A proctometrogram was obtained by infusing a highly compliant rectal balloon at a constant rate (67 ml s⁻¹ min⁻¹) and monitoring pressure by a microtransducer. Volumes (V ml) and pressures (Pcm H₂O) were recorded at threshold and constant sensation and maximal tolerance. Rectal compliance

\[
\frac{\Delta V}{\Delta P}, \text{ ml/cm H}_2\text{O}
\]

was calculated on the linear position of the curve.

There is a significant reduction in rectal volume in the irradiated group compared with controls (threshold sensation 96±23 SEM vs 224±31, p<0.01; constant sensation 122±27 vs 303±23, p<0.001; maximum tolerable volume 224±30 vs 493±25, p<0.001). Rectal compliance was also significantly reduced (2.5±0.4 vs 9.2±0.5, p<0.001). Comparable pressure measurements showed no significant difference.

These results explain many of the symptoms of chronic radiation proctitis. Reduction in volume and compliance is not always obvious radiologically but sigmoidoscopy may give some indication of the damage. The proctometrogram gives a quantitative assessment and may be of value as a prognostic indicator.

F9 High frequency of adenomatous polyps in ulcerative colitis

G C Sturino, R D'Inca, A Martin, G Gurrerii, A Cucchietto, and R Naccarato (Ca’ Foscari University of Venice, Italy) Polyps were observed in ulcerative colitis (UC): they are generally considered inflammatory without premalignant significance, but an unknown proportion of them can be adenomatous. We studied 157 patients (76 women, 81 men, aged 8–70 years) with UC in order to assess the frequency of adenomatous polyps (AP). Two hundred and twenty-four colonscopies were performed showing pancolitis in 72 patients and left sided colitis in 85. The duration of the disease was more than seven years in 37 patients, more than one and less than seven years in 64, and less than one year in 36. We found and removed 15 suspicious polyps – that is, those pedunculated or with a base larger than 0.5 cm or with an irregular surface or with a reddish colour. Eleven of these turned out to be adenomatous (seven tubular, one villous, three mixed) while four were inflammatory. Eight polyps were localised in the left colon and three more proximally. Four patients with AP were under 40 years old. No relationship was found between the duration or the extension of the disease and the presence of AP. Out of a total of 11 cases of moderate or severe dysplasia, six had an AP. In conclusion: (1) we found a high frequency (7%) of AP in UC; (2) dysplasia is frequently associated with AP; (3) AP are frequent also in relatively young patients but there is no correlation with duration and extension of the disease; (4) we suggest that colonoscopy should be used in the follow up of patients with UC and every suspicious lesion should be removed and examined histologically.

F10 Eye lesions in inflammatory bowel disease

A A Santost, E Areias, F Queirado, L M Serra, and J P Correia (Department of Medicine 2 and Department of Ophthalmology, University Hospital Santa Maria Center of Gastroenterology, Lisbon, Portugal) A prospective study was designed to elucidate the prevalence and evolution of eye lesions in IBD. Sixty seven patients were seen (34 with ulcerative colitis) and 33 with Crohn’s disease, with a total of 100 examinations (47 in UC and 53 in CD). Patients age ranged between 14–74 years in UC and 10–62 years in CD. Activity of IBD was measured by a modification of Best et al activity index. Eye complaints were registered only in three patients. Correlations between the activity of intestinal disease and the ocular lesions were analysed.

In active UC (11 observations) one case of uveitis, four keratoconjunctivitis sicca, two reduced Schirmer’s test, three non-specific lesions, and one normal were found. In non-active UC (36 observations) there was also one uveitis, 11 keratoconjunctivitis sicca, 12 reduced Schirmer’s test, three non-specific lesions, and nine normal observations. In active CD (14 examinations) four had uveitis, three keratoconjunctivitis sicca, three reduced Schirmer’s test, one non-specific lesions, and three no alteration. In non-active CD (39 examinations) three had uveitis, six keratoconjunctivitis sicca, eight reduced Schirmer’s test, eight non-specific lesions, and 14 were normal.

We conclude that eye lesions seem more frequent in UC (65.8%) than in CD (47.1%) but no difference was found between active (63.6%) and non-active (66.6%) UC. On the other hand in CD, eye lesions were more frequent in active disease (71.4%) than in non-active (43.5%).

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F11 Angelchik antireflux prostheses: postoperative clinical and objective assessment at 12 months

R M Weaver and J G Temple The Queen Elizabeth Hospital, Birmingham
The Angelchik prosthesis was inserted into 23 patients with intractable gastro-oesophageal reflux.

Postoperative clinical assessment showed that of 21 patients at three months and 17 patients at 12 months available for follow up, 17, and 15 respectively were asymptomatic or had very mild symptoms. Two prostheses disrupted and were replaced. Two further prostheses migrated into the chest and angulated causing dysphagia, for which further surgery was necessary.

Manometric and overnight pH studies were performed preoperatively in 19 patients. These were repeated in 17 patients after three months and 10 patients after 12 months. Results were analysed using the t test for paired comparisons.

The mean percentage of time that intra-oesophageal pH was <4 fell significantly from 37.6% (range 2.7-92%) preoperatively, to 10.3% (range 0-39.7%) at three months, and 8.34% (range 0-64.5%) at 12 months (p<0.01). Mean lower oesophageal barrier pressure rose significantly from 1.41 mm Hg (range 0-6.0 mm Hg) to 6.48 mm Hg (range 0-15.3 mm Hg) at three months, and 9.06 mm Hg (range 1.9-18.6 mm Hg) at 12 months (p<0.01).

These results suggest that the Angelchik prosthesis gives good and continued symptomatic relief with significant reduction in acid reflux and improvement in function of the lower oesophageal sphincter.

**F12**

**Histological and histochemical changes in the columnar lined (Barrett’s) oesophagus**

JANE E PATTERSON, D W DAY, AND C J STODDARD (Departments of Surgery and Pathology, University of Liverpool, Liverpool) A columnar lined oesophagus (CLO) is an acquired condition which predisposes to the development of an oesophageal adenocarcinoma. Patients with intestinal type columnar metaplasia (IM) may be at greatest risk. We have studied the histological and histochemical changes in the oesophageal epithelium and their incidences in patients with a CLO.

Over a 26 month period upper alimentary endoscopies were performed in 2409 patients. Oesophagitis was present in 438 patients (18.2%) of whom 390 (89.0%) had a squamous lined oesophagus and 48 (11.0%) a CLO. Five of the patients with a CLO (10.4%) had a coexistent oesophageal adenocarcinoma. Multiple endoscopic oesophageal biopsies were taken for histological and mucin histochemical evaluation. Intestinal type columnar metaplasia was observed in 41 of the 48 patients with CLO (85%) being present focally in 21, predominantly in 18 (37.5%), and extensively in two (4.2%).

Of the patients with IM 61% had IM of ‘incomplete’ type with sulphomucin production. Seven patients (six with IM) showed dysplasia of the columnar epithelium and three had an associated adenocarcinoma. Four of the five patients with carcinoma had IM of the ‘incomplete’ type.

These results show that IM is common in patients with a CLO. Patients with an incomplete type of IM, especially in the presence of dysplasia, may be particularly at risk of developing an oesophageal adenocarcinoma.

**F13**

**Significance of oesophageal motility disorders**

J BANCEWICZ, H OSUGI (INTRODUCED BY M H IRVING) (Department of Surgery, Hope Hospital (University of Manchester School of Medicine), Salford) Oesophageal motility disorders have recently attracted attention, particularly as a cause of chest pain. The nature of these disorders and their treatment, however, is still uncertain.

Between June 1979 and June 1982 oesophageal manometry was performed on 202 patients with symptoms of chest pain, abdominal pain, or dysphagia. Most also had a Bernstein test and prolonged (12 or 24 hours) recording of oesophageal pH. All but two had prior endoscopy or radiology and 139 had both investigations with negative results in 51. Most of the remainder had minor abnormalities of uncertain significance.

Oesophageal dysmotility was found in 142 patients (70% of total) including 45 (38%) of those with negative radiology and endoscopy. Ninety seven (68%) of those with dysmotility also had significant gastrointestinal reflux and 55 came to surgery (51 Nissen: four Roux-en-Y loop). Five patients without reflux had surgery: two Heller’s procedure: three extended myotomy for diffuse spasm.

After surgery for reflux 25 of 29 patients (86%) with symptoms clearly attributable to the motility disorder – for example, dysphagia or ‘angial’ pain – were improved. This suggests that these disorders were secondary to reflux.

Oesophageal manometry often reveals abnormalities not demonstrable by radiology or endoscopy. Prolonged recording of oesophageal pH; however, is a more relevant investigation for severe symptoms as reflux can be corrected by surgery with good results. Primary motility disorders are less common and do not usually produce severe symptoms.

**F14**

**Gastro-oesophageal scintiscanning in the assessment of gastro-oesophageal reflux**

M M MUGHAL, M OGDEN, M MARPLES, J BANCEWICZ (INTRODUCED BY M H IRVING) (Department of Surgery, Hope Hospital (University of Manchester School of Medicine), Salford) Upper gastrointestinal endoscopy and barium studies are often misleading in patients with symptoms of gastro-oesophageal reflux. In such cases, 24 hour pH monitoring may be required to provide a definitive answer. Whereas pH studies are uncomfortable, gastro-oesophageal scintiscanning (GOS) is both rapid and non-invasive. It is reported to be more sensitive than barium studies and endoscopy, as well as being semi-quantitative.

The use of GOS was studied in 17 asymptomatic volunteers and in 31 patients with symptoms of gastro-oesophageal reflux. All patients also underwent endoscopy, barium meal, and 24 hour pH monitoring. The results of GOS were expressed as a reflux index (RI).

The upper limit of normal RI was determined to be 7.2 by adding two standard deviations to the mean RI of 17 asymptomatic volunteers. The results of 24 hour pH monitoring were expressed as DeMeester scores and endoscopy was considered positive on detection of macroscopic oesophagitis or free reflux.

The sensitivity and specificity of GOS was 36% and 82%, of endoscopy 43% and 71%, and of barium meal 29% and 65% respectively. The correlation between RI and DeMeester score was r=0.55 (p=0.005).

Gastro-oesophageal scintiscanning is a highly specific test for gastro-oesophageal reflux which may be useful when the diagnosis is still in doubt after endoscopy. It is not sensitive enough to either replace endoscopy or to be of use as a screening test.
**F15**

**Teeth and oesophageal stricture**

D G Maxton, S I Grainger, C C Ainley, and R P H Thompson (Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London)

The aetiology of benign oesophageal strictures is unknown, although hiatus hernia and oesophageal reflux are important. We noted that patients with benign oesophageal strictures are often edentulous and examined the relationship between dentition and oesophageal disease in our endoscopy population. The age, diagnosis, and dentition of all patients attending for endoscopy were recorded. Ages were divided into under 30, 30-44, 45-59, over 60, and pathological groups compared.

Of patients over the age of 60, 33 of 37 with benign oesophageal strictures were edentulous compared with 116 of 169 patients with a normal endoscopy (\(p<0.02\), \(\chi^2=6.4\)). There was no significant correlation with dental state in the few patients aged under 60 with strictures. The presence of oesophagitis or hiatus hernia at endoscopy was not associated with either partial or total lack of teeth in any age group.

Absence of teeth is associated with benign oesophageal strictures in the over 60s, but not with hiatus hernia or oesophagitis. The diet of the edentulous, however, will be towards more liquid foods that do not dilate the inflamed oesophagus, while a prolonged reduced volume of saliva, which is known to predispose to early caries and tooth loss, may not adequately neutralise refluxing acid. Both mechanisms may contribute to the development of oesophageal stricture.

We conclude that patients with benign oesophageal disease should be encouraged to use their dentures to eat solid food.

**F16**

**Effect of cimetidine and alginic treatment on oesophageal pH and bile acid concentrations in reflux oesophagitis**

J R Bennett, M R Smith, and G K Buckton (Department of Biochemistry, University of Hull, and Gastro-intestinal Unit, Hull Royal Infirmary, Hull) A double blind trial was performed to evaluate the combination of cimetidine with alginic acid (Gaviscon) in patients with acid gastro-oesophageal reflux (GOR). Forty patients with symptomatic acid GOR shown by oesophageal pH measurement were randomly allocated to receive alginic and placebo or alginic and cimetidine 1 g daily, for six weeks. Bile acid concentrations were measured in fasting gastric juice and in oesophageal fluid aspirated at the same time as 15 hour oesophageal pH measurements before and in the sixth week of the trial.

For intra-oesophageal bile acid concentrations in the post-evening meal samples were significantly lower (\(p=0.06\)) in the alginic/placebo treated group (n=9) when compared with the alginic/cimetidine treated group (n=9). There was a significant difference after treatment with alginic/cimetidine in the number of reflux episodes (\(p=0.002\)) and percentage time pH<5 (\(p=0.014\)). There was also a significant difference after both treatments in the percentage time pH<4 (\(p=0.036\) for alginic/placebo and \(p=0.025\) for alginic/cimetidine). Changes were compared between the two groups, however, no significant differences were observed.

These results confirm the effectiveness of both alginic antacid and cimetidine in reducing acid GOR. Alginic antacid alone also reduced postprandial oesophageal bile acid concentrations. The failure to reduce postprandial oesophageal bile acids by combined alginic/cimetidine therapy may be explained by a reduction in the gastric juice volume response to meals causing a relative rise in gastric bile acid concentrations.

**F17**

**Bile acid levels in stomach and oesophagus of patients with acid gastro-oesophageal reflux**

M R Smith, G K Buckton, and J R Bennett (Department of Biochemistry, University of Hull, and Gastro-intestinal Unit, Hull Royal Infirmary, Hull) Bile acids have been implicated as one of the causative agents of reflux oesophagitis. Previous studies have utilised either bile acid perfusion of the oesophagus in experimental animals or man, or surgery designed to increase oesophageal bile reflux in animals, such as duodenal-oesophageal anastomosis or cholecystogastrostomy. There has been no study of bile acid concentrations in the oesophageal fluid of humans with clinically significant acid gastro-oesophageal reflux (AGOR). We measured total bile acid concentration (TBC) by an enzyme-fluorometric method in the fasting gastric and oesophageal fluid of 40 patients with acid gastro-oesophageal reflux. Oesophageal samples were aspirated in four hour collections for 15 hours with simultaneous intraluminal pH recording. The mean fasting gastric TBC was 55.6 \(\mu\)M ± 161.5 (n=37) with a median of 7.0 \(\mu\)M (range 0-940 \(\mu\)M). Oesophageal TBCs ranged from 0-100 \(\mu\)M with bile acids most frequently detected in the post-meal samples (n=38, x=8.9 \(\mu\)M ± 10, median 8.0 \(\mu\)M, range 0-40 \(\mu\)M). The concentrations of bile acids found in this study differ considerably in magnitude from those used in experimental studies. Perfusion experiments have used 2.5 to 10 mM (2500-10 000 \(\mu\)M) bile acid concentrations and the level of bile acids in gall bladder bile is also of this magnitude. Thus, although there is evidence that bile acids may be of significance in the development of oesophagitis in man, the experimental studies have clearly used concentrations of bile acids much higher than those in the oesophageal fluid of patients with acid gastro-oesophageal reflux.

**F18**

**Ambulatory pH monitoring in the distal oesophagus using radiotelemetry – three year results**

D F Evans, F J Branikli, J Jones, and J D Hardcastle (Department of Surgery, University Hospital, Nottingham) Twenty four hour ambulatory monitoring of oesophageal pH has proved to be a sensitive test in the evaluation of gastro-oesophageal reflux (GOR) in oesophagitis when compared with equivalent tests performed in hospital. A pH sensitive radiotelemetry capsule and portable receiving system have been used to investigate patients with symptoms of GOR to assess the presence and degree of reflux. In the last three years we have performed 203 tests on 90 patients with symptoms of GOR and 30 normal subjects. Twenty nine (12%) of the tests failed due to either technical reasons or capsule intolerance but after repeat studies left a total of 183 (90%) for analysis. Abnormal reflux was defined as those episodes falling to below pH5 that occurred more frequently than 1.7 episodes/hour and of greater cumulative duration than 6.6 min/h. This limit being determined by the highest value (95% confidence limit) seen in our normal group. Using this criteria of a total of 90 patients, 36 (40%) fell within the normal range, 16 (18%) showed moderate reflux and 37 (41%) were defined as having...
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severe reflux. Twenty four of the patients studied were recommended for antireflux surgery and at 30 months after surgery only two (8%) had any further symptoms. Ambulatory monitoring of oesophageal pH is a useful test in the discrimination of gastro-oesophageal reflux from pain due to other causes and has proved helpful in the management of patients with oesophagitis by assessing the benefits of medication and identifying those who may benefit most from antireflux surgery.

F19
Early detection of gastrointestinal cancer – is computer aided analysis necessary?
J.F. Dombal, J. S. Wenham, M. R. Kotwal, and J. M. Brown
(Clinical Information Science Group, University Department of Surgery, St James Hospital, Leeds) At previous BSG meetings, studies have suggested that computer aided analysis may be of value in early detection of GI cancer. However, others have suggested that improved detection rates are due to improved clinical practice, not to computer analysis; and that diagnostic difficulty increases with age.

In this study, 468 patients were studied in five health centres. Mean age was 60 years, and all presented with two weeks of ‘new’ gastrointestinal symptoms to their general practitioner. A detailed interview was carried out by a nursing sister using a structured questionnaire. Subsequently the full patient case record was reviewed by a clinician, and the nurse’s interview data analysed by computer.

Of the 468 patients, 27 eventually proved to have cancer. The clinician’s analysis detected 17 of these (with 125 false positives). Computer aided analysis of the nurse’s interview data detected 22 cancers (with 75 false positives). Replacement of the computer analysis by a scoring system (based on likelihood ratios) resulted in a further marginal improvement. 23 out of 27 cancer cases being detected at the expense of only 61 false positives.

Attempts to use a recently published ‘simple’ scoring system (Mann et al., 1983), however, were unsuccessful, with unacceptable false positive and false negative rates (whatever cut off point was adopted).

These results strongly suggest that GI cancer can be detected earlier than at present; and that this detection is dependent upon detailed careful interview together with multivariate analysis of all symptoms. The results also suggest, however, that such an analysis need not necessarily be computer based.

F20
Recent changes in perforated peptic ulcer
R. M. Watkins, A. R. Dennison, and J. Collin
(Nuffield Department of Surgery, John Radcliffe Hospital, Headington, Oxford) There has been a marked fall in the number of elective operations for peptic ulceration since 1976. Our aim was to assess recent changes in the incidence and pattern of perforated peptic ulcer.

An 18-year review of perforated peptic ulcers in Oxford is presented. The incidence in 1965–76 was 8.4 per 100,000 population compared with 6.9 per 100,000 in 1977–82. There was a significant fall in the male:female ratio from 1965–70 to 1971–76 (4.9:1 to 2.1:1, p < 0.001) and a further fall 1977–82 (1.9:1). The ratio of duodenal to gastric ulcers during the periods 1965–70, 1971–76, and 1977–82 were respectively 6:9:1, 6:4:1, and 8:2:1.

One hundred and sixty six patients (mean age 60.9 years) treated 1977–82 were reviewed in detail. The overall mortality was 13% (22% for gastric ulcers and 11% for duodenal perforations). One hundred and eight patients had an acute ulcer and 52 a chronic ulcer of whom eight were taking cimetidine. Twenty six per cent of patients were taking non-steroidal anti-inflammatory drugs at the time of perforation. Six patients had previously had a perforation and 12 a haematemesis. Nine patients (5.4%) were treated without operation, of whom seven died. Ninety four patients (56.6%) had simple closure of the perforation and 38.0% definite ulcer surgery (58 vagotomy and drainage, five gastrectomy).

We conclude that marked changes have occurred in the sex incidence and type of perforated peptic ulcers in the last two decades. Two thirds of perforations are now of acute ulcers and hence are unlikely to be prevented by improved therapy for chronic peptic ulceration.

F21
Inhibition of early and late postgastrectomy dumping by somatostatin infusion
R. G. Long, T. E. Adrian, and S. R. Bloom
(Gastrointestinal Laboratory, St Thomas’s Hospital, London, and Department of Medicine, Royal Postgraduate Medical School, London) Somatostatin (SRIF) inhibits small intestinal secretion and the release of many pancreatic and gastrointestinal hormones. As such factors have been implicated in the pathogenesis of dumping, we induced the symptoms of early dumping in six patients with either 50 or 100 g oral glucose as a 25% solution. Intravenous SRIF (Serono UK Ltd, 70 pmol/kg/min) was infused on a subsequent day. With SRIF infusion, the symptoms of early dumping were abolished or reduced in five of the six patients and there was a significant reduction at 30 minutes in the pulse rate (187 ± 4 vs 67 ± 3 beats/min, p < 0.005), the packed cell volume (PCV) (0.46 ± 0.01 vs 0.43 ± 0.01, p < 0.005), and the serum glucose (10.4 ± 1.7 vs 7.8 ± 1.2 mmol/l, p < 0.05). At 30 minutes, the mean plasma levels of vasoactive intestinal polypeptide, neurotensin, enteroglucagon, insulin, gastrin, pancreatic polypeptide, gastric inhibitory polypeptide, and motilin were also reduced during SRIF. The serum glucose fell to a nadir of 3.2 mmol/l or less in five of the six patients on the control day, but during SRIF, later mean glucose values were higher – for example, at 120 min. 4.8 ± 1.8 vs 14.7 ± 1.0 mmol/l, p < 0.005 – and the mean insulin response was reduced. Thus SRIF abolishes early dumping symptoms, the tachycardia, the rise in PCV, and the early glucose peak probably by reducing hormone and small intestinal secretion; it also prevents reactive hypoglycaemia by blocking insulin release.
minutes after eating a snack (toasted sandwich and an apple). Blood for alcohol estimation was collected at 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, and 120 minutes. Alcohol estimation was by gas liquid chromatography. Results confirmed that partially gastrectomised patients achieve a higher alcohol peak (mean level = 8.8 mmol/l at 25 min = 41 mg/100 ml) than normal subjects (7.7 mmol/l at 25 min = 35 mg/100 ml). After a snack, however, patients achieved a higher peak more rapidly (9.5 mmol/l = 44 mg/100 ml at 15 min) than normal subjects, in whom the peak was lower and delayed (7.0 mmol/l at 30 min = 32 mg/100 ml). The results suggest that gastrectomised patients may be even more vulnerable to intoxication after combining eating and drinking. While the differences found were not statistically significant, the trend shown appears to be clinically important; one of the patients achieved a peak blood alcohol level above the legal limit for driving (17 mmol/l = 80 mg/100 ml) only when the 50 ml gin was ingested after eating a snack.

HEPATO-PANCREATIC
F23–34

F23
Endoscopic manometric evaluation of exogenous cholecystokinin octapeptide on the pancreatic and biliary sphincters in man

D. L. CARR-LOCKE and S. BENTLEY (Gastroenterology Unit, Leicester Royal Infirmary, Leicester) Cholecystokinin is assumed to have a physiological action on the sphincter of Oddi in man. An endoscopic manometric method, using a pneumohydraulic capillary infusion system and a perfused triple lumen catheter with distal openings spaced 10 mm apart, was used to study 18 subjects during duodenoscopy under midazolam sedation. Ten were asymptomatic subjects after previous cholecystectomy and in these common bile duct (CBD) and bile duct sphincter (BDS) recordings were obtained. Eight were asymptomatic after previous endoscopic sphincterotomy and provided pancreatic duct (PD) and pancreatic duct sphincter (PDS) recordings. Ductal and sphincteric pressures were measured in the basal state and during stepped increasing doses of exogenous cholecystokinin octapeptide (CCK-OP, Kinevac, Squibb) infused at 2.5, 5, 10, 20, 40 and 80 ng/kg/h. All basal recordings were within previously established normal ranges. Pancreatic duct pressure fell from 16.7 ± 2.4 mmHg (mean ± SE) to 11.7 ± 2.9 mmHg and CBD pressure fell from 3.3 ± 1.3 mmHg to 0 at 10 ng/kg/h and greater and were completely abolished at 80 ng/kg/h. As with an intravenous bolus of 20 ng/kg, Pancreatic duct sphincter and BDS phasic pressures were significantly decreased with CCK-OP infusions of 20 and 40 ng/kg/h and were unrecordable at 80 ng/kg/h.

We conclude that CCK-OP has a potent relaxing effect on the PDS and BDS zones at physiological and pharmacological levels.

F24
C4 genotype in children with autoimmune chronic active hepatitis (CAH)

D. VERGANI, L. WELLS, E. T. DAVIS, G. MIELI-VERGANI, AND A. P. MOWAT (Departments of Immunology and Child Health, King’s College Hospital, London and National Blood Transfusion Service, Birmingham) We have shown that children with autoimmune CAH have genetically determined low levels of the complement component C4 and we suggested that this is a predisposing factor as similar findings are associated with autoimmune disorders in experimental animals. C4 is coded for by two separate loci situated in the major histocompatibility region of chromosome 6. Twelve or more allotypes including ‘null’ variants have been described at each of these loci. To investigate whether C4 deficiency in CAH is associated with specific alleles, we have studied 11 such children and their parents. C4 phenotype was determined by immunofixation of electrophoresed desialated samples. C4 serum levels by nephelometry and C4 function by haemolytic assay. At least one null allotype was found in nine of 10 CAH patients whose genotype was deduced. eight having low C4 concentration or function. The genotype was known in 15 parents: 12 had null variants, six of whom had low C4 levels. Null allotypes were present in 42 of 100 blood donors significantly less frequently than in the patients ($X^2$ = 8.4, p < 0.005) or their parents ($X^2$ = 7.5, p = 0.005). This study shows an association between deficient C4 and null variants of C4 in CAH but its pathogenic significance remains to be established.

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F25
Value of serum liver specific protein antibodies as a predictor of relapse in autoimmune chronic active hepatitis

J. E. HEGARTY, C. MCSORLEY, B. MCFARLANE, I. G. MCFARLANE, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital, London) As previous studies have shown that conventional biochemical, immunological and histological indices are of no value in predicting the outcome of corticosteroid withdrawal in patients with autoimmune chronic active hepatitis (CAH), we have prospectively evaluated the use of serum liver specific protein antibodies (anti-LSP), measured by radioimmunossay, as a predictor of outcome in a group of patients with CAH who were participating in a trial of treatment withdrawal.

The 22 patients in whom corticosteroids were withdrawn over a 12 week period had been in clinical, biochemical (AST < 40 IU/l) and histological (chronic persistent hepatitis) remission for one to nine years, and of these 16 had a relapse of disease, as defined by an increase in AST > 120 IU/l and piecemeal necrosis on liver biopsy. Of the 22 patients, eight were anti-LSP positive (titre 1/470 to 1/930) at entry into the trial, and all subsequently relapsed. Of the 14 patients who were initially anti-LSP negative, six achieved sustained remission and remained anti-LSP negative. In seven of the eight remaining patients, anti-LSP antibodies developed during the course of treatment withdrawal. their appearance coinciding with the rise in AST by three to 10 weeks, while in one patient relapse coincided with the appearance of anti-LSP.

The results indicate that serum LSP antibodies are a sensitive predictor of outcome in patients with autoimmune CAH in whom treatment is being withdrawn.

F26
Bone loss in corticosteroid treated patients with HBsAg negative chronic active hepatitis (CAH)

A. J. STELLON, A. DAVIES, AND R. S. WILLIAMS (Liver Unit, King’s College Hospital, London) Cortical bone loss has been detected in 25% of corticosteroid treated patients, with parenchymal liver disease, using metacarpal morphometry. This method may not reflect bone changes at other sites, however, and correlates poorly with trabecular bone loss. This present study evaluates the degree of cortical and
The daily implication of corticosteroids in biochemical, histological, and systemic disease, was undertaken in 50 patients with chronic liver disease, or previous hepatic or bile duct exploration. The study group finally consisted of 47 patients with chronic pancreatitis, 12 with acute pancreatitis, seven with pancreatic cancer and eight with spastic colon syndrome. Cholangiograms were assessed for roughening, irregularity and strictures of the extra-hepatic duct, and also irregularity, roughening, strictures, pruning or nicking of the intrahepatic biliary tree. The frequencies of the various abnormalities in the different groups were compared using Fisher’s exact test. Cholangiographic abnormalities were found in 83% of patients with pancreatic disease (p<0.001 compared with controls).

abnormalities were found in 83%, 75% and 100% of patients with chronic pancreatitis, acute pancreatitis or pancreatic cancer respectively. Excluding patients with constricted distal common bile ducts, 70% with chronic pancreatitis, 55% with acute pancreatitis and 67% with pancreatic cancer displayed cholangiographic abnormalities. Abnormalities of the intrahepatic biliary tree accompany pancreatic disease, and these are not solely due to compression of the intrapancreatic bile duct. The link between sclerosing cholangitis and pancreatic disease might lie at the level of the hepatocyte.

F27 Controlled trial of azathioprine withdrawal in HBsAg negative chronic active hepatitis

A J STELLON, J E HEGARTY, A L W F EDDLESTON, B PORTMANN, AND R WILLIAMS (Liver Unit, King's College Hospital, London) Although randomised placebo controlled clinical trials have established that azathioprine alone is of no value in the treatment of HBsAg negative chronic active hepatitis (CAH), it is nevertheless widely used in this disease in combination with corticosteroids on the basis that it exerts a steroid sparing effect. As such an effect implies that azathioprine is contributing to control of disease, a randomised controlled trial of azathioprine withdrawal was undertaken in 50 patients with CAH who were maintained in clinical, biochemical, and histological remission for prolonged periods (one to five years) on a combination of azathioprine (50-100 mg/ daily) and prednisolone (5-12.5 mg/daily). The group of 27 patients in whom azathioprine was discontinued was similar with respect to age, sex, duration of disease, and remission. previous treatment, presence of cirrhosis, autoantibody status and frequency of previous relapses to the 23 patients who remained on combination therapy. Over a median follow up period of 20 months, reactivation of disease, defined by a three fold increase in serum transaminase concentrations (>120 IU/l) and/or liver biopsies showing the histological features of CAH, occurred significantly more often in the azathioprine withdrawal group (seven of 27 versus one of 23; p<0.02, χ² analysis). The results of the study suggest that treatment measures should be instituted early in the course of the disease.

F28 Sclerosing-cholangitis-like changes in patients with pancreatic disease

R J L ANDERSON, F WARWICK, AND J M BRAGANZA (The University Department of Gastroenterology and the Radiology Department, Manchester Royal Infirmary, Manchester) While abnormal pancreatograms have been noted as an incidental finding in up to 50% of patients with sclerosing cholangitis, the frequency of abnormal intrahepatic bile ducts in patients with pancreatic disease is unknown. The recent finding of abnormal bile in patients with pancreatic disease prompted this retrospective analysis.

Retrograde cholangiograms of patients referred for pancreatic investigation were studied. When the diagnosis was doubtful or follow up inadequate patients were excluded, as were those known to have chronic liver disease, or previous sphincterotomy and bile duct exploration. The study group finally consisted of 47 patients with chronic pancreatitis, 12 with acute pancreatitis, seven with pancreatic cancer and eight with spastic colon syndrome. Cholangiograms were assessed for roughening, irregularity and strictures of the extra-hepatic duct, and also irregularity, roughening, strictures, pruning or nicking of the intrahepatic biliary tree. The frequencies of the various abnormalities in the different groups were compared using Fisher's exact test. Cholangiographic abnormalities were found in 83% of patients with pancreatic disease (p<0.001 compared with controls).
than at that three days (p<0.001). These results show that obstructive jaundice alters pulmonary metabolism of NA which increase with time. This abnormality may be associated with the altered responsiveness to sympathetic stimulation in these animal models. This study was supported by a Ministry of Health Grant, and the Ministry of Absorption.

F30
Role of cholecystokinin in the pancreatic exocrine response to intraluminal amino acids and fat

R S STUBBS AND B E STABLE (INTRODUCED BY L H BLUMGART) (VA Medical Center, West Los Angeles, California, USA) Controversy continues over the relative contribution of hormonal and neural mechanisms in producing the exocrine pancreatic response to ingested food. Using Proglumide, a drug recently shown to be a specific cholecystokinin (CCK)/gastrin receptor antagonist we have reevaluated the role of CCK in this process. Duplicate experiments were performed in each of five adult mongrel dogs prepared with chronic gastric and pancreatic fistulae. Dose response studies to intravenous octapeptide of CCK (CCK-OP), intravenous betahanechol, intraduodenal amino acids (Aminosyn\R) and intraduodenal fat emulsion (Liposyn\R) were conducted with and without simultaneous intravenous infusion of Proglumide 300 mg/kg/h. Ten minute pancreatic juice samples were analysed for protein, volume and bicarbonate outputs. Proglumide infusion competitively inhibited the pancreatic responses to intravenous CCK-OP but produced only minor and not significant inhibition of the responses to intravenous betahanechol. Almost total inhibition of all doses of intraduodenal amino acids and intraduodenal fat was observed from the infusion of Proglumide.

These results strongly suggest that cholecystokinin is indeed the major mediator of the intestinal phase of pancreatic enzyme secretion.

F31
Oral dissolution therapy – a valid option in management of biliary duct stones

W R ELLIS, K W SOMERVILLE, B H WHITTEN, T W BALFOUR, AND G D BELL (Department of Therapeutics, City Hospital, Nottingham) Reports of oral therapy for bile duct stones are few, but suggest less than 30% efficacy for chenodeoxycholic acid (CDCA); 50% success was recorded in the only trial of ursodeoxycholic acid (UDCA), but many patients withdrew because of persistent symptoms or complications. Our experience exceeds any previously published, comprising 31 patients (aged 31–83 years, mean 69 years, 24 cases over 60 years) each with one to nine radiolucent duct stones (4–22 mm, mean 10, 23 over 7 mm). Nineteen patients took Rowachol, a terpene preparation, eight (42%) achieving complete stone disappearance (CSD) in three to 48 months. Fifteen (including three of the above) took Rowachol with bile acid (11 CDCA, four UDCA) for three to 60 months; 11 (73%) achieved CSD within 18 months. Persistent symptoms or complications necessitated withdrawal in only four cases. Eight patients required hospital admission during treatment (two biliary colic, one obstructive jaundice, four cholangitis, one pancreatitis). All settled on conservative management, but the last died of intercurrent illness during recovery: the others continued treatment, two achieving CSD.

We conclude that Rowachol and bile acid combination treatment for choledocholithiasis is superior to bile acids used alone both in efficacy and symptom control. Oral dissolution therapy is a reasonably safe and effective alternative to surgery when endoscopic sphincterotomy is not feasible, or unattainable.

F32
Incidence and outcome of adenocarcinoma of the extrahepatic biliary tree

J B ANDERSON, M J COOPER, AND R C N WILLIAMSON (University Department of Surgery, Royal Infirmary, Bristol) Five year survival rates of 4–8% have been reported for adenocarcinoma of the extrahepatic biliary tree, with most studies emanating from North America. To determine the incidence and outcome of these tumours in Great Britain, the records of 243 consecutive patients with cancer of the biliary tree presenting over a 15 year period were reviewed. There were 87 patients with carcinoma of the gall bladder, 68 of whom were submitted to laparotomy with a 54% operative mortality; only five survived longer than one year with one long term (five year) survivor whose diagnosis was made incidentally on histological examination of a cholecystectomy specimen. Among 31 patients with carcinoma of the ampulla of Vater there was a 27% operative mortality, but 12 were alive at one year and three survived five years. Of 125 bile duct cancers 63 arose proximal to the cystic duct entry; seven of these patients obtained useful palliation by intubation and seven of eight survived resection, but none lived two years. Distal cholangiocarcinomas carried a similar dismal prognosis; resection was accompanied by a 75% operative mortality, with only three patients surviving for two years. For all carcinomas of the biliary tree there was a two year survival rate of 5% and a five year survival rate of 2%.

Modern imaging techniques should facilitate early and accurate diagnosis of these neoplasms. Referral to specialist centres might help to improve the survival and prognosis of these lethal cancers.

F33
Choledocholithiasis: discrepancies between ultrasonography and retrograde cholangiogram findings

M V TOBIN, I T GILMORE, AND G H R LAMB (Royal Liverpool Hospital, Prescot Street, Liverpool) While ultrasonography is of proven value in distinguishing medical and surgical causes of jaundice, with accuracy rates of up to 90%, it is important for clinicians to realise that it may be less successful in particular subgroups such as those with common bile duct stones. We have examined the results in 101 consecutive patients who later had a definitive retrograde cholangiogram performed. Of 26 with choledocholithiasis (31%) had a normal ultrasound, and in a further five ultrasound was technically unsatisfactory; in only 2/26 (8%) were stones detected and in 10/18 biliary dilatation correctly diagnosed. In eight patients with stones but no biliary dilatation, only two (25%) had abnormal ultrasound examinations. Overall, ultrasound examination correctly identified a normal biliary tree in 54/64 patients (84%) and distinguished dilated from nondilated ducts in 83%, confirming previous reports.

Thus, while the overall results are excellent, it should be appreciated that ultrasound examination of the biliary tree may be unreliable in choledocholithiasis, particularly when the biliary tree is not dilated as is the case in approximately 30% of patients. Retrograde cholangiography remains an important investigation when common bile duct stones are clinically suspected.
Comparison of cholecystography and ultrasonography for detection of gall stones

R P JAZRAWI, A E A JOSEPH, A G WILSON, AND T C NORTHFIELD (Departments of Radiology, Ultrasound and Medicine, St. George's Hospital Medical School, London) Ultrasoundography is a safe, simple, and sensitive method of diagnosing gall stones, but its accuracy relative to oral cholecystography is still a matter of controversy. We have therefore carried out a double blind comparison of (a) 102 consecutive patients whose symptoms suggested a diagnosis of gall stones. We also compared the two techniques for (b) diagnosis of complete gall stone dissolution in 71 patients undergoing bile acid therapy; and for (c) diagnosis for gall stone recurrence in 28 patients after a confirmed diagnosis of complete dissolution. In (a) oral cholecystogram showed gall stones in 22 patients, was judged normal in 76, and in four showed no opacification of the gall bladder. Ultrasonography showed gall stones in three of the 76 normal cholecystograms and in three of the four patients who failed to opacify, and in all six patients gall stones were found at surgery. It confirmed the presence of gall stones in 21 of the 22 with a positive oral cholecystogram, but not in one patient in whom the true diagnosis was not clarified by surgery. In (b) complete gall stone dissolution was diagnosed by oral cholecystogram in 31 patients, whereas ultrasound showed the persistence of gall stones in five of these patients. In three of the five, the ultrasound became negative following continued bile acid therapy. In (c) recurrence of gall stones was shown by ultrasound in six patients, whereas cholecystogram detected recurrence at the same time in only three of these patients. A repeat cholecystogram in the next three months confirmed recurrence of gall stones in all six of these patients. We conclude that ultrasonography provides a more sensitive method of diagnosing gall stones, and of monitoring progress during and after bile acid therapy.

F36
Screening of first degree relatives of patients with bowel cancer

N C ARMITAGE AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) There is evidence that first degree relatives of patients with bowel cancer have a three to four times increased risk of developing colorectal tumours. We have screened the families of patients under follow up after operation for colorectal cancer. A full family history was taken, including the names and addresses of all first degree relatives. These were contacted by letter and if agreeable were sent faecal occult blood tests. Those patients who returned tests that were found to be positive were investigated by flexible fibreoptic sigmoidoscopy and double contrast barium enema. A control group of age/sex matched subjects was identified from asymptomatic subjects at the time of entry into a population screening study.

Thirteen patients had no suitable living relatives, and the remaining 112 patients had 436 potentially contactable relatives of whom 267 were able to be contacted by post. Of those contacted, 155 (58%) replied to the first letter and were sent the tests. 120 (45%) completed the tests of which 11 (9.1%) were found to be positive. To date three adenomatous polyps have been identified in these patients. In the control group 104 (40%) individuals completed the tests, of which six (6%) were positive; in these one adenoma has been diagnosed.

A detection rate of nearly 3% of adenomas in first degree relatives of patients with colorectal cancer compared with 1% in a randomly selected asympotomatic population sample would appear consistent with an increased risk of neoplastic disease.

F37
Colorectal carcinoma in the first four decades

H C UMLEBY AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Colorectal carcinoma in young people is reported to be associated with a poor prognosis. We reviewed 85 patients aged 40 or less who presented over a 32 year period with colorectal carcinoma. The incidence was 2.5% of all patients with large bowel cancer (n=3426). Predisposing causes included familial polyposis (eight), panproctocolitis (ulcerative one, Crohn's one) and irradiation (one); four patients were pregnant. Symptoms and signs were the same as at all ages, yet seven patients had an avoidable delay in diagnosis of five to eight months. Twenty eight patients (33%) presented as emergencies: 12 with intestinal obstruction. Fifty nine per cent of tumours were Dukes' C, 31% poorly differentiated and 18% of the mucinous type. Overall five year survival rate was lower.
41% and after 'curative' resection in 61 (73%) was 59%. Survival was equivalent for elective and emergency cases and for mucinous, and non-mucinous carcinomas of moderate histological differentiation. Five year survival rates were poorer when the history was <3 months than >3 months (20% vs 45%, p=0.02) and for rectal and rectosigmoid tumours than colonic tumours (31% vs 50%; p=0.05). Four of five patients with involvement of adjacent viscera and four of six patients with resectable recurrence survived beyond 10 years after radical surgery.

Colorectal carcinoma in the first four decades reflects the disease of the usual older population. Any increase in unfavourable types or stages of the tumour seems to be balanced by greater tolerance to emergency operation. Radical resection of advanced primary disease and of local recurrence is well worthwhile and can be associated with long term survival.

F38 Diet preceding large bowel cancer: increased energy-to-fibre ratio

J B BRISTOL, P M EMMETT, K W HEATON, H C UMPLEBY, AND R C N WILLIAMSON (University Departments of Surgery and Medicine, Royal Infirmary, Bristol) The role of diet in the aetiology of colorectal cancer remains unclear. Studies comparing the diets of patients and healthy controls have been inconclusive, and among possible reasons is the inclusion of patients whose eating habits have changed as a result of their symptoms. Further, most previous reports have not assessed dietary (as opposed to 'crude') fibre intake. In the present case control study, colorectal cancer patients were included only if they met the following criteria: no known predisposing diseases, no previous major gastrointestinal surgery, no appetite loss, no recent weight loss >6-3 kg, no nausea or vomiting. Fifty patients fulfilling these criteria (28 M, 22 F) were interviewed about premorbid eating habits seven to 14 weeks after operation, by the same experienced dietitian using a food frequency questionnaire. Fifty healthy controls matched for age (± three years), sex, social class and marital status were similarly interviewed. Data were analysed by computer to obtain the mean daily intake of energy, nutrients, and dietary fibre. Colorectal cancer subjects had habitually consumed 14% more energy (2p<0.01), 14% more carbohydrate from other sources (2p<0.002), 16% more fat (2p<0.01), and 6% more total protein (2p<0.05) (t test).

No difference was found in the daily intakes of total dietary fibre (patients 17.8±0.9 vs controls 19.4±0.7 g), cereal fibre, vegetable fibre, or natural sugar. Energy intake per gram of dietary fibre was 23% higher in cancer subjects (0.58±0.02 vs 0.47±0.02 MJ/g, 2p<0.001). Thus this group of colorectal cancer patients have tended to eat a diet with a high energy-to-fibre ratio.

F39 Flexible fibreoptic sigmoidoscopy in an outpatient setting

N C ARMITAGE AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Since 1979 flexible fibreoptic sigmoidoscopy using a 60 cm instrument has been a regular outpatient procedure in the diagnosis and follow up of colorectal conditions.

A total of 1339 examinations have been performed on 657 men and 682 women, mean age 59±13 years (range 15-91 years).

Full examination, beyond 50 cm was achieved in 1028 (76.8%), mean time 6-6 minutes. Of those examinations terminating before 50 cm, 84 (6-3%) were because of inadequate bowel preparation. 153 (11-4%) because of patient discomfort or spasm, and 74 (5-5%) because of inflammatory or neoplastic obstructions.

Nine hundred and thirty one examinations were performed for diagnostic reasons. Sixty patients were found to have cancer, 158 to have adenomas, 49 to have inflammatory bowel disease and 129 to have diverticular disease - a positive diagnosis in 396 patients (42.5%).

The diagnostic yield of flexible sigmoidoscopy for neoplastic disease and three to four times that of rigid sigmoidoscopy.

Two hundred and six colorectal cancer follow up examinations were performed with four recurrent cancers and 46 adenomas identified.

One hundred and eighty eight adenoma follow up examinations showed one patient with a colorectal cancer and 60 with further adenomas.

Flexible fibreoptic sigmoidoscopy is quick, easily learned and safe. The increased diagnostic yield can play an important role in the management of colorectal disease.

F40 Place of colonoscopy in the diagnosis of angiodysplasia

R SALEH, A HEMINGWAY, H REES, D ALLISON AND C B WOOD (Departments of Surgery, Radiology and Histopathology, Royal Postgraduate Medical School, London) Angiodysplasia can be diagnosed by selective visceral angiography or by colonoscopy. Colonoscopy can be performed in most centres but detailed visceral angiography is a more specialised technique. The results of colonoscopy in patients shown to have angiodysplasia by angiography were analysed.

Forty five patients were diagnosed as having angiodysplasia by angiography. Thirty one of these had colonoscopy, of which 20 were positive, giving a diagnostic yield of 65%. Of the 11 negative colonoscopies, three had no evidence of angiodysplasia and eight had incomplete examinations; one being due to the presence of a carcinoma at the hepatic flexure. For colonoscopies where adequate views of the caecum were obtained, the diagnostic yield was 87%. Nine colonoscopies were repeated at laparotomy and of these, eight were positive. In patients who had surgery, the resected specimen was submitted for histological and detailed microangiographic examination.

We therefore conclude that colonoscopy is a useful adjunct to angiography in the investigation of angiodysplasia, allowing visualisation of the lesions with the therapeutic possibility of fulguration. Visualisation at laparotomy is good and thus colonoscopy at operation is helpful in assessing the extent of angiodysplasia before resection.

F41 Patients with constipation of different types have difficulty in expelling a balloon from the rectum

P R H BARNES AND J E LENNARD-JONES (St Mark's Hospital, City Road, London) The defaecatory mechanism using a balloon model has been studied in 15 control subjects with normal bowel habit (M8 F7) and 39 patients who complained of constipation, 31 with a normal barium enema and 8 with idiopathic megarectum (M6 F2). Of the 31 patients with a normal barium enema 14 female patients had prolonged whole gut transit times as measured with radio-opaque shapes and 17 (M1 F16) had transit times within normal limits. The ability of the
subject to expel a rectal balloon containing 50, 100, and 150 ml of water was tested in the left lateral position (LLP) and unsuccessful, in the sitting position with the knees raised. The maximum intra-rectal pressure (IRP) outside the balloon was measured with each straining effort and expressed as a mean of the pressure recorded with each balloon in each position. All but one of the patients with normal bowel function could expel all of the balloons in LLP (mean IRP 107±43 SD cm H2O). Only five of 17 patients complaining of constipation with normal transit rates could expel balloons in LLP (p<0.01 compared with controls) while a further three were able to do so when sitting (mean IRP 103±33); nine of 17 could not expel any balloon in either position. None of the 14 patients with constipation and slow transit could expel any balloon in the left lateral position (p<0.001) (mean IRP 90±37) although three were able to do so when sitting (mean IRP 134±38). None of the megarectum patients could expel any balloon in either position (p<0.001) and the mean IRP was 175±60 (p<0.01 compared to controls). A disorder of the defaecatory mechanism is present in many patients with constipation but is not apparently due to an inability to raise intra abdominal pressure.

A I Morris and N Krasner (Gastrointestinal Unit, Walton Hospital, Liverpool) The treatment of patients with recurrent rectal tumours presents a difficult problem particularly in the elderly as does the management of primary tumours in the unifit. We have treated a group of five such patients with either tumour recurrence in Hartman’s pouches, or with primary anorectal tumour in those unfit for surgery. All patients were symptomatic with unpleasant smelling discharge and bleeding per rectum. One of the three patients with a Hartman’s pouch recurrence had failed to improve with deep x-ray therapy and chemotherapy. Treatment using a Neodymium Yag laser was chosen in preference to further surgery or diathermy fulguration. Laser treatment with pulses of up to 100 watts for 0.5–1.0 sec and with an accumulated energy of up to 5000 Joules per session was applied at weekly or fortnightly intervals.

In all these patients there was a consider-

able reduction in discharge and bleeding, and in two complete relief of symptoms. A cirrhotic patient, unifit for surgery, had complete ablation of all visible primary rectal tumour and is alive and well at six months, whereas one patient with inoperable primary anal canal carcinoma, which failed to respond to deep x-ray therapy or chemotherapy has had little benefit from laser therapy. The procedure requires no preparation and can be undertaken with minimal or no sedation. Apart from transient rectal discomfort and an initial transient increase in discharge due to tumour sloughing no serious complications have occurred. The decrease in symptoms has been of major psychological help to these patients. This preliminary series suggest a further use for laser irradiation in addition to its use for oesophageal neoplasms, and in upper gastrointestinal haemorrhage.

F34

Influence of the method of internal sphincterotomy for chronic anal fissure and time after sphincterotomy on the reduction in anal canal pressure

Naomi Chowcat, J G C Araujo, and P B Boulos (Department of Surgery, Faculty of Clinical Sciences, University College London and The Rayne Institute, London) Internal sphincterotomy by relieving sphincter spasm and reducing anal canal pressure heals anal fissures. Incomplete division results in recurrence. This study examines (1) whether division of the sphincter blindly by the subcutaneous method is as adequate in reducing the anal canal pressure as division under vision by the open method and (2) the effect in the long term of healing, where the sphincter had been divided, on the reduction in pressure.

Twenty eight patients with chronic anal fissure were randomly allocated to either method of sphincterotomy. In all patients the fissures were healed at one month and remained healed on completion of the study.

The medians and ranges of the preoperative resting anal canal pressure were similar, 107 (51–138) cm H2O in patients for subcutaneous and 97 (76–129) cm H2O in patients for open sphincterotomy. At one month after sphincterotomy, the pressures decreased significantly (p<0.01) to 52 (17–75) cm H2O and 47 (35–100) cm H2O respectively with 51 (22–77) and 50 (11–68) % reduction of their respective preoperative measurements. There was no statistical difference in these results which justified pooling all the data for further analysis.

In 18 patients the measurements one month after sphincterotomy were 54 (17–100) cm H2O and at three months were 48 (19–85) cm H2O. In 10 patients the measurements at one month, three, and six months after sphincterotomy were 50 (17–68) cm H2O, 47 (19–68) cm H2O and 55 (20–69) cm H2O respectively. Statistical comparisons showed no differences.

These results show that both methods of sphincterotomy are adequate in the extent of sphincter division, as measured by reduction in anal canal pressure which is not transient and is maintained. This information adds to our knowledge of the effectiveness of both methods of sphincterotomy in the treatment of anal fissures.

F44

A randomised clinical trial to compare rubber band ligation with phenol injection in the treatment of haemorrhoids

P C Garrett, R J Sheridan, and F P McGinn (Department of General Surgery, Southampton General Hospital, Southampton, Hampshire) A prospective randomised clinical trial comparing rubber band ligation (RBL) with phenol injection in 269 patients with symptomatic haemorrhoids presenting to one surgical firm over a period of six years has been carried out. Questionnaires were completed by 215 patients (106 RBL and 109 injection) with an average follow up of 2-75 years. A successful outcome was achieved in 89% of those receiving RBL compared with 70% for injection (p<0.001). All symptoms and degrees of prolapse responded more favourably to RBL but only in those patients with bleeding or 2nd degree haemorrhoids did the results achieve statistical significance (p<0.01 and p<0.001 respectively). There was no significant difference in the severity of pain experienced in the two groups, but the duration of pain was significantly longer in those receiving RBL (p<0.01). It is concluded that RBL is a more effective long term therapy for first and second degree piles than phenol injection.

F45

Prospective randomised trial of injection therapy against photocoagulation therapy in first and second degree haemorrhoids
N S AMBROSE, J ALEXANDER-WILLIAMS, AND M R B KEIGHLEY (Department of Surgery, General Hospital, Birmingham) Photocoagulation has proved effective in the treatment of haemorrhoids when compared with rubber band ligation. We have now compared treatment with photocoagulation (P) against injection sclerotherapy (IS) for first and second degree haemorrhoids in outpatients.

Patients with haemorrhoids seen in our rectal clinic were randomised to receive photocoagulation (n=73) or injection sclerotherapy using oily phenol (n=62). Patients were followed and assessed at one, four and 12 months as being excellent, better, the same, or worse. More patients in the photoacoagulation group underwent further similar therapy or other therapy (P=15; IS=4) but similar number required operation (P=4; IS=3). At one month there was no significant difference between the two groups. At four (P=88%; IS=72%) and 12 months (P=72%; IS=56%) a greater proportion of those undergoing photocoagulation were either excellent or better.

We conclude that photocoagulation may require more treatment but is better in the long term than injection sclerotherapy for the outpatient treatment of first and second degree haemorrhoids.

F46 Internal anal sphincter damage in radiation proctitis

J S VARMA AND A N SMITH (University Department of Surgery, Western General Hospital, Edinburgh) Urgency, frequency, and incontinence are common symptoms after radiation injury to the rectum. Many of these symptoms are explainable by reduction in rectal volume and compliance. In order to determine whether there is associated sphincter damage, 10 men with varying degrees of chronic radiation proctitis after prostatic radiotherapy for carcinoma were assessed.

Manometry was carried out to measure maximum resting pressure (MRP cm H2O), length of the high pressure zone (HPZ cm), maximum voluntary contraction (MVC cm H2O) and the presence, amplitude and recovery of the recto-sphincteric reflex (RSR cm H2O) in response to rectal balloon distension by 50 ml of air. The results were compared with a group of 10 normal men in the same age group.

There is a significant reduction in MRP (61.5±7.8 SEM vs 99±6.7, p<0.005), HPZ (2.65±0.2 vs 4.25±0.2, p<0.001) and RSR (25±4.8 vs 46±2.7, p<0.005) in the proctitis group compared with controls. In addition one patient showed absence of the RSR and in four patients it was difficult to elicit and showed a very slow recovery.

Pelvic radiotherapy can result in internal sphincter damage and contributes to faecal incontinence in this group. There appears to be no evidence of significant external sphincter damage.

F47 Oral carbenoxolone protects the gastric mucosa against indomethacin

A MARTIN, N ZARAMELLA, G C STURNIOLO, G GURRERI, AND R NACCARATO (Cattedra Malattie dell’Apparato Digerente, Universita di Padova, Padova, Italy) Previous treatment with prostaglandins (PGs) protects the gastric mucosa against the damaging effects of non-steroidal anti-inflammatory drugs (NSAID). These experiments have little clinical relevance, as it is impractical to pretreat patients with PGs before administration of NSAID. As carbenoxolone (CBNX) increases endogenous PG levels through inhibition of the PG metabolising enzymes, we studied whether simultaneous administration of CBNX could prevent the gastric mucosal damage produced by indomethacin.

Male Sprague-Dawley rats were used in all experiments and drugs were given intragastrically through a plastic tube after a 24 hour fast. All rats were given indomethacin 20 mg/kg and while the 24 control rats simultaneously received only saline, three groups of 10 rats each received CBNX 1.5 or 7.5 or 15 mg/kg.

Control rats had a lesion score (±SE) of 42.4±1.3, while CBNX treated rats had a score of 19.70±3.42 (p<0.01, Wilcoxon’s test), 24.70±3.96 (p<0.05), and 22.30±2.70 (p<0.01) for the three doses, respectively. In CBNX treated rats, gastric PGE2 levels were significantly higher than controls.

We conclude: (1) simultaneous administration of even small quantities of CBNX greatly reduces the gastric damage caused by high doses of indomethacin. (2) this cytoprotection is likely to be mediated by the increased mucosal levels of PGs, and (3) this effect could be exploited clinically.

The British Society of Gastroenterology

F48 Changing pattern of gastric ulcer: are anti-inflammatory drugs involved?

O M J LOLOBE AND R D MONTGOMERY (Department of Medicine, East Birmingham Hospital, Birmingham) The changing clinical pattern of gastric ulcer (GU) has been studied in a series of 528 patients seen in one hospital department during the past 20 years. The male:female ratio in two groups presenting before and after 1973 has declined from 1.89 to 1.08, and age adjusted figures show that this decline applies equally to all age groups. There was a significant decline in midgastric ulcers in men (p<0.01). There was a significant fourfold increased incidence of haemorrhage in proximal as opposed to antral ulcers and a seven-fold excess of haemorrhage in older women as opposed to younger women. Gastric ulcer in women taking non-aspirin non-steroidal anti-inflammatory drugs (NANSADs) showed an increased tendency to bleeding (x2=6.14, p<0.025, corrected for age and ulcer site), accounting for 48% of all haemorrhages in women over 70 years. On statistical analysis, however, NANSAD associated GU showed no other distinguishing features, and NANSAD usage did not account for the changing sex ratio. There is still no satisfactory evidence that these drugs cause chronic gastric ulcer.

F49 Twenty four hour intragastric acidity and overnight acid output in duodenal ulcer patients on a new once daily antisecretory drug

P J MALÈ, M GRIESSEN, N GAROFOLI, T NICOLET, B DE PEYER, AND E LOIZEAU (Division de Gastroentérologie et Polyclinique de Médecine, Département de Médecine, Hôpital Cantonal Universitaire, Geneve, Switzerland) Pyridil-2-tetrahydrothiophène derivative (RP 40749) is a new potent and long acting inhibitor of gastric secretion without anticholinergic or H2-receptor antagonist activity (Lancet 1982; 1: 1179–80).

Using a technique previously reported (Gut 1976; 17: 133–8) we have measured one hour of basal acid output, then 24 hour intragastric acidity and nocturnal acid
secretion in five duodenal ulcer patients in remission. The patients were investigated on three separate occasions: (1) during a single day's treatment with cimetidine, (2) one week later during the first day, and (3) during the tenth day of RP 40749 treatment (cimetidine 200 mg tds, 400 mg nocte; RP 40749 100 mg once daily). Before treatment, mean basal acid output was 5.22±SEM 1.85 mmol/h; for the corresponding hour after 10 days of RP 40749 the mean acid output was 0.46±0.28 mmol/h (p<0.02). Overnight hourly acid output was 0.82±0.26 mmol/h on cimetidine, 1.04±0.27 mmol/h on day 1 of RP 40749, and was reduced to 0.37±0.06 mmol/h on day 10 (NS).

The mean intragastric H⁺ activity during 24 hours was 9.3±±3.1 mmol/l/h on cimetidine, 5.8±±1.3 mmol/l/h the first day on RP 40749 (NS), and was reduced to 0.31±0.13 mmol/l/h the tenth day (p<0.001). On that occasion 90% of the samples had pH >3.5.

RP 40749 once daily is as effective as cimetidine in the reduction of acid secretion. In addition, in contrast with what has been shown previously for H₂-receptor antagonists, its effect increases markedly with duration of treatment, and thus RP 40749 deserves further consideration for duodenal ulcer treatment.

F51
Comparison of tripotassium dicitrato bismuthate (TDB) tablets and ranitidine in healing and relapse of duodenal ulcers

G BIANCHI PORRO, L BARBARA, R CHELI, P R DAL MONTE, AND G MAZZACCA (Department of Gastroenterology, L Sacco Hospital, Milano; 3rd Medical Clinic, University of Bologna; Department of Gastroenterology, St Martino Hospital, Genova; Department of Gastroenterology, Bellaria Hospital, Bologna; Chair of Gastroenterology, University of Napoli, Italy) One hundred patients with endoscopically diagnosed duodenal ulcer were allocated according to a double blind, double dummy, endoscopically controlled trial. The effect on timing of relapses was also studied. Sixty patients (37 men, 23 women, mean age 43 years, range 21–69 years) with DU were randomly allocated to treatment with either BCP (30 patients) or cimetidine (30 patients) for six weeks. Symptoms were recorded on diary cards and at interview at 0, three, and six weeks and ulcer healing was determined by endoscopy at six weeks. In those who had healed, a further endoscopy was done at three months, or earlier if symptoms recurred. Three patients on BCP and one on cimetidine were withdrawn for non-compliance. The groups were similar with respect to age, sex, smoking, alcohol, and duration of ulcer symptoms. Twenty five of 27 (92%) healed on BCP, and 24 of 29 (83%) on cimetidine (p=NS). Relief of symptoms was similar with both drugs and no adverse effects were reported. At three months, six patients of the 16 (37%) given BCP, compared with 11 of 21 (52%) given cimetidine, relapsed (p=NS). Only 43% of relapses were symptomatic. This study shows that healing of DU with BCP is similar to that with cimetidine and that contrary to earlier reports the early relapse rate is not different after healing with either drug.

F52
Twice daily cimetidine in the treatment of gastric ulceration

P BROWN, G V H BRADBY, J M FINDLAY, C GILBERTSON, G D KERR, R MACHELL, J TEMPLE, A C B WICKS, AND J G WILLIAMS (Royal Shrewsbury Hospital, Sandwell District General Hospital, Bradford Royal Infirmary, Nevill Hall Hospital, Abergavenny, West Connwall Hospital, Queen Elizabeth Hospital, Birmingham, Leicester General Hospital, Royal Naval Hospital, Plymouth) Within the UK eight centres contributed 137 patients, all with endoscopic evidence of gastric ulceration to a single blind comparison of cimetidine 400 mg bid, and cimetidine 200 mg tid and 400 mg nocte. Six patients with malignant ulcers were withdrawn, four identified at entry, and two at subsequent endoscopies. Twenty five other patients were excluded, mainly defaulters. Data from 106 patients (55 receiving cimetidine, qid and 51 bid) were statistically analysed for the effects of treatment regimen, age, sex, smoking, and alcohol consumption on healing rates using χ² tests and log linear analysis of contingency tables and the Mann-Whitney U test.

At endoscopy after six weeks' treatment, 73% of patients healed with the qid and 76% with bid regimen (NS). This increased to 94% with qid and 87% with bid after 10 weeks' treatment. There was no effect of sex, smoking, or alcohol consumption on healing rate. There was a suggestion that older patients (an arbitrary age division of 60 years was considered) who had not healed at six weeks healed more frequently at 10 weeks with the qid regimen. There was no difference between treatments in the effect on symptoms or antacid consumption during the trial. Adverse events were mild and resolved in most cases by the end of the trial.

Cimetidine 400 mg bid is as effective as 1 g/day in producing healing and symptomatic improvement of gastric ulceration.
Comparison between ranitidine and conventional therapy in the management of haemorrhagic peptic lesions

A NOWAK, K GIBINSKI, E NOWAKOWSKA, C Z SADLINSKI, Z GORKA, J RUDZKI (INTRODUCED BY J R WOOD) (DEPARTMENTS OF GASTROENTEROLOGY AND SURGERY, SILESIAN MEDICAL SCHOOL, KATOWICE, POOLAND) Previous studies have reported beneficial effects of ranitidine in the treatment of upper gastrointestinal bleeding. Little is known, however, about the changes haemorrhagic lesions undergo during treatment.

In this study 150 patients with endoscopically assessed upper gastrointestinal bleeding were randomly allocated to receive either ranitidine or conventional treatment for 10 days. Both groups were comparable for age, sex, and haemoglobin level.

Endoscopic findings and the need for surgery were compared for the two groups after 10 days' treatment. In the ranitidine treated group 7% of patients with gastric ulcer (GU) required surgery compared with 39% on conventional treatment (p<0.01). Eight per cent of duodenal ulcer (DU) patients receiving ranitidine required surgery compared with 14% of conventionally treated DU patients (NS). In patients diagnosed as having gastritis, none receiving ranitidine and 8% receiving conventional treatment required surgery (NS). In total, 7% of ranitidine patients and 23% of conventionally treated patients required surgical intervention (p<0.01).

Endoscopic healing or improvement after 10 days was seen in 87% of GU patients receiving ranitidine and 43% receiving conventional treatment (p<0.05). Seventy three per cent of DU patients on ranitidine showed healing or improvement compared with 49% on conventional therapy (p<0.05). All patients suffering from gastritis and receiving ranitidine showed endoscopic improvement compared with 67% in the conventionally treated group (NS). Overall, endoscopic healing or improvement was apparent in 81% of patients with ranitidine and 49% of patients by receiving conventional therapy (p<0.05).

These results show a significant benefit of ranitidine over conventional therapy in the treatment of haemorrhagic peptic lesions. The superior efficacy of ranitidine may be particularly beneficial to patients bleeding from gastric ulcers.

Serum pepsinogen I: a non-invasive marker of gastric dysplasia

C N HALL, J O’SULLIVAN, J S KIRKHAM, AND T C NORTHFIELD (DEPARTMENTS OF GASTROENTEROLOGY AND HISTOPATHOLOGY, ST JAMES’ HOSPITAL, AND DEPARTMENT OF MEDICINE, ST GEORGE’S HOSPITAL MEDICAL SCHOOL, LONDON) Detection rates for gastric cancer by endoscopy and multiple biopsies are low even in the precancerous conditions of Polya gastrectomy (PG) and pernicious anaemia (PA). Epithelial dysplasia is a precancerous lesion which may delineate the highest risk individuals for gastric cancer in whom endoscopic surveillances may be more effective. We have previously shown that the incidence and severity of epithelial dysplasia is increased in stomachs of low acidity as determined by gastric aspiration studies. Measurement of serum pepsinogen I is reported to reflect gastric acid secretion.

The aims of this study, therefore, were to validate serum pepsinogen I as an index of gastric acidity and to investigate the relationship between pepsinogen I and gastric dysplasia. Accordingly 30 subjects (12 PG, nine PA, and nine healthy volunteers) underwent endoscopy and multiple biopsies (n=12) and measurement of pepsinogen I in fasting serum by radio-immune assay. In 25 subjects 24 hour intragastric pH profiles were performed.

Epithelial dysplasia was graded into mild and moderate forms (severe dysplasia was not seen) and scores were awarded for these lesions. Serum pepsinogen I was negatively correlated with mean pH (r=-0.58; p<0.005), and the incidence and severity of epithelial dysplasia was increased in subjects (n=15) with a serum pepsinogen I <20 ng/ml (p=0.005). There were 5/15 cases of moderate dysplasia in the <20 ng/ml group compared with 1/15 in the >20 ng/ml group (p<0.025). These data show for the first time a close association between low serum pepsinogen I and epithelial dysplasia and suggest that this non-invasive test may be a useful aid to the selection of high risk individuals in whom endoscopic monitoring for gastric cancer may prove of value.

Gastroduodenal mucosal inflammation in patients with non-ulcer dyspepsia – a controlled endoscopic and morphometric study

A U TOUKAN, M E KAMAL, S S AMR, M A ARNAOUT, A S ABU-ROMIYEH (INTRODUCED BY T W WARNES) (GASTROENTEROLOGY UNIT, JORDAN UNIVERSITY HOSPITAL, AND DEPARTMENT OF PATHOLOGY, FACULTY OF MEDICINE, JORDAN UNIVERSITY, AMMAN, JORDAN) Proper control and quantification are important in the accurate evaluation of gastroduodenal inflammation in dyspeptic patients without ulcers or erosions as proved by endoscopy. Thirty one patients presenting to the GI clinic with non-ulcer dyspepsia (NUD) underwent endoscopy. An age matched group of 32 healthy volunteers were also endoscoped. In both groups the body and antrum of the stomach and the duodenal cap were examined and biopsied. The specimens were oriented on a cucumber slice and processed. Differential cell counts of the mucosal inflammatory cellular infiltrate were carried out with a calibrated eyepiece micrometer.

Endoscopic erythematous changes and mucosal manipulations were noted in a similar frequency and distribution in the NUD patients and the control group. Differential mucosal inflammatory cell count showed a statistically significant (p=0.001) increase in the neutrophil count in the gastric body, antrum, and duodenal cap of the NUD patients as compared with the control group, as well as a slight but significant (p=0.05) increase in the round cell and eosinophil counts of the duodenal mucosa alone. No correlation was found between the endoscopic changes and an increase in neutrophil count above a normal level determined by the mean ± 2 SD of the controls. An endoscopically normal mucosa, however, was more likely to be associated with a normal neutrophil count.

In conclusion, dyspeptic patients without ulcers or erosions have an increased neutrophil infiltration in the gastroduodenal mucosa, and this is not related to endoscopic changes, which are similar in occurrence to healthy controls. Active inflammation of the gastroduodenal mucosa likely accounts for the symptoms in patients with NUD.

Histochemical demonstration of vagal innervation of the whole stomach

A P JAYARAJ, F I TOVEY, AND C G CLARK (DEPARTMENT OF SURGERY, FACULTY OF CLINICAL SCIENCES, UNIVERSITY COLLEGE LONDON, THE ROYNE INSTITUTE, UNIVERSITY STREET, LONDON) Recurrent peptic ulceration has been
claimed to be due to incomplete vagotomy or reinnervation of the stomach after vagotomy. Although there are numerous investigations regarding the distribution of vagus and its branches, there are no reports to show the interlinking neuronal plexuses of the whole stomach.

Ten Wistar rats (220 g) were killed and stomach removed and washed well in Tyrodes. The pylorus was ligated and the stomach inflated with 22 ml of air and the oesophagus ligated. The stomach was floated in the multiplexes of incubating medium containing 5 mg of nitro blue tetrazolium in 15 ml of 0.1 M sodium succinate at 37°C for one hour and fixed overnight in 10% formalin. The staining was localised to the nerve fibres because of their succinic dehydrogenase activity. After cutting the stomach along the greater curvature, the whole stomach was photographed illuminating the surface with fibre-optic light. Microphotographs showed vagal nerve trunks with network of numerous plexuses. The area of the plexus in the lesser curvature was significantly reduced at 0.87±0.75 mm² compared with area in greater curvature at 7.89±1.72 mm² (p<0.001).

The new method visualises the innervation of the whole stomach and is thus suitable for studying the effects of vagotomy. It will be possible to follow the regenerative processes of nerves from the cut ends or collateral sprouting from the nerve trunks.

F57
Acid and gastrin responses during intragastric titration in normal subjects and duodenal ulcer patients with G-cell hyperfunction
R G COOPER, G J DOCKRAY, J CALAM, AND R J WALKER (MRC Secretary Control Group, Physiological Laboratory and Department of Medicine, University of Liverpool, and Gastrointestinal Unit, Walton Hospital, Liverpool) The existence of a subpopulation of duodenal ulcer patients with raised acid output and exaggerated plasma gastrin responses to feeding has been previously recognised. The term G-cell hyperfunction offers a convenient operational definition for this group. Acute normally inhibits gastrin release and a failure of this mechanism would obviously account for the hypergastrinaemia in G-cell hyperfunction. This possibility was examined by comparing amino acid induced acid and gastrin responses during intragastric titration at pH 2.5 and 5.5 in normal subjects and duodenal ulcer patients with G-cell hyperfunction. The latter were identified on the basis of raised basal and maximal acid outputs and increased gastrin responses to feeding. In normal subjects the mixed amino acid meal stimulated only modest increases in serum gastrin, and the highest observed increase was about 30% that after a standard meal. In contrast, in the G-cell hyperfunction group the highest gastrin concentrations were similar to those after a standard meal. In the G-cell hyperfunction group the increment in plasma gastrin at pH 2.5 expressed as a proportion of that at pH 5.5 was 0.29 indicating that the capacity of acid to inhibit gastrin release was well established in these patients. Acid secretory rates were close to maximal at both pH 2.5 and 5.5 during intragastric titration in the ulcer patients, but in normal subjects acid output was about 50% maximal at 2.5 and close to maximal at 5.5. The results suggest that the enhanced gastrin response to feeding in G-cell hyperfunction patients is due to increased sensitivity to amino acid stimulation rather than to diminished acid inhibitory mechanisms.

F58
Dietary fibre intakes in health and functional bowel disease
M A IBBOTSON, J D O'BRIEN, W R BURNHAM, C A VALLANCE, J W DICKERSON, J E LENNARD-JONES, AND D G THOMPSON (Departments of Gastroenterology and Nutrition, Oldchurch Hospital, Romford; The London Hospital, London; The University of Surrey, Guildford, Surrey) The average British diet is said to contain about 20 g of dietary fibre (DF) and a gradual increase has been recommended.

Patients with functional bowel disease (FBD) may eat less DF, but the evidence for this is based upon retrospective assessment and may be inaccurate. We have assessed prospectively (using a seven day dietary diary) the DF intakes of 40 consecutive new patients with FBD diagnosed at a gastroenterology clinic and 40 age/sex matched controls. Dietary fibre was calculated using standard tables.

Dietary fibre intakes of controls (mean 16±6±5 g/day) were lower than those found among the only other UK population previously reported. Dietary fibre intakes among the patients were significantly lower than the controls (12.4±4.2 g; p<0.01. Student's paired t test) and this was mainly because of a lower intake of DF derived from fruit (0.8±1.1 g/d vs 1.6±1.3 g/d; p<0.004) and vegetables (5.3±2.5 g/d vs 7.0±5.0 g/d; p<0.02).

We conclude that the normal dietary habits of populations must be established before appropriate changes are recommended. It remains to be seen whether the low DF intake in FBD patients is a cause or effect of the disease.

F59
Motility of intestinal mononuclear cells in inflammatory bowel disease
P R GIBSON, A HERMANOWICZ, F PALLONE, AND D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) The motility of enzymatically isolated intestinal mononuclear cells (MNC) from patients with ulcerative colitis and Crohn's disease was compared with that of autologous and normal peripheral blood MNC, and intestinal MNC from patients with miscellaneous intestinal diseases. Chemotactic and random migration were assessed in a modified Boyden chamber by measuring the distance of migration through Millipore filters (8 μ) of the leading front of cells. Zymosan activated plasma was used as a chemoattractant. In both Crohn's disease and ulcerative colitis, the random migration of peripheral blood MNC was greater than that from healthy controls. Intestinal MNC exhibited chemotactic and random migration similar to that of autologous peripheral blood MNC except in Crohn's disease where the chemotaxis of colonic MNC was significantly reduced (111±15 μ, n=13) compared with autologous (125±17, n=22) and normal peripheral blood MNC (127±9, n=35). Ileal MNC also tended to migrate more slowly. Disease activity and drug therapy did not influence MNC motility. Patients with Crohn's disease in whom granulomatous diseases were not present, however, had significantly depressed chemotaxis (105±20 μ, n=16) when compared with that of MNC from granulomatous mucosa (133±16 μ, n=9) and from normal peripheral blood.

It is concluded that, in inflammatory bowel disease, motility of intestinal MNC is generally similar to that of autologous peripheral blood MNC except in the subgroup of patients with Crohn's disease in whom granulomata are not present. This could suggest that the formation of granulomatata in Crohn's disease may relate to the ability of macrophages to accumulate at the site of inflammation.
**F60**

Histochemical studies of colonic mucus in ulcerative colitis and Crohn’s disease

J M RHODES, R R BLACK, R GALLIMORE, AND A SAVAGE (Departments of Medicine, Queen Elizabeth and Selly Oak Hospitals, and Department of Histopathology, Selly Oak Hospital, Birmingham) Human faeces of degrading colonic mucus (Rhodes et al, Gut 1983; 24: A1009). We have tested the hypothesis that ulcerative colitis and/or Crohn’s disease may result from increased susceptibility of colonic mucus to desialation or desulphation.

Rectal biopsies were taken from 21 patients with inactive or mildly active ulcerative colitis (UC). 18 patients with ileocolonic Crohn’s disease (CD) and 17 controls (patients with irritable bowel syndrome; IBS). One section from each biopsy was incubated for 12 hours at 37°C in a faecal filtrate prepared by homogenising eight normal faecal samples in 0.2M Tris-acetate buffer (pH 6.0) at a concentration of 0.013 g/ml followed by centrifugation and filtration of the supernatant through a 0.22 μm filter. An adjacent section from each biopsy was incubated in Tris-acetate buffer (pH 6.0) for 12 hours at 37°C. Sections were then stained with HID/Alcian blue (sialomucins blue, sulphomucins black) and graded blindly for staining intensity on a scale 0–5.

Crohn’s disease rectal mucin proved considerably more resistant to desialation than ulcerative colitis or controls: CD 11/18 (61%) unchanged, mean change in grade -1.00±1.41 SD; UC 5/21 (24%) unchanged, mean change in grade -2.18±1.07 SD, p<0.02 by ANOVAR by ranks. Similar resistance to desulphation was shown by CD (94% unchanged), UC (75% unchanged), and IBS control biopsies (88% unchanged).

This increased resistance to desialation of mucus in Crohn’s disease is unexpected and deserves further study.

**F61**

Persistence and location of adhesive and non-adhesive E coli in ulcerative colitis

I F PINDER, E M COOKE, AND A T R AXON (Gastroenterology Unit, The General Infirmary, Leeds, and Department of Microbiology, The General Infirmary, Leeds) Patients with ulcerative colitis have a higher carriage rate of adhesive E coli than normal subjects, but the clinical significance of these potential pathogens is unknown. The possession of adhesive properties implies that these bacteria might persist in the host for longer periods than non-adhesive strains and/or might be found selectively in specific anatomical or pathological areas of the colon.

Thirty colitis patients were studied for persistence of E coli in the stool. Thirteen of 15 patients carrying adhesive E coli in their stool had the same serotype nine months to three years later compared with only four of 15 with non-adhesive E coli originally present (p<0.01).

Thirty colitis patients were studied for location of E coli in the colon. Paired biopsies taken with sterile biopsy forceps through sealed channels of a twin channel colonoscope were taken from inflamed and non-inflamed colonic mucosae.

The biopsies were thoroughly washed in sterile normal saline, homogenised, and plated on to culture medium. E coli isolated was serotyped. In each case, and in 20 normal controls, the same E coli serotype found in the stool was grown from the mucosa as well.

The serotype does not appear to determine the colonic location of E coli in ulcerative colitis but the possession of adhesive properties does seem to be a major factor in the persistence of E coli in this condition.

**F62**

Regional differences in the electrophysiology of normal human colon

G I SANDLE, N K WILLS, W ALLES, J P HAYLETT, AND H J BINDER (Departments of Internal Medicine and Physiology, Yale University, New Haven, Connecticut, USA) Although proximal and distal portions of mammalian colon have different ion transport characteristics which may be important for Na and K homeostasis, it is unclear whether regional differences in colonic ion transport exist in man. Thus, proximal and distal colon from patients undergoing resection for diverticular disease or cancer was studied in Ussing chambers which permitted cell impalements with conventional microelectrodes.

In distal colon (n=13), transepithelial voltage (Vt), total resistance (Rt), basolateral membrane voltage (Vbm), apical membrane voltage (Vam), and the resistance ratio (α = ratio of apical and basolateral membrane resistances) were 14±2 mV, 138±10 ohm/cm², -39±3 mV, 24±3 mV, and 1.5±0.7 respectively under control conditions, and changed to 1±2 mV (p<0.001), 164±14 ohm/cm² (p<0.005), -33±2 mV (p<0.01), 34±3 mV (p<0.02), and 3.4±1.4 (p<0.01) respectively when the Na channel blocker amiloride (0.1 mM) was added to the mucosal solution. In proximal colon (n=4), similar values were obtained under control conditions, but amiloride only changed Vt from -10±3 to -7±3 mV (p<0.02), and Rt from 124±5 to 139±3 ohm/cm² (p<0.1), while Vbm, Vam, and α were not affected. Junctional and basolateral membrane conductances were similar in distal (n=8) and proximal (n=2) colon. Apical membrane conductance (Gα) in distal colon (6±7±1 mS/m²) was greater than in proximal colon (3.4 mS/m², mean of 2), and decreased to 3±0±7 mS/cm² (p<0.005) post-amiloride. Thus, in contrast with proximal colon, distal colon exhibits a marked electrogenic Na transport (VNa) which is inhibited completely by amiloride, and which may be influenced by endogenous aldosterone levels. Gα is similar in distal (post-amiloride) and proximal colon, and may represent an amiloride insensitive apical membrane K conductance.

**F63**

Controlled comparison of the faecal occult blood tests Haemoccult and Fecatwin Feca EIA in population screening for colorectal cancer

N C ARMITAGE, S S AMAR, T W BALFOUR, AND J D HARDCASTLE (Departments of Surgery and Radiology, University Hospital, Nottingham) An asymptomatic population may be screened effectively for colorectal cancer using chemical occult blood tests. To improve the sensitivity and specificity a recently introduced test, Feca EIA, has combined an immunological test for human haemoglobin with a simple guaiac test.

Three hundred two hundred and twenty five subjects aged over 45 years were identified from general practitioners’ age/sex registers and sent by post an explanatory letter. Haemoccult and Feca EIA tests sufficient for three days: 1,306 (40.5%) returned the tests completed, of which 21 were positive for both tests. 19 were Haemoccult positive only, and 88 were Feca EIA positive only.

All persons with a positive test result were investigated by physical examination and flexible sigmoidoscopy: double contrast barium enemas were being performed on all. In the group positive for conditions, and compared to 1±2 mV (p<0.001), 164±14 ohm/cm² (p<0.005), -33±2 mV (p<0.01), 34±3 mV (p<0.02), and 3.4±1.4 (p<0.01) respectively when the Na channel blocker amiloride (0.1 mM) was added to the mucosal solution. In proximal colon (n=4), similar values were obtained under control conditions, but amiloride only changed Vt from -10±3 to -7±3 mV (p<0.02), and Rt from 124±5 to 139±3 ohm/cm² (p<0.1), while Vbm, Vam, and α were not affected. Junctional and basolateral membrane conductances were similar in distal (n=8) and proximal (n=2) colon. Apical membrane conductance (Gα) in distal colon (6±7±1 mS/m²) was greater than in proximal colon (3.4 mS/m², mean of 2), and decreased to 3±0±7 mS/cm² (p<0.005) post-amiloride. Thus, in contrast with proximal colon, distal colon exhibits a marked electrogenic Na transport (VNa) which is inhibited completely by amiloride, and which may be influenced by endogenous aldosterone levels. Gα is similar in distal (post-amiloride) and proximal colon, and may represent an amiloride insensitive apical membrane K conductance.

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All persons with a positive test result were investigated by physical examination and flexible sigmoidoscopy: double contrast barium enemas were being performed on all. In the group positive for
both tests, three cancers (all Dukes' Stage A) have been identified and seven adenomas greater than 1 cm.

In the Haemoccult positive group, 10 adenomas greater than 1 cm have been found. In the Feca EIA positive group, one cancer (Stage C) and seven adenomas greater than 1 cm were found. Sixty five subjects, however, were investigated and no neoplastic disease found.

A total of four cancers, 3-1/1000 subjects tested, and 24 adenomas greater than 1 cm, 18-4/1000, were identified. Of these, Feca EIA increased the yield over Haemoccult by one cancer and seven adenomas. Because of the number of patients investigated in whom no neoplastic cause for bleeding was found, however, the test in its present form would seem unsuitable for population screening.

F64 Lactate dehydrogenase (LDH) isoenzymes and sialomucins in colorectal cancer

D S QUILL, R K S PHILLIPS, J E J BIGLIN, AND H A F DUDLEY (Academic Surgical Unit, St Mary's Hospital Medical School, London)

Both the LDH isoenzyme muscle/heart (M/H) subunit ratio and sialomucin secretion are reported to undergo diffuse change in the cancer bearing colon. This may have diagnostic potential.

We have quantitatively studied the LDH M/H ratio and sialomucin concentrations in the colon of 20 female Wag rats treated with dimethylhydrazine (DMH) (DMH 25 mg/kg/week for 20 weeks). Twelve animals developed colon cancer. Ten untreated animals were used as controls. All animals were killed at 25 weeks. The LDH M/H ratio was calculated following cellulose acetate electrophoresis. Sialomucins were assayed colorometrically using the peridate resorcinol technique.

Our results (mean±SEM) show that sialomucin concentrations (control: 0.96±0.06 μg/mg) were only raised in tumour tissue (1.46±0.23 μg/mg) (p<0.05, Mann-Whitney U). The LDH M/H ratio, however, was significantly raised (2.02±0.04) in tumour (3.08±0.22), colon remote from tumour (2.40±0.05), as well as in the colon of non-tumour bearing animals (2.53±0.05) (p<0.05, Mann-Whitney U).

Similar studies in eight patients with colorectal cancer showed a significant rise of the LDH M/H ratio in histologically normal mucosa between 20 cm proximal and 10 cm distal to tumour in comparison with rectal biopsies from nine control patients with haemorrhoids or fissure (p<0.05, Mann-Whitney U).

These results suggest diagnostic potential for the LDH M/H ratio in colon cancer and document extensive field change in the tumour bearing colon.

F65 Cell proliferation in normal appearing mucosa as a marker for colon tumours

O T TERSTRA, J DEES, AND M VAN BLANKENSTEIN (Departments of Surgery and Gastroenterology, University Hospital 'Dijkzigt' and Erasmus University, Rotterdam, The Netherlands)

The development of colonic adenomas is associated with an increased risk for colon cancer. The majority of these adenomas and cancers arise in the distal large bowel. The aim of the present study was to investigate the cell proliferation in different parts of the colon in patients with neoplastic disease of the colon.

At colonoscopy biopsies were taken from normal appearing mucosa in the caecum, hepatic and splenic flexures, descending colon, mid sigmoid, and rectosigmoid. Autoradiography was performed after in vitro labelling with ³H-thymidine as described by Deschner (J Nucl Cancer Inst 1966; 36: 849). The labelling index (LI) and distribution of labelled cells in the crypts were determined in 21 patients with small adenomas (diameter ≤1 cm) and in 13 patients with large adenomas (diameter >1 cm) or colon carcinoma. Individuals without a history of colon neoplasm and a normal colon at colonoscopy served as controls (n=16). At least 25 crypts per patient were analysed.

No differences in LI or labelling distribution between the proximal and distal colon could be shown, neither in adenoma or cancer patients, nor in controls. The LI in patients with large adenomas or cancer was 8.4±1.9 (±2 SD, p<0.001 vs controls, p<0.02 vs small adenoma patients), while the LI in patients with small adenomas was 6.1±1.5 (p<0.02 vs control patients in whom LI was 4.9±0.8). In adenoma or cancer patients 23-32±6% of the labelled cells was found in the middle third of the crypts, compared with 19-42±6.7% in the control group (p<0.05), indicating an enlargement of the proliferative zone. In five additional patients at risk for familial polyposis coli an abnormal LI corresponded with the presence of polyps.

These preliminary results suggest that this method is a useful tool for the screening and follow up of individuals at risk for the development of colon cancer.

F66 Effect of high and low dose warfarin on preneoplastic changes and tumour incidence in induced colorectal cancer in the rat

NICOLA GOETING, G A TROTTER, N KIRKHAM, T COOKE, AND I TAYLOR (University Surgical Unit, Southampton General Hospital, Southampton) We have previously presented to this society evidence to suggest that preneoplastic changes occur in the rat colon with induced carcinogenesis. Microadenomas were observed early during induction, and increased in size and number with time. In the present study, the effect of low and high dose warfarin on micro-adenoma formation, tumour incidence, and cell kinetics was assessed.

One hundred and sixty eight male Wistar rats receiving subcutaneous injections of azoxymethane (12 mg/kg/week) were randomly allocated to one of three groups: (1) azoxymethane alone, control (n=72); (2) azoxymethane + low dose warfarin, LDW (n=48); and (3) azoxymethane + high dose (‘therapeutic’) warfarin, HDW (n=48). Warfarin was given in drinking water for eight weeks and clotting times monitored using the thrombostest technique. Rats were killed at five, 10, 15, 20, and 25 weeks after initial injection. Scanning electron microscopy and crypt cell production rate calculations were performed on segments of colon.

The mean number of micro-adenomas per low power field significantly reduced at each time interval in both LDW and HDW groups (at 20 weeks 9-5 in control, 0-76 in LDW, and 1-10 in HDW, p<0.05). There was no difference in size of microadenomas, number of crypts per microadenoma, or crypt cell kinetics. The number of tumours at 25 weeks was significantly reduced in both LDW and HDW groups (control 37, LDW 17, and HDW 17, p<0.05).

These results suggest that warfarin, even at a low dose, reduces initiation of pre-malignant change at a cellular level, rather than preventing malignant transformation of adenomas.

F67 Bile acid receptors and colorectal cancer growth in the rat model
F68 Failure of gamma glutamyl transpeptidase and mean corpuscular volume to detect potentially dangerous levels of alcohol consumption in self referred ‘drinkwatchers’

1 G BARRISON AND I M MURRAY-LYON (Gastroenterology Departments, West Middlesex Hospital and Charing Cross Hospital, London) Gamma glutamyl transpeptidase (GGT) and mean corpuscular volume (MCV) are the most commonly used blood markers of alcohol abuse. The value of these tests has been established mainly in medical and psychiatric patients and in health screening programmes. The aim of our study was to correlate levels of GGT and MCV with alcohol consumption and liver size and also to assess the sensitivity of these tests in detecting heavy drinking in self-referred individuals who wished to control excessive drinking through our ‘Drinkwatchers’ project. Ninety subjects (37 men, 53 women, mean age 40 years), who had consumed more than 80 g alcohol/day for more than two years, were studied; 37-8% had raised MCV, and 29-9% had raised GGT. 28/90 (30-1%) had normal MCV and GGT. 13/26 patients with hepatomegaly had normal MCV and GGT. For the group as a whole, GGT correlated significantly with current alcohol consumption (CALC) (r=0.26; p=0.005), liver size (r=0.02; p=0.005), and MCV (r=0.22; p=0.008). MCV did not correlate with GGT or liver size. The sensitivity of MCV was 50% and GGT 28-8%; the sensitivity of MCV and GGT combined was 64-4%. Sixty per cent of women who had raised MCV, but only 18% had raised GGT. Significantly more men than women (11/17 vs 2/9) with hepatomegaly had normal MCV and GGT (x²=6.1, p<0.01). We conclude that MCV and GGT will fail to detect 30% of heavy drinkers overall and 50% of heavy drinkers with hepatomegaly. These blood tests are not adequate substitutes for detailed history taking and clinical examination.

F69 Monocytosis: a feature of alcoholic liver disease

U MCKEEVER, C O’MAHONEY, E LAWLOR, D G WEIR, AND C FEIGHERY (Immunology Department, St James’ Hospital, Dublin) Altered cellular and humoral immune responses are present in patients with alcoholic liver disease (ALD). The reported abnormalities in T cell suppressor function and number may explain the hypergammaglobulinaemia of ALD but do not explain the lymphocyte hyporesponsiveness. It has recently been suggested that monocyte suppressor cells play a role in the peripheral lymphocyte hyporesponsiveness of chronic liver disease. With the exception of early reports on monocytosis, based on morphological criteria, in cirrhosis, the literature concerning monocyte numbers in ALD is scarce.

Because of the reported defects in the monocyte function associated with cirrhosis the present study used the monoclonal antibody MO-2 to precisely identify and enumerate peripheral blood monocytes in 12 patients with acute-on-chronic ALD. These results were compared with nine age and sex matched healthy laboratory volunteers. Peripheral blood T lymphocytes were also counted using Leu 1, a monoclonal antibody which is specific for these cells.

Both proportions (mean=38±20%) and absolute numbers (mean=0.87±0.69 x10¹⁰/l) of MO-2 positive cells were significantly higher in the severe ALD group when compared with healthy controls (66±11%; 1.5±0.5 x10¹⁰/l).

In this study, with the aid of a specific monoclonal marker of monocytes, a significant excess of these cells was discovered in the peripheral blood of severe alcoholic patients. In addition, a significant T cell lymphopenia was observed. The combination of these findings may help explain the lymphocyte hyporesponsiveness characteristic of severe ALD.

F70 Natural killer activity in hepatitis B positive chronic active hepatitis and the in vitro response to lymphoblastoid interferon

M G ANDERSON, M BAKHTIAR, A W L F EDDLESTON, I M MURRAY-LYON, AND R WILLIAMS (Liver Unit, King’s College Hospital, and Gastroenterology Unit, Charing Cross Hospital, London) The observations that interferon (IFN) may be of value in the treatment of HBsAg positive chronic active hepatitis (CAH), that natural killer (NK) activity may be reduced in this disease and that IFN increases NK activity, had led us to investigate NK activity and its modulations by IFN in vitro in a group of patients with HBsAg positive CAH.

Natural killer activity of peripheral blood lymphocytes (PBL) was assessed using a standard 51Cr release assay and the tumour cell line K562. Effector:target (E:T) ratios of 50:1, 25:1, and 12.5:1 were used in four and 16 hour incubation. At an E:T ratio of 50:1, NK activity in 15 healthy controls after four hours was 55±15 (mean % cytotoxicity ± SD) and after 16 hours 68±15. The values were not reduced in 21 patients with HBsAg positive CAH (four hours, 52±12; 16 hours, 68±14) or in four HBsAg carriers with minimal liver disease (four hours, 65±8; 16 hours, 77±9). A similar pattern was seen at E:T ratios of 25 and 12.5:1. NK activity was significantly increased after in vitro incubation of PBL for one hour with a-IFN (1000 units/ml) in HBsAg CAH (four hours, 69±9), an effect comparable to that in normal subjects (four hours, 72±11).

The results indicate that NK activity in HBsAg CAH is not impaired. The increase
in activity after interferon treatment may in part be responsible for the therapeutic effect of this agent.

F71
Do H₂-receptor antagonists affect liver blood flow and why?

S L GRAINGER, C C AINLEY, AND R P H THOMPSON (Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London) Ranitidine is a 'cleaner' H₂-receptor antagonist than cimetidine, but studies suggest both alter liver blood flow (LBF). H₂-receptors, however, probably have no physiological role in the splanchnic circulation, and the methods of measuring LBF have not always been valid. We have measured LBF on these drugs from the plasma disappearance of 1IV indocyanine green (ICG) using an analysis that determines hepatic extraction of ICG without hepatic vein catheterisation.

Twelve patients with normal liver function and duodenal ulcer or duodenitis were studied. Six received cimetidine 400 mg bd and six ranitidine 150 mg bd. Liver blood flow measured was 0.25 mg/kg ICG after an overnight fast, two hours after drug administration, three weeks after starting, and again at least three weeks after stopping therapy.

Ranitidine had no effect on LB but cimetidine reduced LBF by a mean 11% (mean change during and after cimetidine 1.7 ml/kg/min, SE 0.6, p<0.025). Cimetidine but not ranitidine also reduced intrinsic hepatic clearance of ICG, a measure of hepatocellular function (mean change during and after cimetidine 11.7 ml/kg/min, SE 5.3, p<0.05); this cannot be due to the known inhibition of microsomal enzymes by cimetidine, because ICG is not metabolised. We suggest: (1) cimetidine, in contrast with enzyme inducers, reduces liver mass by inhibiting liver enzymes; (2) this change is not mediated by H₂-receptor blockade since ranitidine was without effect; and (3) the fall in blood flow simply accompanies reduced hepatic metabolic activity.

F72
Prednisolone pharmacokinetics and autoimmune chronic active hepatitis: effects of cimetidine and spironolactone

B POWELL-JACKSON, J ENGLISH, AND R S WILLIAMS (Liver Unit, King's College Hospital, and Dental Schools, London, and Department of Biochemistry, University of Surrey, Guildford, Surrey) The wide variations in prednisolone dosage required to maintain sustained remission in patients with autoimmune chronic active hepatitis (CAH) may be because of interindividual differences in prednisolone pharmacokinetics and to inhibition or induction of drug metabolism by concomitant administration of cimetidine and/or spironolactone respectively.

Four patients with 'unresolved' CAH had lower prednisolone clearance (51–25±7–01 ml/min) and greater area under the concentration time curve (5526±813 ng/ml/h) than six patients with CAH in remission (96±13–2 ml/min (p<0.05); and 3073±452 ng/ml/h (p<0.02) respectively) and six prednisolone treated patients without liver disease (76–8±5–2 ml/min (p<0.02) and 3556±268 ng/ml/h (p<0.05)). In patients with inactive disease, these parameters did not correlate with prednisolone maintenance doses and were not affected by cimetidine 400 mg bd and spironolactone 50 mg bd administration for 14 days in a randomised, double blind crossover trial. In one of the four patients with active disease, clearance decreased by 23% with cimetidine and was associated with a decrease in serum AST from 434 to 187 IU/l. With spironolactone, clearance increased by 41% and was associated with symptomatic relapse within one week and a rise in AST to 368 IU/l.

These results indicate that prednisolone pharmacokinetics are abnormal only in patients with active disease and that clinically significant interactions may occur with cimetidine and spironolactone. Variations in the dose of prednisolone required to maintain remission are not due to differences in prednisolone metabolism.

F74
Dietary protein supplementation from vegetable sources in the management of chronic hepatic encephalopathy

A KESHAVARZIAN, J H MEEK, C SUTTON, V M EMERY, E A HUGHES, AND H J F HODGSON (Royal Postgraduate Medical School, Hammersmith Hospital, London) Clinical trials suggest that patients with portal systemic encephalopathy can tolerate larger intakes of vegetable than animal protein. In a controlled crossover trial, we have compared a conventional 40 g protein diet (30 g animal and 10 g vegetable, diet A) with an 80 g vegetable protein supplemented diet (30 g animal and 50 g vegetable, diet B) in the treatment of five patients with chronic stable portal-systemic encephalopathy, requiring dietary and lactulose therapy. Each diet was given, in random order, for five days in hospital. EEG, clinical indices of encephalopathy, and the plasma amino acid profile was assessed at the end of each treatment period.
The increase in vegetable protein intake was associated with minor improvement in EEG and clinical performance in two patients, and no change in the others. Fasting plasma phenylalanine and tyrosine were higher on diet B (phenylalanine 108±6±9-3 (SEM) μmol/l vs 99±6±8-37, p<0.05 (paired t test); tyrosine 153±3±5-2 μmol/l vs 140±1±4, p<0.05). Plasma branched chain amino acid levels did not change, and branched chain:aromatic amino acid ratio (BCAA/AAA) was lower on diet B (p<0.02). Faecal weights were not significantly altered.

These results indicate that patients with chronic portal systemic encephalopathy are tolerant of protein supplementation from vegetable sources. A minor improvement in parameters of encephalopathy was seen in some individuals, despite a lowering of BCAA/AAA which some authors have thought important in the pathogenesis of encephalopathy.

**F75**

**Hepatocyte and Kupffer cell function in liver disease assessed by single photon emission tomography (SPET)**

E M ALSTEAD, A I MORRIS, I T GILMORE, J S GRIME, AND M CRITCHLEY (University Department of Medicine and Department of Nuclear Medicine, Royal Liverpool Hospital, Liverpool) We have previously described and validated a technique for quantification of Kupffer cell uptake and liver volume measurement using 99Tcm sulphur colloid by SPET. In an attempt to differentiate better between the type and severity of various liver diseases we have extended the above technique using 123I bromosulphthalien (BSP) as a specific hepatocyte label. Seventeen patients with diverse liver disease received 111 MBq (3 mCi) 123I BSP intravenously. Tomography using an IGE 400T tomographic camera was performed at 10 minutes after injection before bileary concentration was apparent. Three dimensional reconstruction of the liver was obtained using SPET software, allowing absolute volume determination and quantification of total BSP uptake. All patients also had tomography after 99Tcm sulphur colloid administration. The mean percentage uptakes (±SD) of 123I BSP and 99Tcm sulphur colloid respectively were 40±4±8-1 and 19±4±5-2 in patients with decompensated cirrhosis, 65±7±4-8 and 39-3±3±5 in those with moderate liver disease, and 75±3±11-6 and 56±7-1 in patients with minimal hepatic dysfunction.

These results correlate well with clinical, biochemical, and histological findings. The technique offers the prospect of both structural and functional hepatocyte assessment simultaneously and additionally will permit the investigation of quantitative differences in Kupffer cell and hepatocyte function in liver disease.

**F76**

**Alterations in hepatic adenine nucleotide metabolism in patients with liver dysfunction**

D LAMBERT AND P D WRIGHT (University Department of Surgery and Freeman Hospital, Newcastle upon Tyne) The structural and functional integrity of the cell requires the continual expenditure of energy in the form of adenosine triphosphate (ATP). Mechanisms controlling the utilisation and resynthesis of ATP are therefore of paramount importance. Animal studies have demonstrated that hepatic energy balance is disturbed in various types of hepatic dysfunction. This study investigates these changes in patients with normal and abnormal liver function. Three groups undergoing elective surgery have been studied: group 1, controls (n=20); group 2, obstructive jaundice (n=8); group 3, cirrhotics (n=7). A freeze clamp technique was used following liver biopsy. Adenine nucleotides were determined and hepatic energy charge calculated from these values. Significant reductions in ATP levels were found in patients with jaundice (2±9±0-11 mol/g) and cirrhosis (2-69±0-18) compared with controls (3-64±0-12). This reduction in ATP was accompanied by a significant increase in adenosine monophosphate and a reduction in the total adenine nucleotide pool. Energy charge was significantly lower in group 2 and 3 patients and in group 2 showed a negative correlation with the serum bilirubin (r=−0.75, p<0.05).

These results indicate reduced availability of ATP to meet metabolic demands in liver disease and also a relative lack of the precursors necessary for its resynthesis, as the total adenine pool is reduced. A shift towards a less phosphorylated state is shown by the lowered energy charge values, indicating loss of normal metabolic control. These findings have important therapeutic implications as clinical measures specifically aimed at improving the hepatic energy economy should benefit overall liver function.

**F77**

**Evaluation of the use of fluorescein during injection of oesophageal varices**

K R HINE, D I MORRIS, P J TOGHLILL, AND P W DYKES (University Hospital, Queen’s Medical Centre, Nottingham, and General Hospital, Birmingham) The management of patients with oesophageal varices by injection sclerotherapy is increasing in popularity because of its simplicity and proven improvement in survival. The optimal site for injection is probably into the varices themselves (intravariceal) rather than into the submucosa (para-variceal). Unless radio-opaque contrast is mixed with the sclerosant and radiograph screening is used, however, it is difficult to be certain whether a particular injection is intravariceal or submucosal.

Fluorescein fluoresces bright yellow under ultraviolet light and a standard endoscopic light source was shown to produce sufficient ultraviolet light to give this fluorescence. In initial animal studies using canine stomach submucosal injection of fluorescein was visible as bright fluorescence whereas injection into a gastric vein produced a different effect with fluorescence following a linear path and partly flowing away. The same phenomenon was shown in human necropsy material.

In four patients with oesophageal varices undergoing a total of 10 courses of sclerosant injections, the sites of injection were positively identified by the use of fluorescein (0.5 ml of 10% solution mixed with 5 ml of sclerosant). Submucosal injection retained the fluorescence for a long period whereas an intravariceal injection there was a very rapid loss of fluorescence. Free sclerosant in the oesophageal lumen could very easily be identified.

The use of fluorescein mixed with sclerosant may be of value in identifying the site of endoscopic injection of oesophageal varices.

**F78**

**Small bowel: a source of gastrointestinal bleeding**

A P HEMINGWAY AND D J ALLISON (Royal Postgraduate Medical School, Hamme-smith Hospital, London) The purpose of this study is to determine the incidence of small bowel lesions causing gastrointestinal bleeding detected at angiography.

Patients with acute and chronic gastro-
Jejunal secretory effect of intraduodenal perfusion of nutrients in man

R Palma, B Miazza, J R Lachance, J A Chayvialle, P Jonard, and R Modigliani (INSERM U54 – Hôpital Saint-Lazare, Paris, and INSERM U45 – Hôpital Edouard Herriot, Lyon, France)

The effect of the presence of food in the intestinal lumen on fluid transport by an intestinal loop isolated from nutrients is debated and seems species dependent. The aim of the present work was to investigate this problem in man. Fluid and ion transport by a 30 cm jejunal loop was measured by the perfusion of a plastic like solution below an occlusive balloon inflated at the angle of Treitz. Meanwhile the duodenum was infused at the papilla by saline (control period, CP) or one of the following solutions (test period, TP): protein hydrolysate (P; 135 g/l), starch hydrolysate (S; 135 g/l), lipids (L; 20% Intralipid; 270 ml/l), mixed nutrients (MN; P=25.4 g/l, S=53.6 g/l, 20% Intralipid: 112 ml/l). The four solutions (pH = 7, 300 mOsml/l) were infused intraduodenally in six normol subjects (order randomised). Each TP was preceded and followed by a CP. Blood samples were taken for radioimmunoassays of gastrin, secretin, CCK-PZ, motilin, VIP, GIP, PP, and somatostatin.

Itraduodenal MN reduced jejunal H2O absorption (ml/min/30 cm; mean ± SEM; −=absorption, + =secretion) from -1.06±0.27 to -0.42±0.23 (p<0.05), and stimulated plasma CCK and PP (p<0.02). Intraduodenal L and P reversed H2O jejunal absorption to a secretion (respectively from -1.02±0.3 to +0.25±0.37, p<0.01, and from -0.64±0.52 to +0.21±0.49, p<0.01) and increased plasma CCK, PP, and GIP (p<0.02). Intraduodenal G did not change jejunal H2O transport and increased plasma GIP (p<0.02). Moreover, L and P stimulated and G decreased motilinaemia (p<0.10). Ion transport variations followed those of H2O.

We conclude that (1) an intraduodenal mixed meal inhibits H2O and ion absorption by a jejunal loop isolated from the nutrients; (2) this is due to the L and P content of the meal; and (3) this effect might be mediated by CCK and/or motilin.

F80
Mucosal recovery and permeability in gluten sensitive enteropathy

I Bjarnason, M N Marsh, A J Levy, A Price, and T J Peters (MRC Clinical Research Centre, Harrow, Middlesex, and University Department of Medicine, Hope Hospital, Salford, Manchester) The aim of this study was to assess the 51Cr-EDTA absorption test in the detection of altered intestinal permeability (IP) in patients with coeliac disease (CD) and dermatitis hermiformis (DH), correlating such changes with mucosal structure and the effects of gluten withdrawal.

Thirty four healthy Caucasians served as controls: 61 adults with CD (42 treated for an average of five years) and 16 with DH (11 treated by gluten withdrawal for an average of three years) were studied. A 100 μCi dose of 51Cr-EDTA was taken orally and results are expressed as the per cent 24 hour urine excretion (mean ± SD). Jejunal biopsies were obtained within a week of study in CD patients and analysed morphometrically and intraepithelial lymphocytes/100 enterocyte nuclei were counted.

While controls excreted 1.9±0.5% of the tracer, increased excretion was found in CD, untreated (5±2.6%) or treated (4.2±2.4%) and DH, untreated (4.6±4.2%) or treated (3.0±0.6%). All untreated CD and DH had increased IP; 83% of treated CD and 73% of treated DH patients had increased IP. No significant difference was found between the patient groups. Intestinal permeability correlated significantly with intraepithelial lymphocytes (r=0.33, p<0.01) and inversely with mucosal height/crypt depth ratio (r=-0.35, p<0.01) in CD patients. Although 21 treated CD patients had normal intraepithelial lymphocytes and 19 normal morphometry, only 14 (33%) had an entirely normal mucosa, 11 of whom had abnormal IP.

We conclude that (1) the 51Cr-EDTA absorption test is a sensitive reliable measure of IP, (2) intestinal permeability is increased in all untreated CD/DH patients and despite gluten withdrawal persists in approximately 75% of patients, and (3) no CD patient treated for less than four years had a normal intestinal mucosa.

F81
In vitro determination of ileal Na+ dependent taurocholate uptake, values from colonoscopic ileal biopsies in relation to in vivo bile acid loss

F W M de Rooij, J W O van den Berg, M van Blankenstein, E P Bosman-Jacobs, and A C Touw-Bloemestein (Department of Internal Medicine II, Erasmus University Rotterdam, POB 1738, 3000 DR Rotterdam, The Netherlands) Increased faecal bile acid loss (FBAL) is found in a variety of gastrointestinal diseases and may result from ileal dysfunction or motor disturbances. We have been able to characterise ileal Na+-dependent taurocholate transport (INBAT) at the brush border membrane level by preparing brush border membrane vesicles (BBMV) from microquantities (15–200 mg) of ileum allowing the use of endoscopic biopsy specimen, according to an adaptation of the Ca2+ precipitation method (Kessler et al). Uptake of 3H-taurocholate (4 μM) into the BBMV in the presence of a 100 mM NaCl gradient is followed during one minute by sampling at 20, 40, and 60 seconds. Taurocholate uptake was quantified in pmol/20 sec/mg membrane protein. The assay was validated on rabbit and human jejunum and ileum. Normal values were based on data from ileal biopsies in 59 patients with endoscopic normal mucosa and no clinical signs of ileal disease. In 27 patients faecal bile acid loss (FBAL) was also measured. In seven patients with normal FBAL, a normal INBAT was found. In 20 patients with increased FBAL, INBAT was normal in 12 patients and decreased in eight patients.

We conclude that this technique can be applied in analysing the pathophysiology of increased FBAL.
F82
Complications of jejunoileal bypass – still at risk after 12 years

R J McFarland, J-C Gazet, and T R E Pilkington (St George’s Hospital Medical School, London) Effective and permanent weight loss has been achieved in 175 morbidly obese patients by performing a 35 cm jejunoileal bypass during the years 1971–1982 with considerable psychological and social benefit. Sixty per cent of patients developed a complication, two thirds of these within two years. Fifteen per cent had simple electrolyte disturbance and a further 5% electrolyte disturbance and liver dysfunction associated with excessive weight loss. Seven patients died, one operative death and five within the first two years. No patient has died in hospital since 1976, which we attribute to experience and a policy of early reversal for patients with serious metabolic disturbance.

Even up to 10 years after weight has stabilised, however, patients are at risk of serious complication which may be new, recurrent or precipitated by intercurrent illness. Twenty eight patients (15-5%) have required reversal; half of these more than five years after bypass. The common indications for reversal after this interval were metabolic problems (five), urinary calculi (four), and arthritis (three). Failure to associate the new problem with the bypass may lead to a delay in diagnosis – particularly of late metabolic failure which begins with insidious weight loss. Indefinite outpatient follow up is mandatory and this sets the limit on the number of patients that can be admitted to the programme.

There was, however, no significant difference between the groups tested. In previous experiments, alpha gliadin was shown to significantly inhibit leucocyte migration in cells from coeliac patients while having no effect on control cells (p<0-001).

To assess the specificity of binding of crude gliadin to peripheral blood mononuclear cells (PBMCs), rosetting experiments were carried out using gliadin labelled ox red blood cells (ORBCs). Gliadin coated ORBCs bound to similar percentages of PBMCs from normal individuals (10), untreated (six) and treated (eight) coeliac patients. Respective percentages rosettes were 4-0±1-5, 4-5±1-0, and 3-5±1-6.

In further experiments, alpha gliadin was shown to bind specifically to PBMCs of coeliac patients but not to control cells. Using a monoclonal antibody to alpha gliadin and an indirect immunofluorescence technique, there was a five-fold increase in the percentage of PBMCs from treated (six) and untreated (five) coeliac patients which bound the purified wheat protein when compared with cells from control subjects (eight), p<0-001.

These findings indicate that there is an intrinsic difference between the cells of coeliac patients and those of normal individuals in that the former bind alpha gliadin. The lectin like properties of crude gliadin probably cause it to bind non-specifically to normal and coeliac cells. The specific binding of alpha gliadin to cellular plasma membranes in coeliac patients may represent a central event in the pathogenesis of coeliac disease.

F83
Alpha gliadin binds specifically to coeliac lymphocytes

Cliona O’Farrelly, C A Whelan, C O’Mahony, C Feighery, and D G Weir (Departments of Immunology and Clinical Medicine, Trinity College, and St James’s Hospital, Dublin, Ireland) The in vitro reactivity of cells from normal and coeliac subjects with two wheat protein fractions, alpha gliadin, and crude gliadin was investigated.

Using the leucocyte migration inhibition factor assay, crude gliadin was found to have a non-specific effect on cells from normal individuals (12) and from untreated (11) and treated (10) coeliac patients in that a variety of responses was elicited. For possible associations which would confirm evidence for a specific chromosomal locus for this condition.

Forty two patients with coeliac disease were investigated for (1) HLA surface cell markers including DR typing, (2) immunoglobulin allotypes. HLA and DR loci were determined by standardised antisera in a lymphocytotoxicity assay. Immunoglobulin allotyping was undertaken by a haem-agglutination inhibition assay. Immunoglobulin allotype markers included G1m (1, 2, 3), G3m (5, 11, 12). High incidences of the HLA types included A1 (80%), B8 (76%), DR 3 (96%), and DR 7 (54%). Only one patient had neither DR 3 nor DR 7. In contrast with previous reports, no disturbance of Gm allotype frequencies was found for the limited number of allotypes investigated.

The association of coeliac disease with HLA DR 3 and 7 is higher than the previously reported value. These results suggest a specific abnormal chromosomal locus in patients with coeliac disease.

F85
Are routine duodenal biopsies useful during endoscopy of patients with dyspepsia?

H W Jones, C J Durkin, W Grey, and A M Hoare (Wycombe General Hospital, High Wycombe, Bucks) No abnormality is found at endoscopy in a large proportion of patients with dyspepsia. Biopsies of the second and third part of the duodenum have been shown to be reliable in diagnosing coeliac disease. Therefore biopsies at initial endoscopy could pick up any of these patients who had coeliac disease.

This study of duodenal biopsies was taken over two years from all patients presenting with dyspepsia in whom no cause for the dyspepsia was found. In addition their symptoms were analysed to see if a subgroup of patients requiring biopsy could be selected.

Over two years there were 2938 endoscopies of which 520 were negative endoscopies in patients with dyspepsia. Four of these had villous atrophy and three giardia on their biopsies. Their symptoms responded to the appropriate treatment. Six of the seven patients had the following factors to suggest small bowel disease. Therefore duodenal biopsies need only be performed if endoscopy is negative if patients have anaemia, weight loss, diarrhoea (however mild), or a family history of coeliac disease in addition to dyspepsia.
F86
Secretory dose-response studies in the pancreas made hyperplastic by pancreatocholecystokinin-2 (PBD) or 90% small bowel resection (SBR) in the rat

N H STACE, S VAJA, A BUTT, G M MURPHY, AND R H DOWLING (Gastroenterology Unit, Department of Medicine, Guy's Hospital Medical School, London Bridge, London) Although pancreatic hyperplasia can be induced by several methods, little is known about the secretory potential of these large glands. Therefore, eight weeks after surgery, we measured exocrine secretion in two models of pancreatic adaptation associated with hypercholerhectokinin-2 - PBD, achieved by interposing 50 cm of jejunum between pylorus and ampulla, and SBR - and compared results with transected controls (TC). The volume, protein, and trypsin outputs in pancreatic juice were measured during a basal hour and after 6x30 minute infusion periods with continuous secretin (20 CU/kg/h) + doubling doses of CCK-OP (0-25-80 mg/kg/h) in fasting (24 hour), anaesthetised, bile duct ligated rats (n=8).

Both models induced pancreatic growth, the pancreatic weight (mg/100 g bw) increasing from 351±22 in TC to 441±25 (p<0.02) after SBR and to 587±43 (p<0.001) after PBD. In keeping with this hyperplasia, mean maximum volume (ml 30 min/kg) increased from 620±61 in TC to 1002±77 (p<0.01) after SBR and to 1567±127 (p<0.001) after PBD. Mean maximum protein and trypsin outputs (mg and U 30 min/kg) showed a similar pattern with 15 and 10% increases after SBR (NS) and 41 and 66% increases after PBD (p<0.05 and 0.01). When expressed per g pancreatic weight, however, protein and trypsin secretion were comparable in all three groups although maximum trypsin was still significantly higher in PBD.

We conclude that (1) PBD induces greater pancreatic growth than 90% SBR; (2) when stimulated maximally, these hyperplastic glands secrete more pancreatic juice than TC; (3) after PBD, maximum outputs of protein and trypsin were markedly increased; after SBR, the increases were modest and NS; (4) this functional adaptation is due mainly to more cells, with little or no change in secretion/unit weight pancreas.

F87
A new approach to gall stone dissolution

R O KING, C J HAWKEY, A H SHORT, AND G D BELL (Departments of Therapeutics and Physiology/Pharmacology, University Hospital, Nottingham) A possible explanation for the lengthy dissolution times observed with bile acid therapy for cholesterol gall stones is an interfacial barrier between crystalline cholesterol and biliary micelles. Benzalkonium chloride, a cationic amphiphile, has been shown to increase cholesterol dissolution rates by reducing interfacial resistance. In the present study, a rotating disc apparatus was used to study the effects of drugs on the dissolution rates of compressed cholesterol (‘artificial gall stones’) into sodium cholate solutions and ox bile.

In 2% sodium cholate-phosphate buffer (pH 7.4) the following results were obtained (activities given are drug rate/ control rate ± SEM, ratios greater than 1 indicate enhanced dissolution): 3 mM amitryptiline 6-74±0-70 (n=7), 3 mM diphenhydramine 6-40±0-43 (n=8), 3 mM diclofenac 5-91±0-44 (n=7), 3 mM propamphamide 5-01±0-38 (n=7), and 0-3 mM loperamide 6-49±0-14 (n=3). These activities were similar to 3 mM benzalkonium chloride (6-33±0-35, n=4).

In ox bile the following results were obtained: 3 mM amitryptiline 1-92±0-14 (p<0.001, n=4), 3 mM diphenhydramine 1-67±0-12 (p<0.05, n=4), 3 mM diclofenac 1-45±0-09 (p<0.01, n=4), and 3 mM diphenhydramine 1-2±0-01 (p<0.01, n=4).

Structural features common to these drugs are (a) quaternary or tertiary nitrogen group and (b) a lipophilic ring system. If these drugs or their structural analogues are excreted in bile in sufficient quantities and in an active form, they may represent a new approach to medical gall stone dissolution.

F88
Reconstruction of the upper gastrointestinal tract after duodenopancreatectomy

N J LYGIDAKIS AND W H BRUMMELKAMP (Department of Surgery, Academic Medical Centre, Amsterdam, The Netherlands) Although a variety of reconstructive techniques have been reported after duodenopancreatectomy (DP), it seems likely that none had affected significantly the short and long term results of the procedure. The present study reports a new approach of reconstruction. The technique uses end-to-side jejuno-jejunostomy of the specimen of DP is closed and the jejunum is again transected 30 cm distal to it. The so created segment is transferred to the supra-mesocolic space and anastomosed end-to-side with the pancreatic remnant and the common bile duct. The distal jejunal segment is anastomosed end-to-end with the gastric remnant after hemigastrectomy.

Bilateral truncal vagotomy is added and an end-to-side jejunostomy is carried out 60 cm distal to the gastrojejunostomy between the distal end of the proximal jejunal segment and the distal jejunal segment. Fourteen patients underwent this type of reconstruction. Two patients died, one because of haemorrhage and the second because of myocardial infarction. Two patients developed pancreatic anastomotic leakage, but none required further surgery. Twelve patients were followed up through clinical history, weight measurements, physical examination, endoscopy, radio-isotope gastric emptying studies, Hida-scan, and gastric secretory studies.

We conclude that after DP fashioning of gastrojejunostomy and of hepatopancreaticojejunostomy, a separate intestinal segment from the gastrojejunostomy after hemigastrectomy and bilateral truncal vagotomy (1) makes early oral feeding feasible, (2) because there is no food passage along dangerous anastomotic lines, healing along these lines is less interfered with and any possible leakage is less dangerous, (3) the construction reduces dumping, and (4) eliminates reflux gastritis and offers satisfactory quality of life.

F89
Serum lipase, a better screening test for acute pancreatitis?

P G MCCULLOCH, S OATES, ROSALIND CAMPBELL, AND C W IMRIE (Departments of Surgery and Biochemistry, Royal Infirmary, Glasgow) Serum lipase concentrations rise during acute pancreatitis (AP). Complicated assay methods with poor reproducibility have hitherto minimised its value as an early diagnostic test, but more modern methods allow reassessment of this.

In a prospective trial involving 20 patients with AP and 20 age and sex matched controls admitted with severe acute abdominal pain of other origins, admission serum lipase was more frequently diagnostic than admission serum amylase (100% sensitivity vs 40%). Specificity was 100% for both assays and lipase estimations. There was a trend for higher lipase values to occur in patients
with pancreatitis associated with biliary tract disease compared with AP due to alcohol abuse, but this did not achieve significance (0·1>p>0·05, unpaired t test).

The assay used requires similar time and technical ability to that used for Phadebas amylase assay. Using modern methods with improved speed and reliability, initial serum lipase appears to be more sensitive than initial serum amylase in the early diagnosis of acute pancreatitis.

F90 Connective matrix changes after acute pancreatitis (AP) in the rat
L USCANGA, R H KENNEDY, R CHOUX, J A GRIMAUD, AND H SARLES (INSERM U 31, Marseille, and Institut Pasteur, Lyon, France) The changes following intrapancreatic ductal injection in rats of 0·2 mg of trypsin solution (n=12) or normal saline (n=12), were compared with a control group (n=12). Three animals from each group were killed at one, two, four, and eight days after operation and the tissue examined by light microscopy. Indirect immunofluorescence (IF) was used to label specific antihuman antibodies to collagen types I, III, pro-III, and IV, fibronectin and laminin.

Light microscopy in the control group was normal apart from slight oedema in two cases. After injection, acute oedematous pancreatitis occurred in 12 rats, all within four days. Perilobular and intralobular fibrosis was present at four days in four animals, but was minimal at eight days.

Immunofluorescence in the control group was normal. Fibronectin IF showed a strong amorphous reaction one day after injection in rats with AP. At four days it was colocalated with areas of fibrosis and at eight days the changes had disappeared. Collagen type III and pro-III reactions were markedly increased at four days, being colocalated with fibrosis and the fibronectin deposition. At eight days the reaction was again normal. In contrast, alterations in collagen types I, IV, and laminin IF were minimal.

Thus in the rat, AP produces an initial fibronectin deposition, followed by reversible type III/pro-III fibrosis. This may be analogous to man and would explain the lack of progression to chronic pancreatitis.

F91 Bile duct calibre – the value of ultrasonic and cholangiographic measurement in the postcholecystectomy patient
H J O’CONNOR, R J BARTLETT, J HAMILTON, W R ELLIS, J K WATTERS, D J LINTOTT, AND A R AXON (Gastroenterology Unit and Department of Radiology, General Infirmary, Leeds) The differential diagnosis of jaundice by ultrasound is based on measurement of bile duct diameter. In the postcholecystectomy patient, however, where ductal changes may result from previous disease or surgery, it is not known if assessment of bile duct calibre can be used to diagnose or exclude biliary tract obstruction. We have prospectively evaluated the role of ultrasound and the relation between ultrasound and radiographic bile duct measurements by performing dynamic biliary tract sonography on 50 symptomatic postcholecystectomy patients two to three hours before endoscopic retrograde cholangiography (ERC). At both examinations the maximum diameter of the extrahepatic bile duct and its site were recorded; the diagnosis of biliary tract obstruction was based on the cholangiographic findings. The mean maximum sonographic diameter was 7·9 mm (SD=3·3 mm) compared with 13·1 mm (SD=4·5 mm) at cholangiography (t test, p<0·001). The sonographic diameter was plotted against the corresponding ERC measurement and the correlation coefficient was 0·730. Twenty three of 37 patients shown to have duct dilatation at ERC (>10 mm) had biliary tract obstruction (predictive value, 62%) compared with 21 of 29 with sonographic (>6 mm) dilatation (predictive value, 72%). Eight of 13 patients shown not to have dilated ducts at ERC were not obstructed (predictive value, 62%) compared with 14 of 21 with non-dilatation at ultrasound (predictive value, 66%). We conclude that in the symptomatic postcholecystectomy patient, bile duct calibre assessed by ultrasound or ERC cannot be used to predict the presence of biliary tract obstruction and significant discrepancy exists between cholangiographic and sonographic bile duct measurements.

F92 Remission of symptoms and shrinkage of metastasis with long term treatment with somatostatin analogue
M E KRAENZLIN, J L C CH’NG, S M WOOD, AND S R BLOOM (Department of Medicine, Royal Postgraduate Medical School, London) Somatostatin is a potent inhibitor of peptide release and is potentially useful in the treatment of patients with peptide secreting tumours. The use of somatostatin has been limited, however, by its short half life. A long acting somatostatin analogue, SMS 201 995, has recently been developed for subcutaneous use. Short term administration of this analogue has shown an effective suppression of peptide secretion from pancreatic endocrine tumours. We have treated for eight months a patient with metastatic VIP-oma in whom the conventional measures of surgery, chemotherapy, and hepatic artery embolisation failed to control his severe life threatening diarrhoea. SMS 201 995 reduced the VIP secretion from the tumour considerably (mean before treatment with SMS, 361±91 pmol/l; mean on SMS, 161±68 pmol/l) and has prevented the torrential diarrhoea ever since. Serial computerised tomographic scanning has also now shown a marked reduction in the size of hepatic metastasis. Except for mild discomfort at the time of injection, no untoward effects of the SMS 201 995 have been observed.

The long acting somatostatin analogue SMS 201 995 provides a valuable new alternative treatment for the diarrhoea of VIP-omas. The absence of growth inhibitors may be as important as the role of growth factors in cancer formation and this agent may therefore offer more general tumour therapeutic possibilities.

F93 Congestive gastritis – a clinical and pathological entity
T T MCCORMACK, J GOEPEL, J M SIMMS, H KENNEDY, D R TRIGER, AND A G JOHNSON (University Departments of Surgery, Medicine and Pathology, Royal Hallamshire Hospital, Sheffield) Although oesophageal varices are the most common cause of haemorrhage in portal hypertension, gastritis is an important, though often unrecognised cause of blood loss. Over a four year period gastritis occurred in 61 of 123 patients with portal hypertension. Thirty one patients had mild transient gastritis and 30 patients had severe or persistent gastritis which caused clinically significant bleeding in 26 patients.
and accounted for 24.4% of the bleeds from all sources. Gastritis was independent of the type or severity of liver disease or the rise of wedged hepatic venous pressure. There was no difference in the age, sex, or the drugs prescribed in patients with or without gastritis but the mean follow up period and the number of sclerotherapy treatments was significantly greater (p<0.0005) in those with gastritis. Full thickness gastric biopsies in 18 patients (11 necropsy, seven surgical specimens) showed dilated and tortuous submucosal veins. Endoscopic biopsies in 13 of 23 patients showed some degree of mucosal vascular ectasia. The clinical and pathological evidence suggests that gastritis is caused by a congested mucosa. As injection sclerotherapy improves survival from variceal bleeding, congestive gastritis may become more common. The response to conventional (‘anti-erosive’) therapy is poor and the logical approach to treatment is a reduction of the gastric portal pressure by medical or surgical means.

**F94 Portal hypertension in precirrhotic liver disease**

D J VAN LEEUWEN, P J SCHEUER, SHEILA SHERLOCK, AND R DICK (Departments of Medicine, Surgery, Histopathology and Radiology, Royal Free Hospital and School of Medicine, London) This study assessed portal hypertension, as measured by the wedged hepatic venous pressure gradient, in patients with chronic hepatitis before the development of cirrhosis. Thirty seven patients were investigated. Liver biopsies were diagnosed by light microscopy as chronic active hepatitis (n=12), chronic active hepatitis in transition to cirrhosis (n=9), and cirrhosis (n=8). A control group showed minor changes including mild chronic persistent hepatitis (n=8).

Hepatic venous pressure gradients were measured with a balloon catheter using the femoral approach. The mean wedged hepatic venous pressure gradients and their standard deviations were 6.2±2.6 mm Hg in chronic active hepatitis, 10.3±4.8 mm Hg in chronic hepatitis in transition to cirrhosis and 15.4±7.1 mm Hg in cirrhosis, but only 3.4±1.4 mm Hg when minor changes were found, a figure in keeping with the accepted normal values for the pressure gradient. The differences between the groups were highly significant (p<0.005).

We conclude that (1) relatively minor alterations of hepatic architecture as seen in chronic active hepatitis without cirrhosis may be accompanied by a significant degree of portal hypertension. (2) The pressure pattern reflects the progression of disease. (3) Pressure gradients might be a useful method of monitoring the efficacy of drugs intended to prevent the development of portal hypertension in chronic hepatitis.

**F95 Observer variation in the endoscopic assessment of oesophageal and gastric varices**

A THEODOSI, D WESTABY, B R MACDOUGALL, AND R WILLIAMS (Liver Unit, King’s College Hospital, London and MRC Biostatistics Unit, Cambridge) The presence of large and small varices has been suggested as a risk factor to predict bleeding, and has been used to select patients for prophylactic therapy. To validate the grading of varices it is important to show a close agreement between different observers with respect to such assessment. To investigate the extent of this agreement, three experienced observers independently assessed, at endoscopy, the varices of 28 patients with portal hypertension. After passing the endoscope the patients were examined by each observer who noted the presence or absence of oesophageal and gastric varices; the number of cords of oesophageal varices and the size of the largest varix (graded small or large) using the gastro-oesophageal junction as the reference point. In only one instance were varices stated to be absent by one observer and present by the other two observers. Exact agreement on the number of variceal cords present occurred in 33 (40%) of the 84 comparisons with a difference of two or more cords between any two observers in 12 instances (14%). Using Kappa statistics, the agreement on the presence or absence of gastric varices was no better than expected by chance alone. With respect to variceal size, agreement occurred in 74% of comparisons, with a Kappa value of 0.37; significantly better than expected by chance. In practical terms, however, the use of variceal size to select patients for treatment would lead to disagreement between two observers on management in one in four cases.

**F96 Factors affecting variceal recurrence after endoscopic sclerotherapy**

**J D R ROSE AND P M SMITH** (Department of Gastroenterology, Llandough Hospital, Penarth, S Glam) Fifty patients, (mean age 54-6 years, range 17-77 years) have been followed for 1184 patient months (mean 23.7 months) after endoscopic sclerosis of oesophageal varices; 64% more than one year, 40% more than two years and 12% more than three years. All eight non-cirrhotics were Child’s grade A and of the cirrhotics 21 were grade A, 14 B and 7 C at the time of initial treatment. Thirteen cirrhotics died, seven of hepatic failure, three of infection, two of gastric bleeding and one of hepatoma. The probability of survival was 0.84 at one year, 0.75 at two and 0.63 at three years and was worse for primary biliary cirrhosis (PBC) compared with the eight non-cirrhotics (Gehan statistic=3.94, p<0.05). The three year survival for 10 cryptogenic, 19 alcoholic and the 10 patients with PBC was 0.88, 0.75 and 0.17 respectively. The survival of cirrhotics with different Child’s grades was, however, similar.

Of 11 episodes of haemorrhage in 10 patients, only three were from recurrent varices, all in grade A patients – a risk of 0.0025 variceal bleeds/patient month. In 20 varices patients recurred, 85% within the first year, unaffected by Child’s grade but recurring more in patients with PBC than in non-cirrhotics (Gehan statistic=4.11, p<0.05).

Mortality and variceal recurrence after sclerotherapy are determined by the patient’s diagnosis rather than the initial Child’s grade. Bleeding is three times as common from sources other than varices after successful sclerotherapy, and variceal recurrence after the first year is rare.

**F97 Results of oesophageal staple transection for acute variceal haemorrhage in a series of 53 patients**

G HAMILTON AND K E F HOBBS (Academic Department of Surgery, Royal Free Hospital School of Medicine, Pond Street, London) The results of treatment by oesophageal staple transection (OST) of acute variceal haemorrhage uncontrolled by conservative means were analysed. Of the 53 patients treated there were 18 postoperative deaths (34%; Child’s B – two; Child’s C – 16); two patients were lost to follow up. Sixteen patients have not rebled with a mean survival of 21 months (48-5%). Using Life Table Analysis, survival without rebleeding was 75% at six
months, 52% at one year, 33% at 18 months and 27% at two years. In the 17 patients who rebled the mean time before reblooding was 8-4 months. Of the patients who rebled there were none in Child's C group (Child's A – five; Child's B – 12), but of those who did not rebled, seven were in Child's C group (Child's A – six; Child's B – three).

Oesophageal staple transection is a procedure which will stop acute variceal haemorrhage irrespective of the severity of liver disease, with a reduction in the reblooding rate at one year. Injection sclerotherapy (IS) for acute bleeding is technically difficult, requiring multiple procedures in the majority of patients, has a similar mortality and carries a complication rate of up to 55%. These results suggest that OST compares favourably with IS in management of variceal haemorrhage and requires further evaluation by prospective randomised trial.

F98 Effect of sclerosants used in oesophageal sclerotherapy on vein and muscle
J D R Rose (Department of Gastroenterology, Llandough Hospital, South Glamorgan) It is inevitable that during variceal injection sclerosants will extravasate. Their effect on vein and muscle has been examined in 46 rats by perivenous injections of physiological saline, 3% sodium tetradecyl sulphate (STD), 5% ethanolamine olate and 5% hydroxy polyethoxy dodecanoic acid made next to the femoral vein and compared with intravenous injections of saline and STD. The neurovascular bundle and adjacent muscle were removed at 30 minutes, two, six, 12 and 24 hours, three and seven days, four and eight weeks and examined histologically.

Intravenous saline produced no change but after perivenous injection there was transient inflammation from six and 12 hours. Intravenous STD produced thrombosis from 30 minutes onwards with an increase in perivasculare connective tissue and conversion of the veins to fibrous cords with haemosiderin-containing macrophages. There was no muscle necrosis. The changes after extravasation of all three sclerosants were indistinguishable: immediate oedema of muscle and perivenous tissue with infiltration of polymorphs at two hours and necrosis of muscle maximal at seven days. Thrombosis occurred initially but after three days had disappeared. Overlying connective tissue was considerably thickened. Fibroblast conversion of necrotic muscle was begun by seven days and complete by four weeks.

Extravasated sclerosants increase connective tissue around veins, which they do not thrombose and are extremely damaging to muscle.

F99 Peptide YY, a new gut hormone, distribution in the human intestine
T E Adrian, A J Bacarese-Hamilton, G-L Ferrer, J K Polak, and S R Bloom (Department of Medicine and Histochemistry, Royal Postgraduate Medical School, London) Peptide YY (PYY) is a newly discovered 36 amino acid peptide localised to endocrine cells of the intestinal tract; low dose infusion of PYY in man causes a substantial reduction of pentagastrin stimulated, gastric acid and pepsin secretion.

The distribution of PYY in the human gastrointestinal tract was measured in surgical tissues using a specific radioimmunoassay. PYY was found throughout the lower intestine with concentrations increasing distally (ileum 68±6 pmol/g, n=4; ascending colon 51±6, n=5; sigmoid colon 176±34, n=6; rectum 528±69, n=8) PYY was undetectable (<3 pmol/g) in the fundus, antrum, duodenum and jejunum.

Layer separation of bowel showed that the PYY immunoreactivity was localised to the mucosal epithelium. High resolution, isocratic, reverse phase HPLC of human gut, revealed a single, major peak of PYY-like immunoreactivity which eluted in an identical position to the porcine standard, suggesting that the human peptide may be identical to that already isolated from the pig.

Thus the new hormone PYY is present in very high concentrations in the large bowel. The further investigation of the role of this peptide may help explain colonic influence on digestive function.

F100 Effect of truncal vagotomy and pyloroplasty and of highly selective vagotomy alone, on gall bladder emptying dynamics: a prospective study
W A Brough, T V Taylor, and H B Torrance (Department of Surgical Gastroenterology, Manchester Royal Infirmary, Oxford Road, Manchester) Duodenogastric reflux is increased after vagotomy with pyloroplasty, cholecystectomy, and gastric surgery. Eighty four patients have been studied using 99mTc-EHIDA, measuring the bilirubin output of resting gastric juice, frequency and amount of duodenogastric reflux. The patients were divided into six groups: Asymptomatic controls (n=10); vagotomy with pyloroplasty (VP, n=15); vagotomy with pyloroplasty and cholecystectomy (VPC, n=15); modified highly selective vagotomy (HSV, n=15); modified HSV and cholecystectomy (HSV C, n=9) and cholecystectomy alone (n=20).
Symptomatic patients after VP showed a significant increase in amount of duodenogastric reflux (control p<0.002, HSV p<0.002). VPC showed a significant increase in the refluxate in the symptomatic patients when compared with VP (p<0.002) but not when compared with patients after cholecystectomy. The HSV group, with pyloric preservation showed no significant difference in frequency or amount of reflux, but the addition of cholecystectomy resulted in a highly significant increase in both amount (p<0.001) and frequency (p<0.001) of reflux. This study shows that cholecystectomy alone, and when in combination with either pylorus preserving or deforming procedures can lead to increased duodenogastric reflux. We suggest that such increased reflux may be a critical factor in the pathogenesis of bile gastritis after surgery.

F102
Epigastric impudence: a non-invasive method of monitoring gastric volume?

J A SUTTON, SYLVIA THOMPSON, D LEVINE, AND R SOBNACK (Human Pharmacology Unit, Beecham Pharmaceuticals, Harlow, Essex, and The Medical Unit and Radioisotope Department, The London Hospital, London) Impedance is an established, non-invasive and sensitive method of monitoring rates of change in cardiac or lung volumes which logically is applicable equally to the stomach. We measured impedance changes in a 100 KHz, 4 mA current passing between two pairs of Ag/AgCl skin electrodes positioned so that the stomach lay between them. When volunteers drank water or orange squash (conductivity 0.2–1.1 mS) large impedance increases 1–4 Ω occurred during gastric filling. Then followed a gradual decline, the rates and monoexponential patterns of which suggested that it reflected the dispersal of the meal from the stomach.

This decline was compared simultaneously with a dye-dilution method in five fasting volunteers in a 40–45° semi-recumbent position. Impedance group mean half-emptying (xt1) of water of 6.7, SD 2.8 min was statistically comparable with dye-dilution (4.2, SD 3.2 min). For 5% glucose solutions both methods recorded an equally statistically significant slowing (xt1 was 12.1, SD 7.7 min and 12.0, SD 10.9 min respectively). In a radioisotope imaging comparison 150 μCi 99mTc DTPA was mixed 600 ml dilute orange cordial. The six male volunteers lay flat, drinking the meal through a wide-bore tube. xt1 was 30-4, SD 14-3 min and 35-2, SD 17-7 min for impedance and 99mTc respectively (uncorrected for tissue attenuation). Within-subject correlations were good. In eight normal volunteers metoprololamide 10 mg iv produced xt1 of 7-5, SD 6-9 min in a within-subject crossover comparison with placebo (13-5, SD 12-8 min: p<0.04 Student’s t test).

The non-invasiveness of epigastric impedance permits serial assessments of drug effects or surgery. Equipment is relatively inexpensive and produces a full emptying pattern in real-time, ideal attributes for a practical outpatient screening method.

F103
Prospective testing of a scoring system to predict the individual risk of serious pathology in patients undergoing GI endoscopy

G HOLDSKOV, C PATEL, AND M HARMAN (Southampton General Hospital, Southampton) A recently described scoring system to assess the individual risk of finding serious pathology in patients undergoing endoscopy has been prospectively tested in two hospitals with differing endoscopic practice. A total of 749 patients were studied. The six features which are involved are age, sex, smoking habits, and a history of vomiting, prior peptic ulcer or hiatus hernia. Patients referred to an open access system were found to have significantly lower scores than those referred to a hospital-based one (p<0.006), mirroring the incidence of serious pathology in the two units (24% vs 34% p<0.007). The incidence of serious pathology varied from 1.5% in those patients scoring less than 350 points to 70% in those scoring more than 650 points. By utilising the system and limiting examination to those patients with a score of more than 400, 23% fewer endoscopies would be performed and only 2.5% with major pathology missed. Restriction to a score of more than 450 would result in a 43% reduction examination and 15.6% of major pathology being missed, but would still result in all malignant disease being detected. To date, 70 patients with GI malignancy have been studied and all scored more than 464 (mean 584±56), compared with a mean score of 444±99 for patients in whom no abnormality was detected. A simple table is described which allows for easy calculation of individual score without the use of a computer. It is suggested that the scoring system can be used as a guide to the value of endoscopy in individual patients and that it allows for rational development of open access endoscopy service.

F104
Therapeutic peritoneal lavage in patients with severe acute pancreatitis

A D MAYER, M J MCMAHON, A P CORFIELD, M J COOPER, R C N WILLIAMSON, A P DIXON, M G SHEARER, AND C W IMRIE (The General Infirmary, Leeds, The Royal Infirmary, Bristol and The Royal Infirmary, Glasgow) Peritoneal lavage therapy for severe acute pancreatitis was evaluated in a multicentre, prospective, controlled clinical trial. Patients referred to the study from 24 hospitals were assessed by an investigator from one of three participating centres and were entered into the study if they fulfilled laboratory criteria of severe pancreatitis or if more than 20 ml of ascitic fluid or dark coloured ascitic or lavage fluid was found on diagnostic peritoneal lavage. Patients randomised to the control group received intensive conservative treatment including monitoring of arterial oxygen and central venous pressure. Patients randomised to the treatment group received, in addition, continuous peritoneal lavage (2 litres of dialysis solution hourly) for three days. Seventy nine patients were included in the study. There were 12 deaths (29%) and 14 major complications (34%) in the 41 patients in the control group and 11 deaths (29%) and 11 major complications (29%) in the 38 patients in the treatment group. Eight of the deaths in the control group (67%) occurred within 10 days of admission compared with five (46%) in the treatment group (NS). The probability that a 50% reduction in mortality had been achieved in the treatment group was 2%. The results indicate that the regime of therapeutic peritoneal lavage used in this study may delay death from severe acute pancreatitis but does not reduce overall mortality.

F105
Symptomatic gall stone disease: before and after cholecystectomy

T BATES, J C MERCER, AND M HARRISON (The William Harvey Hospital, Ashford, Kent) In a prospective study of gall stone disease
115 consecutive patients who were considered to have gallstone-related symptoms completed a questionnaire before cholecystectomy was carried out. One year later they were sent a follow-up questionnaire which was completed by all but three patients who had died of unrelated causes.

Previous hospital admission for gallstone disease had occurred in 39 patients (34%) and the majority had had periods of time off work or being unable to cope at home. All patients had more or less typical biliary pain preoperatively although jaundice was the presenting symptom in 15 patients (13%). Postoperative recovery was slow in that 62% of patients did not return to work or resume normal household activities within six weeks of their operation.

Twelve months after cholecystectomy 49 patients (43%) still rated their operation less than completely successful. The commonest persisting symptoms were excessive flatulence (47%), indigestion (46%), abdominal distention (33%), and nausea (23%), although when these had been mentioned specifically before the operation it had been explained to the patient that they would probably not be relieved by cholecystectomy. Abdominal pain, however, most often in or deep to the scar, persisted in 27% of patients. Twenty-two (19%) had consulted their general practitioner for persisting symptoms and nine had been referred back to hospital.

It is concluded that even when cholecystectomy is limited to patients with typical biliary pain or jaundice, nearly half of them still have some symptoms a year later.

Operative cholangiography on selected patients – a safe alternative to routine use?

J P Linehan, A J Spriggins, P B Boulos, and C G Clark (Department of Surgery, Faculty of Clinical Sciences, University College London, The Rayne Institute, University Street, London) Operative cholangiography (OPC) is intended to define stones in the biliary tree and also to avoid unnecessary common bile duct exploration (CBD) which is known to increase mortality threefold. Its cost effectiveness, however, is disputed as 85% of routine OPC shows no abnormality. The former method of applying clinical criteria in selecting cases for OPC has been disregarded and had not been carefully evaluated. We have therefore examined retrospectively the feasibility of adopting such an approach by correlating defined clinical indications with the findings on OPC to determine whether a more selective OPC can be used.

Preoperative criteria (history of jaundice or pancreatitis, abnormal liver function tests, ultrasound or radiological evidence of CBD stones) and operative criteria (small stones, wide cystic or CBD, palpable stones in CBD) were used to divide patients into those in whom OPC was mandatory and those in whom it was not. Of 129 patients studied, 45 (35%) would not have required OPC, all had normal cholangiograms. In 84 (65%) OPC was indicated because of either preoperative (70%) or operative (30%) criteria but only 22 (26%) proved to have CBD stones on cholangiography. There were no demonstrable differences in clinical criteria in the remaining 62 patients in this group to explain the discrepancy on the cholangiographic findings.

These results show that by adopting such a policy, unnecessary OPC can safely be avoided in a third of routine cholecystectomies. This made the detection rate of CBD stones higher, 26% compared with 17% on routine OPC in this series, and avoided unnecessary exploration in the majority to justify its use in these selected cases.

Gastric antisecretory and cytoprotective activity of MDL 646, a new PGE₄ analog, in man

G Bianchi Porro, M Petrillo, M Lazzaroni, L M Fuccella, and D Sassella (Gastrointestinal Unit, L Sacco Hospital, Lepetit Research Labs, Milan, Italy) MDL 646 is a 16-methyl-16 methoxy PGE₄ analog which has been shown to inhibit gastric acid secretion and to protect the gastric mucosa against the damaging effects of indomethacin, alcohol and stress in various experimental animals.

No change in blood pressure or heart rate nor any important side effects were observed in a preliminary single oral rising dose tolerability study carried out in 18 healthy subjects given 1-400 mcg of the compound.

The efficacy of MDL 646 in reducing pentagastrin stimulated acid secretion was investigated in a randomised single blind placebo controlled crossover study carried out in 10 healthy male subjects given single oral rising doses (32-56 years) in the range 500-1000 mcg. The minimal antisecretory dose was found to be 800 mcg, which caused a 25% decrease of acid output within 2 h after administration, with maximal inhibition during the first hour. The results obtained with 1000 mcg suggest
a dose-dependence of both the entity of inhibition and the duration of action (about 36% and 2 h respectively after 1000 mg).

In another randomised single blind, placebo controlled crossover study, carried out in eight male healthy subjects (30–72 years), we tested the effect of single oral doses of 500 mg of MDL 646 in preventing the fall in gastric potential difference (PD) induced by intragastric instillation of 600 mg of aspirin. After pretreatment with placebo, within 10 min after aspirin administration, PD decreased by about 26% and started recovering only one hour later. MDL 646 completely prevented this aspirin induced drop in potential difference, which on the contrary was maintained above baseline values for the whole duration of the test (one hour after aspirin challenge). No side effects nor changes in bowel habits were reported in either study.

We conclude that MDL 646, because of its antisecretory and cytoprotective activity, is a potential antulcer agent and is warrant of further investigation.

We conclude that ranitidine 300 mg as a single night time dose for the healing of DU is at least as good – and probably better – than the conventional 150 mg bid. The trial also highlights the importance of overnight gastric acidity in DU.

**F11 Intragastric bacteria, nitrate, nitrite, and n-nitroso compounds before and after treatment with omeprazole**

B K SHARMA, J A SANTANA, R P WALT, R E POUNDER, M PEREIRA, P NOONE, P L R SMITH, AND C L WALTERS (Academic Department of Medicine and Department of Microbiology, Royal Free Hospital, London, and Leatherhead Food Research Association, Surrey) Omeprazole is a potent inhibitor of gastric acid secretion. Omeprazole 30 mg/day raises median 24 hour intragastric pH from 1.4 to 5.3 in duodenal ulcer patients. The object of this study was to measure the bacterial flora, and the nitrate, nitrite, and N-nitroso compound concentrations, of gastric contents before and after omeprazole treatment.

Ten healthy male volunteers were studied before treatment, and one, four, seven, 10, and 16 days after 14 daily doses of omeprazole 30 mg taken at 0900 h. The subjects ate a standard meal at 1730 h and were intubated at 2030 h. The pH of aliquots of gastric juice was measured hourly from 2100 to 0700 h. The samples of gastric juice aspirated at 0700 h were cultured for bacterial growth and also analysed for nitrate, nitrite and N-nitroso compound concentration.

After 14 days of treatment with omeprazole 30 mg/day, mean nocturnal intragastric acidity in these healthy volunteers was decreased by 76%. The number of bacteria in the gastric juice was only raised for 24 hours after the last dose of omeprazole. Similarly, mean intragastric nitrite and N-nitroso compound concentrations were raised one day after cessation of treatment with omeprazole (14-fold and four-fold, respectively), but three days later they were not significantly different from the before treatment values. Intragastric nitrate concentration was not affected by treatment with omeprazole.

The results of this study show that during treatment with omeprazole there is an increase in the number of bacteria in the stomach, with increases of nitrite and N-nitroso compound concentration. The changes, however, disappear within three days of stopping treatment.
Evaluation of the nitrosamine hypothesis of gastric carcinogenesis in man

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Hypochlorhydric conditions such as PolyA gastrectomy (PG) and pernicious anaemia (PA) predispose to gastric cancer. According to the nitrosamine hypothesis, high intragastric pH leads to overgrowth of bacteria, which convert nitrate into nitrite, and then nitrite plus dietary amines into carcinogenic N-nitroso compounds. We have studied nine PG eight PA and nine matched control subjects by hourly measurement of intragastric pH, bacteria (total and nitrate-reducing), nitrite and N-nitroso compounds (total and stable) over a 24 hour period. Clear differences were not apparent between controls and PG or PA, because the control and PG groups were heterogeneous for gastric acidity. Although 8/8 PA subjects were hypochlorhydric (intragastric pH >4 for >50% of the time), only 5/9 PG subjects and 2/9 control subjects were hypochlorhydric. When subjects were rearranged into hypochlorhydric (n=15) and acidic (n=11) groups, bacterial counts (p<0.01) and nitrite concentrations (p<0.01) were higher, whereas total and stable N-nitroso compounds tended to be lower in the hypochlorhydric group (NS). In individual subjects we found a positive association between pH and both total and nitrate-reducing bacterial counts (r=0.82, p=0.001) and between pH and nitrite concentrations (r=0.61, p<0.001). By contrast, a negative association was found between pH and both total (r=0.52, p<0.01) and stable (r=0.74, p<0.001) N-nitroso compound concentrations. We conclude that, although hypochlorhydria predisposes to bacterial proliferation and nitrite generation, it does not enhance nitrosation. Thus, the nitrosamine hypothesis that bacteria mediate nitrosation at high intragastric pH is not supported.

9Tcm red cell scintigraphy and rebleeding from peptic ulcers

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Patients who rebleed from peptic ulcers constitute a 'high risk' group and their early identification would be desirable. We have evaluated the technique of 99Tcm red cell scintigraphy as a means of identifying patients at risk of significant rebleeding.

Any patient admitted to hospital with haematemesis or melena in whom endoscopy within 24 hours of admission showed a peptic ulcer was eligible for the study. Following endoscopy the patient's red blood cells were labelled in vivo with 750 MBq 99Tcm and scintigrams were obtained at least once in the succeeding 24 hours.

Twenty seven patients have been studied to date. Eighteen (67%) had scintigraphic evidence of rebleeding. The rebleeding was clinically significant in seven patients (in four of whom the scintigraphic evidence of rebleeding antedated the clinical evidence) and four of them required emergency surgery. Nine (33%) patients had negative scintigrams and none of these bled clinically during hospital admission.

Of the patients with positive scans 14 (77%) had either active oozing or clot in the base of their ulcers at endoscopy including five of the seven who rebled clinically. Two of the patients with negative scans (22%) had clot in their ulcers at endoscopy.

These results show that rebleeding is common, occurring in as many as 67% of patients admitted with bleeding peptic ulcers, although this is often not clinically manifest. 99Tcm red cell scintigraphy may be more reliable than endoscopic stigmata as a means of predicting which patients are liable to significant rebleeding.

Somatostatin or surgery for massive upper gastrointestinal haemorrhage?

I MAGNUSSON, T IHRE, C JOHANSSON, U SELIGSON, S TÖRNGREN, AND K UVNÄSMOBERG (Department of Surgery, Södersjukhuset, Stockholm and Department of Pharmacology, Karolinska Institutet, Stockholm, Sweden) A randomised double-blind trial of somatostatin (SST) in the treatment of massive upper gastrointestinal bleeding from peptic disorders has been performed in 95 consecutive patients during a 28 months period. All patients were endoscoped within eight hours of admission to the hospital, whereupon the source of bleeding and types of stigmata were assessed. Forty six patients were given a 72 hour infusion of SST, 250 μg/h, and 49 received infusion of placebo. No additional treatment except blood was given. The two groups were well matched regarding sex, age, and source of bleeding. On the day after admission, a control endoscopy was done.

A total of five patients in the SST-group and 14 in the placebo group were operated on (χ² p<0.05). Rebleeding occurred in six patients in the SST-group, of which five experienced rebleeding after completion of the SST treatment. In the placebo group rebleeding occurred in five patients, of which four rebled on the day after admission. The need of blood transfusions and the mortality rate did not differ between the two groups. No toxic side effects were found as a result of the infusion of SST.

In conclusion, SST significantly reduced the number of emergency operations in cases of massive upper gastrointestinal bleeding. The protective effect of SST against bleeding was also indicated by the finding that rebleeding in the SST-group occurred when the infusion of SST was completed.

Psychiatric assessment of patients with severe constipation

D M PRESTON, J M PFEFFER, AND J E LENNARD-JONES (St Mark's Hospital, London and The London Hospital, Whitechapel, London) Women with severe constipation often appear to have a personality disorder. We therefore studied a series of 20 consecutive patients (Mean age 24-5 years) who complained of severe constipation and who had a normal barium enemas but slow whole gut transit time. As a disease control group 20 patients with Crohn's disease matched for age, sex, length of history and number of hospital admissions were also studied. These groups were compared with a normal population of young women using the Crown Crisp Experiential Index (CCEI) and the Hostility and Direction of Hostility Questionnaire (HDHQ). They also completed the General Health Questionnaire (GHQ) and a Quality of Life Questionnaire (QLQ). On the CCEI patients with constipation showed less
phobic anxiety (p<0.01) than normals and patients with Crohn’s disease. In contrast, the Crohn’s disease patients showed more free-floating anxiety (p<0.05) and phobic anxiety (p<0.01) than normal subjects and significantly more obsessiolanility than the constipated patients (p<0.02). Both disease groups had more somatic anxiety than normal subjects. On the HDHQ the Crohn’s disease group showed an abnormal degree of inwardly directed hostility whereas the constipated group were normal (p<0.005). There were no significant differences between the two groups on the GHQ or the QLO.

The constipated patients were interviewed by a consultant psychiatrist who found a very high incidence of a disturbed childhood, psychosexual problems, and personality difficulties. These findings which correspond with the impression of most clinicians are, however, at variance with the assessment by questionnaire which showed a minimal deviation from normal, in contrast with another group of patients with a similar degree of disability from a gut disorder.

Daily stool weight which rose during bran treatment (bran, mean=148 g; placebo, mean=125 g) was significantly correlated with dietary fibre intake (p<0.05). After the initial three months therapy, there was no significant differences in total symptom scores between the bran and placebo treated groups, but there were significant improvements in symptom scores compared with pretreatment in both the bran treated (p<0.01, n=14) and placebo treated (p<0.05, n=14) groups. When crossover data were combined – that is, n=28 – separate and total symptom scores after three months treatment with bran did not differ from those after treatment with placebo.

We conclude that these data suggest that there are similar symptomatic improvements with both treatments and do not support the contention that bran is specifically efficacious in IBS.

F116

Is bran efficacious in irritable bowel syndrome?

M R LUCY, M L CLARK, J LOWNDES, AND A M DAWSON (Departments of Gastroenterology and Medical Electronics, St Bartholomew’s Hospital, London) Despite widespread use, it is uncertain whether addition of dietary fibre is efficacious in irritable bowel syndrome (IBS). We therefore conducted a double blind placebo controlled crossover trial of fibre supplements in patients with classical IBS. Patients were asked to add to their normal diet a daily supplement of either 12 bran biscuits (1=0.87 g fibre) or 12 placebo biscuits (1=0.29 g fibre) each for three months. Biscuits were given in random order with crossover to the second biscuits at three months. Assessment of dietary fibre intake and symptoms were made monthly and a score for single and total symptoms reckoned. Three day stool collection were made at three and six months. Twenty eight patients completed the study. Their age (median 32 years, range 22–78; 19 women, nine men) duration of symptoms (median 60 months, range 2–360) initial total symptom score and random allocation of treatment did not differ from the 16 patients who withdrew.

F117

Fimbriae of colonisation factor antigen II positive enterotoxigenic Escherichia coli: morphology and role in mucosal adherence

S KNUTTON, D R LLOYD, P RISTAINO, AND M M LEVINE (INTRODUCED BY A S MCNEISH) (Institute of Child Health, University of Birmingham, Edgbaston, Birmingham and Centre for Vaccine Development, University of Maryland, Baltimore, USA) Three different surface antigens designated coli surface-associated antigens CS1, CS2 and CS3 have been identified in enterotoxigenic Escherichia coli (ETEC) bearing colonisation factor antigen II (CFA/II). CS1 and CS2 have been shown to be fimbrial in nature but the morphology of CS3 has not been described. ETEC of serotype 06:H16, biotype A possessing CS1 and CS3 and ETEC of serotype 08:H9 possessing only CS3 have been examined by electron microscopy and for their ability to adhere to human intestinal mucosa and to isolated human enterocytes. Both on bacteria (06:H16, biotype A and 08:H9 strains) and in the pure state CS3 has been found to consist of thin (2 nm) flexible fibrillar fimbriae. In contrast, CS1 exist as wider (6 nm) rigid fimbriae on the surface of 06:H16 biotype A strains. Using monospecific antisera to CS1 and CS3 and immuno gold labelling CS1 and CS3 were found to be immunologically as well as morphologically distinct.

In an enterocyte adhesion assay, 06:H16, biotype A and 08:H9 ETEC strains possessing CS1 and CS3 were found to adhere to the brush border of isolated human duodenal enterocytes to a much greater extent (2.2 and 1.7 bacteria/brush border respectively) than the same strains grown at 18°C which lack CS1 and CS3 (0 bacteria/brush border). In the same assay adhesion of a CFA/I producing 078:H11 ETEC strain was 2-1 bacteria/brush border. Immunoelectron microscopy of human colonic enterocytes and adherent bacteria show that CS1 and CS3 fimbrial antigens both function to promote brush border attachment of bacteria and are thus both probably important in pathogenesis.

F118

Sigmoid hypermotility is not a feature of the irritable bowel syndrome (IBS)

I F TROTMAN AND J J MISIEWICZ. (Department of Gastroenterology, Central Middlesex Hospital, London) Colonic hypermotility is believed to be the basis of IBS. In contrast with previous work manometric studies in the true sigmoid colon were done in 20 subjects with IBS (11 women: nine men; median age 43 years, range 22–77 years) and compared with 13 controls (six women: seven men; median age 49 years, range 25–80). Basal and standard meal stimulated intraluminal pressures were recorded with four perfused tubes positioned at colonoscopy 25–55 cm from the anus. Records were analysed for per cent activity and median maximal amplitude and a motility index (MI) derived as their product. All the IBS patients had abdominal pain, 17 bloating, and 10 alternating constipation/diarrhoea. All were symptomatic at the time of study and medication was stopped 48 h previously. Controls underwent colonoscopy for polyp check (five), rectal bleeding (five) and inconclusive barium enemas (three). All were asymptomatic. Colonoscopy was normal in both patients and controls. The meal equally and effectively stimulated MI in both groups (p<0.01). Mean log MI was significantly lower in IBS before (IBS=3.10±0.46; control=3.46±0.22; p<0.02) and after the meal (IBS=3.38±0.49; control=3.69±0.156; p<0.01). Taking control mean log MI±2 SD as the normal range, sigmoid hypermotility was present in only two of 20 IBS patients, while in nine the MI was below the lower limit of normal. These results suggest that colonic hypermotility is not a feature of IBS.
Treatment of irritable bowel syndrome with domperidone and pinaverium bromide

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We tested the therapeutic effect of the dopamine receptor antagonist domperidone (D) and the antispasmodic pinaverium bromide (P) in a randomised double blind crossover trial. Twenty two consecutive patients (11 men, 11 women, aged 19-54 years) with irritable bowel syndrome (IBS) entered the study and were prescribed bran 30 g/day for the two weeks preceding and throughout the therapeutic trial. In the first three weeks, 11 randomly selected patients received D (10 mg tid) whereas the others received P (50 mg tid). After a seven day washout interval, the patients switched treatment for the second three week period. Patients graded the severity of their symptoms on an analogue scale before starting the study, after bran only and at the end of each treatment period. A higher score (range 0-10) indicates a more severe symptom.

Abdominal pain decreased from 3.07±0.50 (±SE) before treatment (B) to 1.12±0.37 after D (p<0.01, Student's t test) and to 1.89±0.57 after P. Abdominal distension improved from 4.39±0.61 (B) to 2.01±0.41 after D (p<0.01) and to 2.51±0.57 after P (p<0.05). Flatulence decreased from 3.95±0.64 (B) to 2.41±0.42 after D (p<0.05) and to 2.23±0.61 after P. Treatment with bran only did not alter symptoms significantly, while D and P reduced symptoms to 48% (p<0.001) and 60% (p<0.05) of the baseline scores respectively. Side effects were rare and generally mild for both drugs. In conclusion D significantly improved symptoms of IBS; P was also found to be effective, though to a lesser extent.

Fat and fibre restriction is not helpful in the short bowel syndrome

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Patients with a short small intestine have been recommended a low fat diet with the aim of reducing the volume of diarrhoea and calcium and magnesium losses but this practice has recently been challenged. To determine whether the amount of fat or fibre in a diet was an important factor in fluid, calorie and mineral balance three whole food diets were constructed to contain (1) normal fat (68-106 g), high fibre (26-29 g), (2) reduced fat (42-51 g), high fibre (24-29g) and (3) reduced fat (39-46 g), normal fibre (11-15 g) daily while maintaining fluid input constant, and with an oral supplement of 12 mmol magnesium daily. Four patients with a residual jejunum of 60-150 cm ending in a terminal stoma took each of the diets in random order for two days. Twenty four hour collections were made of stoma effluent and urine. The wet weights (mean ± SEM) of effluent on diets (1), (2) and (3) were 3093±658 g, 3070±607 g, 3330±462 g and dry weights 248.6±47.3 g, 224.1±37.4 g and 234.6±26.7 g respectively. Calorie absorption by bomb calorimetry as a percentage of those available was 42.7±6.8%, 44.7±7.2% and 43.9±5.4% respectively, but absolute calorie absorption tended to be greater on the normal fat diet. Fat losses tended to be higher on the normal fat diet, 43.5±6.8 g compared with 21.9±3.2 g and 22.8±3.7 g on the reduced fat diets. Magnesium excretion was similar on all diets, 18.2±2.1, 19.1±1.5 and 16.2±1.9 mmol/day respectively, and all patients remained in positive balance. Calcium excretion was more variable between patients but three of the four maintained positive calcium balance on all diets. This study suggests that patients with a short small intestine should be allowed to take fat normally to improve palatability of the diet and to increase total calorie intake.

Home parenteral nutrition

R H White and M H Irving (Department of Surgery, Hope Hospital, (University of Manchester School of Medicine), Salford) Between October 1978 and November 1983 Hope Hospital home parenteral nutrition (HPN) programme treated 32 patients, 17 women and 15 men. The mean age of the patients was 36.09 years and ranged from 14.5 to 76.2 years. The primary disease was Crohn's disease in 19 cases, mesenteric vascular disease in four, and radiation enteritis in one. A further seven patients had varied pathologies. The primary disorder was complicated by the short bowel syndrome in 13 instances, enterocutaneous fistula in 13.

Apart from three patients who were unemployed, all were involved in some occupation before starting HPN, and once on the programme two-thirds returned to work, 16 of these full time and six part time.

Strict protocols are observed for insertion and care of central feeding lines. Feeding catheters are inserted in the operating theatre with full surgical aseptic technique. Under the direction of the staff of the nutrition unit patients rapidly acquire techniques for connecting and disconnecting their nutrition, dressing the lines and heparin locking catheters. Using these methods only two patients have had catheter sepsis and metabolic problems have been minimal. Sixteen patients have completed HPN, the mean duration of therapy being 124-75 days (range 9-503). Nine of these have returned to a normal diet, five due to adaptation of short bowel and four to closure of fistula. There were five deaths (15-6%), three unrelated to their disease or HPN and two related to their disease alone. Mean duration of HPN for those still on the programme was 326-63 days range 20-1293 days. Home parenteral nutrition is a valuable treatment for both short and long term intestinal failure.

Body composition in ileostomy patients with and without ileal resection

J C Cooper, A Laughland, L Burkinshaw, and N S Williams (University Department of Surgery, The General Infirmary, Leeds) Recent evidence suggests that modest ileal resection (IR) during protecocolectomy (PC) results in malabsorption of fat and nitrogen, in addition to water and electrolytes. Serious nutritional deficits may thus ensue.

Body composition (BC) was therefore studied in nine ileostomy patients (resected group: mean ± SD: age 43±17 y; height 172±14 cm; M:F 4:5) who had undergone significant IR (70±28 cm range 50-120 cm), and nine ileostomy patients (control group: age 43±13 y; height 170±9 cm; M:F 4:5) who had undergone minimal IR (4±3 cm p<0.001). Time since operation was similar (resected 5±6±4:9 y, controls 7:3±4:5 y) Values were compared with predicted values for normal subjects, based on age, sex and height. All patients (17 ulcerative colitis, one Crohn's disease) had undergone PC and had a normal residual small bowel.

Body weight and 24 hour ileostomy volumes were determined. Total body
nitrogen (TBN) and minerals were measured using neutron activation analysis. Total body weight was measured using tritiated water, and total body fat (TBF) was calculated using skin fold measurements. Twenty four hour ileostomy volume in the resected group (1809±1614 ml) was significantly greater than the control group (570±159 ml p<0-01). Total body nitrogen in both resected (1468±471 g) and control groups (1446±471 g) was significantly less than predicted (1677±484 g p<0-02; 1627±371 g p<0-001 respectively). Body weight (60±9-5 kg) and TBF (12-8±4-4 kg) in the resected group were reduced compared with predicted (wt: 69-5±9 kg p<0-01, TBF: 17-5±6-0 kg p<0-02) and controls (wt: 67-5±15 kg, TBF: 18-5±7-0 kg p<0-06).

Thus the only serious nutritional deficit shown in ileostomy patients without IR was a reduction in TBN, which could in part be explained by resection of the large bowel. Modest IR during PC however, caused significant loss of weight which was primarily because of loss of body fat.