British Society of Gastroenterology

The 1990 Annual Meeting of the British Society of Gastroenterology was held at the University of Southampton from 26–28 September 1990 under the presidency of Dr Roger Williams. Below are printed the 314 abstracts selected by the Programme Committee of the Society for oral and poster presentation in the scientific sessions.

**COLORECTAL NEOPLASIA**

A new approach to the in vivo measurement of gastrointestinal mucosal kinetics combining flow cytometry and histochemistry

D A REW, M KELLETT, C S POTREN, S ROBERTS, I TAYLOR, AND G D WILSON (University Surgical Unit, Southampton and the Cancer Research Campaign, Northwood and Manchester) In vivo bromodeoxyuridine (BrdU) labelling is a new tool with which to study human mucosal cell kinetics, using histochemistry and flow cytometry (FCM). The ploidy profile, the crypt labelling index (LI), the crypt turnover rate (CTR), and the S phase duration (tS) of proliferating cells in large, heterogeneous samples (>10,000 nuclei) can be analysed.

Eighty five patients undergoing resection for colorectal carcinoma received an intravenous bolus dose of 250 mg BrDU between 2.4 and 16 hours before surgery. Mucosal specimens (n = 137) were excised from resection specimens, at least 10 cm from the tumour, and stored in ethanol. Sections from 50 colorectal mucosal blocks were stained by a peroxidase method and subjected to counting of longitudinal crypts. Samples for FCM were disaggregated using pepsin. Some 10,000 nuclei were analysed per specimen. The total tissue LI and CTR were calculated, using a factor which took account of the proportions of crypt and stromal cells in the mucosa. The median crypt LI of the mucosa was 2.7 (range 0.8–15.2)% and the median CTR was 12.0 (range 1.7–54.3) days. There was no change in mucosal proliferation with anatomical site from the ileum to the rectum. The FCM findings correlate with static crypt cell counting and in vitro studies of crypt cell thymidine labelling and turnover. This technique is a valuable asset in measuring altered mucosal proliferation of the gastrointestinal tract.

Synergistic stimulation of growth in HT29 colorectal cancer cells by peanut lectin (PNA) and epidermal growth factor (EGF)

D L RYDER, J A SMITH, E G ROHDES, AND JONATHAN M ROHDES (University Departments of Medicine, Haematology, Biochemistry and Walton Hospital, Liverpool) The peanut lectin (PNA) receptor (gal-galNAc) becomes expressed in colonic carcinomas and adenomas, and as lectins often pass through the gut undigested, studies are being performed to assess the functional importance of this receptor. We have previously shown that PNA stimulates growth in HT29 cells but it is possible that lectin binding might also indirectly affect the response to other growth factors by causing clustering of receptors.

After initial experiments to determine optimal concentrations of PNA and EGF (PNA tested at eight concentrations from 1 to 100 ng/ml, EGF at concentrations from 1 pg/ml to 100 ng/ml), HT29 cells (25 wells with 10 cells/well) in each PNA concentration were grown for 40 hours in the presence of PNA (25 μg/ml) and EGF (100 ng/ml) separately or in combination, pulsed for 18 hours with 1H thymidine and beta counted. PNA caused significant better uptake. CTR and CTR in combination caused 119% more than their predicted additive effect. PNA and EGF had similar synergistic effects on cell counts.

Interactions between dietary lectins and growth factors may have considerable importance in growth and oncogenesis in the colon.

High dose high affinity antibody and dexa-methasone increase antibody uptake by colorectal cancer

A R ATTARD, G D THOMAS, M J CHAPPELL, D N TAYLOR, J A FRANK, P W DIXES, AND A B BROADWELL (Walsgrave Hospital, Coventry and IDRL, University of Birmingham) Antibody targeting of tumours holds great potential for diagnosis and therapy but has been limited by poor uptake efficiency. We have constructed a computerised biomathematical model which suggested two fundamental requirements to improve uptake - very high affinity antibody and a large injected dose. This was tested in six patients with primary colorectal tumours using a high affinity (10^6 M^-1) technetium labelled-anti-CEA monoclonal antibody (B431/26). Each patient was scanned after 1 mg of antibody and again after a higher dose (1 mg labelled, 12-30 mg cold antibody). Tumour background uptake ratios (UR) were calculated from tomograms obtained. Tumour URs following the higher dose were significantly increased from a mean of 2.0-2.7, an average increase of 35% (p < 0.023; Wilcoxon test). Correlation of the patients' pharmacokinetic data with the model predictions suggested that available tumour antigen was 10 times less than total antigen content as determined from tumour biopsy specimens. Therefore in an attempt to increase antibody accessibility, three patients with recurrent colorectal cancer (eight tumour sites), were given a 24 hour course of dexamethasone between two scans. This resulted in an average increase in UR of 60% (from a mean of 1.5 to 2.4; p = 0.005; Wilcoxon rank test). These results indicate that high doses of high affinity antibody and increased antigen access can improve antibody targeting of colorectal cancer.

Reduction of low density lipoprotein by N-3 fats is associated with impaired growth of human colorectal cancer cell growth in vivo

C H IMRAY, M SAKAGUCHI, A DAVIS, S ROWLEY, C JONES, N LAWSON, M R REIGHLET, P BAKER, AND J P NEOPTOLEMOS (Academic Department of Surgery, Dudley Road Hospital and Clinical Research Block, University of Birmingham) Studies with COLO-320 and HT-29 human colorectal cancer cell lines have suggested that reduced growth by N-3 fats is related to reduced arachidonate in tumours. We have studied the growth of SW-620 and LS174T human colorectal cancer cell lines and in addition the effects on plasma lipids, a nutrient source for the tumour.

1 x 10^6 cells were inoculated into 90 nude mice receiving three iso-caloric diets: A = control, B = 20% saturated fat, C = 20% N-3 fat. After 5 weeks, tumours weights (mean (SEM) g) for SW-620 and LS174T, respectively were: A = 0.38 (0.06), 1.33 (0.33); B = 0.43 (0.08), 0.47 (0.19); C = 0.2 (0.04), 0.38 (0.14) g (p < 0.001, ANCOVA; least for C, p < 0.001). Tumours from groups A and C showed increased values of lipolate and arachidonate compared with diets A and B (p < 0.01). The plasma triglycerides and phospholipids (mean (SD) mmol/l) were respectively: A = 2.13 (0.38), 3.32 (0.51); B = 3.02 (0.29), 3.73 (0.28); C = 0.88 (0.19), 2.27 (0.24) (C least for all lipids, p < 0.01). The plasma cholesterol, high density lipoprotein, and low density lipoprotein (mean (SD) mmol/l) were respectively: A = 2.58 (0.25), 2.15 (0.24), 0.53 (0.13); B = 4.52 (0.4), 3.47 (0.59), 1.05 (0.45); C = 1.71 (0.19), 1.51 (0.3), 0.22 (0.11) (C least for all lipids, p < 0.01).

We have confirmed that inhibition of colorectal cancer growth by N-3 fats is related to reduced tumour arachidonate. We have also shown reduced low density lipoprotein by N-3 fats indicating another important mechanism of action.

Pattern of cyclic AMP binding protein expression in colorectal cancer and benign mucosa

A W BRADBURY, W R MILLER, AND D C CARTER (University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh) Cyclic AMP (cAMP) exerts its effects through activation of protein kinase A (PK-A). The regulatory units (R) of PK-A bind cAMP and exist as two forms RI (MW 47-50 kDa) and RII (MW 50-54 kDa). Using a [3H] 8-azido-cAMP photoaffinity labelling technique followd by polyacyrlyamide gel electrophoresis, cAMP binding proteins were identified in the cytosol of 17 paired colorectal cancers and related mucosa. The relative expression of each as a percentage was then determined by laser densitometry.

Three cAMP binding proteins of molecular weights 52, 50, and 47 kDa were identified and termed R52, R50, and R47, respectively. R47 (RI) is relatively overexpressed in cancer tissue (n = 17, mean (SEM) 55.9 (4.1)%) compared with related benign mucosa (44.7 (9.9)%p < 0.005).
The c-myc protein product is a marker of DNA synthesis but not of malignancy in colorectal tissues and tumours

D A REW, I TAYLOR, J W WATSON, AND G D WILSON (University Surgical Unit, Southampton and The Medical Research Council, Cambridge) C-myc is a putative oncogene. c-myc gene transcript values by Northern blotting are reported to be increased in cancerous adenomas and cancers. The gene product is a nuclear bound 62 000 MW phosphoprotein (p62-c-myc). Measurement of the gene product may be a better indicator of gene function in vivo than is measured by RNA transcript analysis.

The mean p62-c-myc content was measured in units of fluorescence in the G1 and G2 diploid (D) and aneuploid peaks of the cell cycle by multiparameter flow cytometry using the 6E10 monoclonal antibody. Studies were performed on 113 tumour blocks from 87 patients with colorectal cancer, on blocks from four villous adenomas, 52 colorectal muco sa samples and 7 mucosal samples from two patients with polyposis coli.

Mean (SD) G2D values of p62-c-myc were higher in normal mucosa (303 (17) U) than in tumours (186 (13) U). No differences in peak c-myc expression were found in relation to histological grade, ploidy, anatomical site or in vivo bromodeoxyuridine labelling indices. The highest mean levels of p62-c-myc were found in polyposis coli mucosa (502 (63) U, n = 7).

Multiparameter FCM is a valuable tool for studying gene expression. P62-c-myc values are cell cycle related but the protein has not been shown to be a marker of tissue proliferation or of colorectal malignancy.

Deoxycholic acid and calcium have opposite effects on colon proliferation in vitro

R G WILSON, A N SMITH, AND C C BAIRD (University Department of Surgery, Western General Hospital, Edinburgh and Department of Pathology, University of Edinburgh Medical School) Increased dietary calcium may protect against colon cancer by precipitating irritant secondary bile acids. The proliferative response of colorectal mucosa to deoxycholic acid (DCA) has been examined in 15 hour organ culture from the sigmoid mucosa of 12 adenoma patients before measuring the crypt cell production rate (CCPR). The CCPR decreased with increasing concentration of calcium; DCA in low concentration stimulated proliferation.

To assess the response to DCA, 10 μM and calcium 0.3 mM, biopsy specimens from 10 patients were cultured for 15 hours before flash-labelling with bromodeoxyuridine. DCA increased the % labelling index (LI) compared with biopsy specimens cultured in standard medium (14 (10) n = 11.3, p < 0.01); calcium decreased the LI (8.1 ± 11.3, p < 0.02). The positions of the proliferative compartment within the crypts were compared by generation of cumulative labelling distributions. Kolmogorov-Smirnov analysis showed a significant expansion of the proliferative compartment towards the surface epithelium in the DCA group compared to controls (00-01 =6-8, Omax =10), with a significant reduction towards the base of the crypt in the calcium group (00-01 =7-7, Omax = 9-0).

We conclude that while bile acids may stimulate proliferation, the mode of action of dietary calcium can also be explained by a direct antiproliferative effect on colon mucosa.

Vitamin D inhibits cell proliferation in human colorectal mucosa

M G THOMAS, R J SWIFT, AND R C N WILLIAMSON (Royal Postgraduate Medical School, Hammersmith Hospital, London) Vitamin D inhibits cell proliferation and stimulates cell differentiation in various human cancer cell lines, but its effect on normal colorectal mucosa is largely unknown. Sigmoidoscopic biopsy specimens were obtained from macroscopically normal rectal mucosae of patients with incidental anal condations. Samples were divided into 2 mm explants and established in organ culture with or without the addition of vitamin D (either 1 μM or 10 nM). After 15 hours, the vitamin D (0.6 μM) was added to the culture medium, and samples were removed 1–3 hours later for counting of metaphase arrests in microdissected crypts. Crypt cell production rate (CCPR) was determined by linear regression analysis. Vitamin D 1 μM reduced CCPR from the control value of mean (SEM) 47/6 (0-52) cells/crypt/hr to 2-07 (0-61) cells/crypt/hr (p < 0.01). Likewise, vitamin D 10 nM reduced CCPR from 5-25 (0-63) to 2-74 (0-54) (p < 0.02). Thus CCPR was roughly halved by vitamin D, irrespective of concentration. This inhibitory effect suggests that vitamin D, like calcium, may have a protective role against colorectal carcinogenesis.

LIVER PHYSIOLOGY

Defective export of HBsAg in long standing chronic hepatitis B virus (HBV) infection: relation to viral replication and pre-S antigen expression

J Y N LAU, V G RAIN, S E DAVIES, H M SMITH, G J M ALEXANDER, AND ROGER WILLIAMS (Liver Unit, King's College Hospital and School of Medicine and Dentistry, London) An inverse correlation between the proportion of hepatocytes expressing HBsAg and the serum titre of HBsAg has been established recently. To elucidate the underlying mechanism, hepatocytes isolated from 30 liver biopsies/hepatocyte specimens were cultured and HBsAg or HBcAg production and export were studied by measuring cellular and secreted antigens respectively using radioimmunoassay. These were correlated with serum HBsAg and HBV-DNA, and intrahepatic expression of HBsAg, pre-S1, and HBcAg were assessed by immunohistochemical staining.

High values of serum HBsAg were associated with markers of active viral replication; serum HBV-DNA (p < 0.001) and intrahepatic HBcAg (p < 0.001). There was an inverse relation between intracellular HBsAg and serum HBsAg (R = 0.37, p = 0.44) and HBsAg export (R = 0.45, p = 0.013). HBsAg export correlated with the presence of serum HBV-DNA (p < 0.05) and intrahepatic HBcAg (p < 0.05), and was significantly lower in CAH/cirrhosis (p < 0.05). Intrahepatic pre-S1 and pre-S2 expression correlated with intrahepatic HBsAg (pre-S2: R = 0.79, p < 0.001; pre-S1: R = 0.75, p < 0.001). Absence of intrahepatic pre-S1 in the presence of intrahepatic HBsAg occurred only in patients with minimal changes/CHPH (n = 5).

These data confirm our previous observation that intrahepatic HBsAg correlated inversely with serum HBsAg in patients with long-standing chronic HBV infection and further suggest that (1) HBsAg export is more efficient during active viral replication; (2) HBsAg export is not related to underexpression of intrahepatic pre-S antigens.

Importance of a raised serum bile acid (SBA) value in liver disease

R P JAZRAWI, J DE CAESTECKER, P M GOGGIN, A BRITTAIN, J NISBET, J D MAXWELL, A A JOSEPH, AND T C NORTHFIELD (Departments of Medicine and Nuclear Medicine, St George’s Hospital Medical School, London) A raised fasting SBA is a sensitive index of hepatic dysfunction. It has high specificity for the presence of liver disease, but not for the type of liver disease, although it is one of the criteria for the diagnosis of cirrhosis. Our aim was to define its pathophysiological importance by determining what aspect of hepatic bile acid handling is deranged in patients with a raised SBA. We studied 12 patients with primary biliary cirrhosis, eight patients with biopsy proved cirrhosis due to other causes, and eight healthy controls. After an intravenous bolus of 5’-S’-HbC, we carried out simultaneous γ-camera scanning and serial blood sampling for 90 minutes as previously described. We measured plasma disappearance, hepatic uptake, transit time, and net excretory rate for 5’-HbC. The patients with cirrhosis also had total fasting SBA measured enzymatically. Plasma disappearance was related to each other (r = 0.59, p < 0.005), and also individually with SBA (r = 0.56, p < 0.005) and r = 0.61, p < 0.005 respectively). Hepatic excretory rate and transit time were measured for the patients who were related with each other (r = 0.59, p < 0.005), and also individually with SBA (r = 0.56, p < 0.005). Hepatic excretory rate and transit time were therefore not correlated with plasma disappearance or hepatic uptake. Furthermore, neither correlated with SBA (r = 0.06 and r = 0.14 respectively). We conclude that plasma disappearance depends on hepatic uptake, and transit time on hepatic excretion and that a raised fasting SBA implies a specific defect in hepatic uptake and not in hepatic excretion as previously assumed.

Cholesterol transport in human hepatocytes: enhancement in cholesterol gall stone disease

H AHMED, P M GOGGIN, AND T C NORTHFIELD (Division of Biochemical Medicine, St George’s Hospital Medical School, London) Little is currently known about the mechanism(s) of cholesterol transport from the site of synthesis in the endoplasmic reticulum (ER) to the site of
secretion on the bile canalicular membrane (BCM). We separated vesicular fractions from the microsomes of hepatocytes in 15 cholesterol gall stone (GS) patients and 10 controls by centrifugation. One vesicular fraction showed enrichment in marker enzymes of both the ER (13 times) and BCM (25 times) over homogenate, suggesting a transport role between these two sites. Both the cholesteryl: phospholipid and the cholesteryl: protein ratios were higher in GS patients (mean (SEM) 0.60 (0.02) and 0.26 (0.01)) than controls (0.47 (0.01), p<0.001 and 0.1, p<0.002, respectively). That is, there is an absolute enrichment in cholesteryl in GS patients. Both ratios showed a direct correlation in GS patients with the ideal body weight per cent (r=0.81, p<0.001 and r=0.91, p<0.001, respectively). The vesicular cholesteryl: phospholipid ratio showed a 0.68, 0.87 and 0.91 velocity in GS patients, as this ratio. In all patients, we have studied the correlation between the ideal body weight and the vesicular cholesteryl: phospholipid ratio in both GS patients and controls.

A role for hepatotropin in human fetal liver development

A C Seldén, and H J F Hodgson (Department of Medicine, RFMS, Hammersmith Hospital, London) Hepatotropin, a hepatic growth factor, is a major determinant of liver regeneration in rats and man after injury. We have investigated whether hepatotropin plays a role in liver growth during fetal development. Total RNA was prepared from human foetal liver, spleen, pancreas, and kidney (9-6-21-5 weeks' menstrual age). RNA (5 μg) was resolved on agarose/formaldehyde gels, transferrred onto nylon membranes, and hybridised under low ionic strength conditions using a 569 bp cDNA 32P-labelled probe. Autoradiography of the membranes showed a 6 kb RNA species in foetal liver, as found in adult liver, which was considerably overexpressed in human foetal liver as compared with the adult, at all time points of foetal development studied (9-6, 11-7, 14-6, 18-2, and 21-5 weeks). RNA from foetal kidney (19-6 weeks) showed just detectable expression of the 6 kb RNA. Foetal spleen (20-4 weeks) and pancreas (17-9 weeks) showed similar levels of expression of the 6 kb RNA as that of normal adult human liver. These results show a role for hepatotropin in liver development. The increased hepatotropin mRNA values in foetal liver compared with kidney, spleen, and pancreas strongly support the liver as a major site of synthesis of this protein.

Autonomic dysfunction and hepatic function in chronic liver disease

M T Hendrickse, and D R Trigger (Department of Medicine and Pharmacology, University of Sheffield) Although autonomic dysfunction is well recognised in chronic liver disease (CLD), there has been no systematic study of its relation to the severity of hepatic damage. We investigated the autonomic system using a series of standard cardiovascular (CVS) tests (as described by Ewing and Clarke together with the heart rate variation at rest and during intra-venous atropine), in a group of patients with CLD. Fifty one patients (31 alcoholic, 10 primary biliary cirrhosis, five chronic active hepatitis, five others; 35 Child's A, 11, B, and 5) and 29 controls of comparable age and sex were studied.

Cardiovascular autonomic impairment was closely associated with hepatic function with 23% (eight of 35) of Child's A and 69% (11 of 16) of Child's B and C having one or more abnormal CVS tests correlated closely with the Child-Pugh score (r=0.72, p<0.0001). The Child-Pugh score correlated with the response to atropine (r=0.5146, p=0.0006) and the valsala ratio (r=0.5419, p=0.0057). Autonomic dysfunction was equally common in alcoholic and non-alcoholic liver disease (35% vs 35%), and occurred independently of age, duration of liver disease, diuretic use, and serum sodium and creatinine values. These results indicate that the prevalence and severity of autonomic neuropathy in chronic liver disease increases with advancing hepatic dysfunction.

Radiological diagnosis of coarctation of the inferior vena cava

V JAYANTHI, S VICTOR, and N MADANAGOPALAN (INTRODUCED BY DR J F MAYBERRY, LEICESTER GENERAL HOSPITAL) (Department of Digestive Diseases, Kilpauk Medical College and Hospital and Cardiothoracic Surgery, Vijaya Hospital, Madras, India) Chronic Budd-Chiari syndrome (CBCS) due to coarctation of the inferior vena cava (IVC) is a common cause of portal hypertension in Indians. Twenty five patients were investigated by venography or ultrasonography, or both. Of the 18 patients with functional hemiplegograms, the right hepatic vein (RHV) was occluded in four, with drainage through inferior hepatic veins and in one via the portal vein. Transcaval venacavography in 22 patients showed obstruction of the IVC in its inrtheastic portion with characteristic diagnostic appearances. In three patients the procedure was unsuccessful due to extensive collaterals and in three there was reflux of contrast into the RHV. Simultaneous transarial and transferomal venacavography in five patients delineated the cephalic end of the obstruction. The length of the obstruction varied from 0 to 3 cm. Twenty patients were successfully treated with a dorsal cavoval bypass graft whose patency was confirmed radiologically. Real time ultrasound was used in the pre- and postoperative assessment of 13 and seven patients respectively. In 16 patients the RHV was patent. Twenty patients were followed post operatively (two to 12 years) and in all a patent graft could be shown.

Value of duplex Doppler ultrasound in patients with postprandial abdominal pain and normal endoscopy

R F MULLER, K A STAINER, L FULLWOOD, M HAWKINS, and A J COWLEY (INTRODUCED BY DR C J HAWKLEY (Department of Medicine,
The British Society of Gastroenterology

University Hospital, Nottingham) The manifestations of chronic mesenteric ischaemia are often protean, but it has been claimed that Doppler ultrasound analysis of the abdominal vasculature may discriminate between predominantly fistomatous and be a useful non-invasive screening tool before angiography. Six patients aged (mean (SEM)) 63 (3) years were referred for Doppler scanning. All described postprandial abdominal pain in the presence of a normal vmscopy. Two gave a history of weight loss and all had evidence of vascular disease. The following Doppler parameters of superior mesenteric (SMA) and coeliac arteries (CA) were examined preprandially following an overnight fast and a meal of 800 kcal meal: peak systolic (Vmax) and end diastolic (Vmin) velocities, pulsatility index (PI) and velocity of flow (V). Peak changes were accepted. Twenty volunteers (20 SMA's and 10 coeliac arteries) aged 20-65 years were similarly examined to establish normal values. The superior mesenteric artery was inconsistently insonated.

Mean (SEM) coefficients of variance for parameter control were all less than 10%. Food in the control group increased SMA Vmax from 100-5 (4-2) cm/s to 154 (7-8) cm/s, Vmin (16 (0-9) cm/s to 46 (2-5) cm/s, V (35 (1-1) cm/s to 59 (2-5) cm/s) whilst PI fell from 3-9 (1-4) to 1-8 (0-8) units. For CA changes were: Vmax (120 (7) cm/s to 130 (22) cm/s), Vmin (30 (3-3) cm/s to 40 (4-8) cm/s, V (30 (3-3) cm/s to 41 (3-3) cm/s), and PI (1-5 (0-2) to 5 (0-1) units. All patients had normal fasting SMA and CA parameters. Postprandially, one patient's SMA Vmax/Vmin fell from 96/14 cm/s to 63/12 cm/s and V from 25 to 22 cm/s (heart failure). One patient increased SMA Vmax/Vmin significantly over controls from 108/20 cm/s to 312/28 cm/s with V from 28 to 70 cm/s. A third patient had CA Vmax/Vmin from 127/36 cm/s to 225/70 cm/s. These changes may represent non-occlusive and obstructive mesenteric ischaemia. When vascular ischaemia is suspected, Doppler ultrasound may be a useful screening test. Symptomatic patients should be scanned pre and post prandially.

Value of computed tomography (CT) in detection of subradiological calcification of gallstones and in predicting their response to bile acid therapy

M L PETRONI, R P JAZRAWI, A GRUNDY, A LANZINI, M G FOIOZZI, A BIASIO, K W HEATON, J VIERI, AND C T NORTHELFIELD (St George's Hospital, London; Spedali Civili, Brescia, Italy; Royal Infirmary, Bristol) Computed tomography is now advocated for selection of patients for non-surgical treatment of gall stones, but there is little controlled data to support this view. Our aims were to compare the sensitivity of CT with plain x ray in detection of calcification; and to assess the value of CT in predicting response to bile acid therapy. Fifty-eight patients with 84 gallstones, 43 patients with gallstones considered potentially suitable for non-surgical therapy. Compared with CT, the sensitivity of plain abdominal x ray was 36%, accuracy of prediction of 62% in detection of calcification. In 32 consecu-tively untreated gall stone patients with radio-luent stones on oral cholecystogram, and no calcification detected on plain x ray, seven (22%) had calcification on CT (Hounsfield units $>90$). Of 17 patients receiving bile acid therapy, seven showed a definite response. Median attenuation value in these seven responders was 35 HU before treatment, compared with 142 HU in the 10 non-responders (p<0.01). CT detected calcification in all 10 non-responders and in only one of the seven responders (p<0.005).

We have shown that CT is more sensitive than x ray in the detection of gall stone calcification and that this is of value in predic-tively predicting response to bile acid therapy.

OESOPHAGEAL MOTILITY

Ballon distension in patients with painful oesophageal motor disorders: a clue to the edrophonium response?

J S DE CASTECKER, A PYDE, AND R C HEADING (Department of Medicine, Royal Infirmary, Edinburgh) The mechanism of action of edrophonium, used to provoke symptoms in patients with suspected oesophageal chest pain, is unclear. Ten healthy controls and 13 patients with both chest pain and oesophageal motility disorders were studied. A 2.5 cm long latex balloon was tied around an Arndorfer manometry catheter and placed in the distal oesophagus, inflated with air in a step-wise fashion before and after intravenous injection of edrophonium (80 mg/kg) and again after atropine (1.2 mg). Intraballoonal pressure was measured at each volume increment, and the pressure and volume at which chest discomfort occurred were recorded. At each volume increment, balloon pressure recorded on the workbench was subtracted from the corresponding intraballoonal pressure to reflect oesophageal wall tension. Within 13 groups, net balloon pressure was significantly less after atropine than after edrophonium (p<0.05), but control subjects and patients did not differ. Volume, but not pressure, at the point of discomfort was significantly less in patients after edrophonium than during pre-injection inflation or after atropine in either patients or control subjects (p<0.005). Balloon volume at the point of discomfort during basal inflation did not differ between participants and controls. We conclude that: (1) oesophageal wall tension during balloon distension is modified by a cholinergic mechanism; and (2) edrophonium causes increased sensitivity to stretch in patients with painful motility disorders. This effect cannot be wholly explained by differences in oesophageal wall tension.

Role of head position in postural control of transient lower oesophageal sphincter relaxations

A IRELAND, J DENT, AND R H HOLLOWAY (Gastroenterology Unit, Royal Adelaide Hospital, Adelaide, Australia) Transient lower oesophageal sphincter relaxation (TLOSR) is the mechanism underlying gastro-oesophageal reflux (GOR) of acid and gas. Gastric distension with gas is a potent stimulus for TLOSRs and gas GOR in the sitting position but in normal subjects the response is suppressed when supine. The mechanisms underlying the postural suppression of TLOSRs are unknown, and this study investigates whether visual stimuli influences acting through head position may be responsible.

We studied 17 healthy volunteers aged 19-38 years. The effect of gastric distension with 750 ml CO₂ on the occurrence of TLOSRs and gas

GOR was studied in two head positions, tilted back and upright, in each of two body positions, sitting and supine. Oesophageal manometry was performed using a sleeve/sidehole assembly and measurements were made over 10 minute intervals before and after gas distension. Oesophageal contractions common episodes were used as markers of gas GOR.

When supine, the rate of TLOSRs was low (0.6 (0.2-10) min) and no gas GOR occurred. Tilted the head up significantly increased the rate or the gas rate of GOR. When sitting the rate of TLOSRs (3.0 (0.8) and gas GOR (5.0 (1.0)) were significantly greater than when supine (p<0.01) but this rate was not affected by tilting the head back. In this study head position is not the factor responsible for suppression of TLOSRs and gas GOR when supine.

Healing of oesophagitis does not improve oesophageal function

P SINGH, A ADAMOPoulos, R H TAYLOR, AND D G COLLIN-JONES (Royal Naval Hospital, Haslar, Gosport and Queen Alexandra Hospital, Cosham, Portsmouth) Lower oesophageal sphincter (LOS) hypotension and impaired oesophageal peristalsis occur commonly in patients with gastro-oesophageal reflux disease. Whether these abnormalities are primary phenomena or they result from repetitive injury caused by acid reflux is not clear. We designed this study to determine whether oesophageal motility abnormalities found in patients with oesophagitis could be reversed with prolonged sustained healing.

Eleven patients with endoscopic oesophagitis were recruited. LOS pressure was recorded using rapid pull through technique. The mean of nine measurements was regarded as the LOS pressure. Oesophageal body amplitudes were calculated at 5, 10, and 15 cms above LOS as the mean of 10 consecutive values using wet swallows. Twenty four hour oesophageal pH monitoring was performed which showed evidence of appreciable acid reflux in 10 of 11 patients. The tests were repeated six weeks after injection of a bolus of acid (M70 for 20 min) and 48 hours before and after a second endoscopy on the same day for a median duration of nine weeks). Endoscopy showed complete healing of oesophagitis in all the patients. Eleven healthy volunteers served as controls. Patients had significantly lower median LOS pressure than the control group (13.3 vs 20.0; p<0.05). There was a significant difference between the two groups in median distal (D) and middle (M) oesophageal amplitudes (D=48 vs 107; p<0.01 and M=4644 vs 98.2; p<0.01). There was no significant change in the median LOS pressure and the distal (D) and middle (M) oesophageal amplitudes after healing of oesophagitis (LOS: D=13.3 vs 11.6; D=48 vs 49; M=4644 vs 45.6).

We conclude that LOS hypotension and impaired peristalsis in GORD are primary phenomena rather than being the consequence of injury from acid reflux.

Improvement in oesophageal function after healing of oesophagitis

D WILLIAMS, D G THOMPSON, M MARPLES, V MANI, C M BATE, T O'HANRANAM, AND J BANCZKIEWSZ (Hope Hospital, Salford; Leigh Infirmary and Royal Albert Edward Infirmary, Wigan) Background: Oesophageal motility is impaired in oesophagitis but whether this is the
cause or the effect, of reflux is unknown. Aim: To compare oesophageal motility and clearance forces before and after healing of oesophageal peptic (40 mg·day·1). Method: Nine patients (age range 32–67 years) with endoscopic and histological evidence of erosive oesophagitis were studied both by standard manometry and using a novel intraluminal traction device to measure: (1) peristaltic force, and (2) the myenteric plexus mediated clearance forces induced by intraluminal distension. Results: Before treatment, standard manometry showed that lower oesophageal sphincter pressure (LOSP) was low (4–2–9 mmHg) and distension induced clearance was impaired. After treatment, all patients showed endoscopic and histologic healing. LOSP was unchanged (5–3–7 mmHg, p=0.4 v pretreatment). In contrast, peristaltic force improved (4–2–5 mmHg, p<0.05 v pretreatment). Clearances to distension (5–4–5 mmHg, p<0.05 v pretreatment). Conclusion: These improvements in clearance forces with healing indicate that inflammation induced myenteric plexus dysfunction contributes to the motor abnormality of oesophagitis although the LOSP disorder remains unaffected.

COLORECTAL POSTERS

Deficiency of a mucosal trypsin inhibitor in patients with ulcerative colitis

W J Playford, T Freeman, C Quinn, and J Calam (Departments of Medicine and Histopathology, RPM, Hammersmith Hospital, Du Cane Road, London W12 0NN) Pancreatic secretory trypsin inhibitor (PSTI) is a powerful protease inhibitor produced in high concentrations in colonic mucosa. We have shown that human mucus can be digested by trypsin, which is present in colonic contents, and that PSTI can prevent this. Mucus turnover and secretion in patients with ulcerative colitis. We therefore investigated whether mucosal PSTI was deficient in these patients. Colonoscopic biopsy specimens were collected from six patients with left-sided ulcerative colitis (four M, two W, aged 66 years (range 60–74)) and seven controls with a normal colon (three M, four W, mean age 41 years (range 25–67)). The mean weight of biopsy specimens was 11 mg. Paired biopsy specimens were taken for routine histology, radiomunous assay (RIA), and immunohistochemical staining for PSTI. Normal subjects had median (range) mucosal PSTI concentrations of 200 (150–450) ml·g d.w. in all regions of the large bowel. Patients with ulcerative colitis had normal PSTI concentrations in the right colon 140 (40–210) (NSD), but significantly decreased levels in the sigmoid 70 (40–170) (p<0.05 v control) and transverse colon 40 (20–80) (p<0.01 v control). This decrease was confirmed by immunostaining. Active ulcerative colitis is associated with decreased mucosal trypsin inhibitor concentrations. This may contribute to the abnormalities of colonic mucus seen in these patients.

Pathogenesis of inflammatory bowel disease: mucosal cell mediated immunity to mycobacterial and non-mycobacterial antigens

J P Ibbotson, J R Lowes, H Chahal, H Gastong, D S Kumanovitch, J Alexander-Williams, and R N Allan (Departments of Medical Microbiology, Immunology, and Rheumatology, University of Birmingham, and Gastroenterology Unit, General Hospital, Birmingham) We have examined mucosal responses to mycobacterial and other antigens in mesenteric lymph node lymphocytes (MLN) and peripheral blood lymphocytes (PBL) from patients with Crohn’s disease (CD), ulcerative colitis (UC), and controls. In a six day lymphocyte proliferation assay antigens included: Chlamydia, Salmonella, Yersinia, E coli, influenza, Candida, PPD, and the 65 kD heat shock protein of mycobacteria (rHSP). Some 5×10 Cell cultures were 18 hours before harvesting, cultures were pulsed with U C T indicated thymidine. A positive proliferative response was defined as >5000 DPM/well. MLN cells from CD patients recognised a range of non-mycobacterial antigens (30/72 positive assays). PBL also recognised a range of antigens (23/72). In UC, eight/24 assays were positive for MLN and six/24 positive for PBL. Cells from control subjects were negative; three/24 MLN positive, four/24 PBL positive (p<0.05). Proliferative responses to the mycobacterial antigens PPD and rHSP for MLN for UC, and controls were three/24, three/eight, and one/ eight and for PBL five/24, three/eight, and two/ eight respectively. In conclusion, there is evidence of increased CMI to a range of non-mycobacterial antigens by MLN and PBL from patients with both UC and CD but not UC over CD. We have found no evidence for specific cell mediated immunity to mycobacterial antigens in CD.

Virulence properties of Escherichia coli isolated from patients with inflammatory bowel disease

M H Giaffer, C D Holdsworth, and B I Duerden (Gastroenterology Unit, Royal Hallamshire Hospital, Sheffield, and Department of Experimental and Clinical Microbiology, University of Sheffield) We have studied the virulence of E coli isolated from the faeces of 40 patients with Crohn’s disease, 34 with ulcerative colitis, and 18 healthy controls. Haemolysin production was examined in solid media using sheep erythrocytes, verotoxin production by the effects of E coli on vero cells, and their adherence to baby hamster kidney cells. Enterotoxin (LT) production was examined on vero cells. Haemolytic E coli strains were isolated from 18% of patients with Crohn’s disease, 24% with ulcerative colitis, and 11% of normal controls. A new ELISA technique has been developed. Haemolytic E coli strains were isolated from patients with Crohn’s disease and ulcerative colitis were more adhesive (mean adhesiveness index 42.2 (6.4) and 43.2 (6.2) respectively) than those in normal controls (mean 13.2 (3.4); p<0.0001). When cultured, E coli strains from patients with Crohn’s disease and ulcerative colitis were more adhesive (mean adhesiveness index 42.2 (6.4) and 43.2 (6.2) respectively) than those in normal controls (mean 13.2 (3.4); p<0.0001). Altogether 62% of Crohn’s patients and 68% with ulcerative colitis harboured adhesive E coli compared with 6% of controls (p<0.0002). Adhesiveness was not dependent upon disease activity, anaemia, or infliximab therapy. No verotoxin producing strains were detected among the 216 E coli isolates tested. However, five strains produced a distinctive cytotoxic effect on vero cells that could not be explained by VT or LT production. Enterohemorrhagic E coli are frequently associated with inflammatory bowel disease regardless of disease site or activity. Their role in the pathogenesis of these conditions remains to be established.

Postprandial hypergastrinaemia in patients with colorectal cancer

K Wong, R Beardsull, J Calam, and G J Poston (Ashford Hospital, Middlesex, Gastroenterology Department, RPH, Hammersmith Hospital, London; and Academic Surgical Unit, St Mary’s Hospital, London) Gastrin is trophic to colorectal cancers possessing gastrin receptors. The purpose of this study was to measure the effects of food and resection on serum gastrin in patients with colon cancer.

Serum gastrin was measured by RIA in 16 patients with non-obstructing colon cancer before and 10 days after tumour resection, and in 14 healthy age and sex matched controls. In each case, samples were taken before and 10, 20, 30, 40, 60, 90, and 120 minutes after a standardised hospital meal. At surgery, both tumour and adjacent colon mucosa were assessed for gastrin content. Data were analysed by ANOVA (p<0.05 significant).

Preoperative fasting and postprandial serum gastrin levels were consistently higher in patients compared with postoperative values, in turn these values were consistently higher than controls. These differences were significant at 20 (gastrin pmol/l: preop 51 (11–7), p<0.01) and 10 days after tumour resection (gastrin pmol/l: preop 49.0 (10.4), postop 30.2 (7.0), control 25.3 (4.5), and 90 minutes (gastrin pmol/l: preop 38.5 (8.7), postop 30.1 (9.4), controls 21.0 (4.0)). No gastrin was detected in either the tumours or colon mucosa.

Patients with colon cancer have significant postprandial hypergastrinaemia which is corrected by tumour resection. These tumours (and gastrin producing mucosa) may be producing endogenous gastrin release and this is of possible aetiological importance in tumour development.

Pathogenesis of inflammatory bowel disease: virulence properties of mucosal and submucosal associated Escherichia coli

J P Ibbotson, H Chahal, A Loaan, P E Pease, and R N Allan (Departments of Medical Microbiology, University of Birmingham and Gastroenterology Unit, General Hospital, Birmingham) We determine the pathogenic potential of Escherichia coli in the gut lumen of patients with IBD. Since E coli in the mucosa or submucosa may possess pathogenic properties distinct from normal faecal flora we have studied mucosal biopsy specimens from patients with active (n=30) and inactive (n=16) Crohn’s disease, active (n=17) and inactive (n=25) ulcerative colitis, and normal controls (n=20). After washing, samples were homogenised and cultured for enterobacteria. Isolates of E coli were examined for virulence factors including mannose resistance (MR), adherence to baculal epithelial cells (BEC), MR. coli motility (MCM), verotoxin production, haemolysin production, and antibiotic resistance. E coli were isolated from 36 of 47 patients with active IBD (76%) but from only 22 of 71 histologically normal biopsy specimens.
(31%). E. coli from active disease tissues were commonly either haemolytic or adherent, or both, and MR haemagglutination was frequently shown by isolates possessing these virulence factors, but was not a prerequisite for adherence to BEC. Only one isolate from inactive disease or normal control tissue possessed virulence-associated properties.

No differences were detected between active ulcerative colitis and Crohn’s disease. Since IBD may result from a lymphocyte mediated hypersensitivity reaction to bacterial antigens, these findings suggest that the antigenic relationship between these mucosal isolates may share common chromosome or plasmid encoded surface antigens not present in commensal strains of E. coli.

Inhibitory effect of long chain fatty acids (LCFAs) on colonic bacteria

L THOMPSON, R EDWARDS, D GREENWOOD, and R R KAWANE
(Department of Therapeutics and Microbiology, University Hospital, Nottingham)
Malabsorbed fat induces diarrhoea and stimulates colonic motility. The present study aims to determine whether LCFAs also disturb the colonic flora.

LCFAs were deposited on the wall of empty culture tubes and a defined culture medium added together with 0.1 ml of a 24 hours culture of Bacteroides fragilis (NCTC strain 9344). Growth was expressed as the ratio of viable counts after six hours’ anaerobic culture to counts at time 0. Final LCFAs concentration were 1% w/v.

Mean (SD) – oleic acid (C18:1) significantly reduced growth to 77-6 (8-5)% of control values, p<0-02. Increasing unsaturation increased this inhibition, growth being 16-9 (1-9), 4-6 (1-2), and 1-9 (0-2)% of controls for linoleic (C18:2), linolenic (ω3C18:3), and gamma linolenic (ω6C18:3) respectively (all p<0-001).

Arachidonic (C20:4) and eicosapentaenoic (C20:5) acids also exerted an inhibitory effect, growth being 23-0 (5-9) and 9-7 (2-0)% under strict anaerobic conditions to avoid peroxidation (all p<0-001).

Dietary LCFAs significantly inhibit a major component of the colonic bacterial flora. This may contribute to the diarrhoea seen in fat malabsorption.

Colonicoscopy in severe attacks of ulcerative colitis: correlation with clinical and pathologic features

F CARBONNEL, A LAVENGUE, M LÉMANN, A BTOUL, J VAUVEIL, G AGLIÂN, P HAUTEFEUILLE, R BARGUE, and C BAMBARD (Hôpital Pierre-Laraze, Paris) Between 1981 and 1989, 91 patients with ulcerative colitis (UC) were admitted in our centre. All these patients were evaluated using Truelove’s criteria and examined using colonoscopy, without any complication. Endoscopic signs of severity were: deep and extensive ulceration(s), mucosal detachment, well-like ulceration, and total mucosal abrasion. When at least one of these signs was found in colon, the patient was selected for emergency surgery, in the absence of contraindication. Colectomy specimens were examined to assess the depth of ulceration according to previously defined criteria (Buckell et al, Gastroenterology 1980; 79: 19–25).

Fifty four patients (group I) had colonicoscopic signs of severity. Forty three of them underwent surgery, none died. Eleven patients were treated medically. Three achieved a complete remission with one subsequent death, and eight had to undergo surgery because of treatment failure. Thirty seven patients (group II) had no colonicoscopic signs of activity and only four of them had surgery because of medical treatment failure (no mortality). All five Truelove’s criteria were found in 17% of patients in group I and 4% of patients in group II. Pathological examination showed that ulcers or erosions reaching or extending into the circular muscle coat were present in 96% of the 51 coloectomy specimens in group I and in two of the four colectomy specimens in group II.

In our experiences, Truelove’s criteria were specific of severe lesions in patients with UC attacks but had a low sensitivity. Colonoscopic assessment of these patients is safe and may be useful to select candidates for emergency surgery.

Experience with 1286 outpatient 60 cm flexible sigmoidoscopies without pre-examination: diagnosticyield and missed lesions: is it worthwhile?

S DOODS and M R THOMPSON (St Mary's Hospital, Portsmouth) A total of 1286 consecutive new patient outpatient flexible sigmoidoscopies (OF) were reviewed to determine the number of neoplasms diagnosed and missed. The 1286 OFS diagnosed 64 carcinomas (5-9%) and 125 polyps (10%). Most were in patients over 60 years (54 carcinomas, 85%: 93 polyps, 74%). Some 106 of 198 neoplastic lesions (55%) were at least 20 cm above the anus and the reach of rigid sigmoidoscopy. All polyp patients had colonoscopies and one further caecal carcinoma was diagnosed. Altogether 288 barium enemas were done when OFS did not show a neoplasm. One further polyp and nine further carcinomas were diagnosed (3-1% yield); two caecal, one ascending, three transverse, three descending, and only one sigmoid carcinoma which had been missed on OFS. Some 280/288 barium enemas (97%) were normal. Two patients with persistent rectal bleeding, one of whom had been discharged from the clinic, had a sigmoid polyp diagnosed on a subsequent OFS. There have been no cases of carcinoma presenting at a later date.

Seventy four carcinomas and 128 polyps were diagnosed in 1286 new patients, of which 64 carcinosmas (87%) and 125 polyps (99%) were diagnosed by OFS. One sigmoid carcinoma and three polyps were missed on initial OFS. OFS on the unprepared bowel is more effective than rigid sigmoidoscopy and should be used for the first examination in new patients with coloectumal symptoms.

Gut: first published as 10.1136/gut.31.10.A1162 on 1 October 1990. Downloaded from http://gut.bmj.com/ on September 21, 2023 by guest. Protected by copyright.
sodium succinate (G0), irrigation and phosphatidylcholine (G1), and irrigation alone: controls (G2). All animals were sacrificed at two weeks. One control animal was excluded due to early death. Adhesions were found in: 13 of 19 (p = 0.056, Fisher's exact test), 6 of 20 of G0 (p = 0.025) and 3 of 20 of G1 (p = 0.001). These data suggest that in this model postoperative adhesions can be significantly reduced by phosphatidylcholine.

'Hot' ultrason in 120 acute abdomens

A H DAVIES, I MOSTARAKOU, R COBB, D LINDSELL, AND N J MCC MORTENSEN (Departments of Surgery and Radiology, John Radcliffe Hospital, Oxford) A misdiagnosis in the acute abdomen can be associated with morbidity and mortality. The role of emergency ultrasound in the management of the acute abdomen and its possible use by surgical trainees are controversial. A total of 120 consecutive patients (66 men, 54 women) of mean age 54 years (range 1–94) presenting with an acute abdomen were studied. All patients were clinically assessed by a middle grade surgeon and a management plan was formulated. An ultrasound examination was then performed by a radiologist, the surgeon was informed of the result, and any influence on management was noted. Ten patients (8%) would have had an emergency ultrasound requested, 49 patients (41%) would have had a request for a routine ultrasound, and 61 patients (59%) would not have had one. Ultrasound altered the diagnosis in one patient from probable appendicitis to cholecystitis. Ultrasound missed one abdominal aortic aneurysm, one appendicitis, and one empyema of gall bladder. In 22 patients who underwent appendicectomy, 20 had appendicitis. In this group ultrasound had a sensitivity of 95%, a positive predictive value of 95%, and an accuracy of 91% in detecting appendicitis.

In most cases of the acute abdomen 'hot' ultrasound was rarely helpful, with the exception of appendicitis where we found a surprisingly high accuracy. Where an urgent ultrasound is necessary on clinical grounds the skills of a radiologist are required, whereas in specific areas, for example the diagnosis of appendicitis there may be a place for training staff.

Effect of a xanthine oxidase inhibitor (allopurinol) in patients with pouchitis after ileal pouch-anal anastomosis

K E LEVIN, J H PEMBERTON, S F PHILLIPS, A R ZINSMEISTER, AND M E PEZIN (Mayo Graduate School of Medicine, Division of Colon and Rectal Surgery and Gastroenterology, Rochester, Minnesota, USA) Our hypothesis was that most pouchitis in oxygenated, free radical production by xanthine oxidase, contributes to the clinical syndrome of 'pouchitis' in ileo-anal pelvic reservoirs. We therefore evaluated the effect of allopurinol, a xanthine oxidase inhibitor, in patients with acute and chronic pouchitis. Acute pouchitis was defined by increased frequency and decreased viscosity of stools occurring in the context of fever, malaise, and pelvic discomfort. Usually, the syndrome responds to metronidazole. Chronic pouchitis was characterised by persistent pouchitis controlled by antibiotics which recurred within one week of stopping treatment.

Twelve patients (10 M, 2 W) with chronic pouchitis had chronic antibiotic therapy stopped; they were then given allopurinol (300 mg PO bid) for 28 days. Eight patients (6 M, 2 W) with acute pouchitis were treated with allopurinol (300 mg PO bid) during the episode.

Seven of the 12 patients with chronic pouchitis responded completely, with no new onset or exacerbations during the 28-day period. The five remaining patients failed, prompting return to standard therapy. None had any side effects. Acute pouchitis resolved promptly in four patients (50%). The other four patients with acute pouchitis failed; they were then treated with their usual regimen. Two patients had transient side effects (headache, joint pains, and skin rash).

The efficacy of allopurinol treatment in 58% of episodes in pouchitis patients is consistent with a role for mucosal ischaemia and free radical production by xanthine oxidase in the aetiology of pouchitis. Controlled studies are therefore indicated.

Creative protein in right iliac fossa pain

A H DAVIES, F BERNAU, A SALISBURY, AND R G SOUTER (INTRODUCED BY N J MCC MORTENSEN) (Milton Keynes General Hospital, Milton Keynes) Accuracy rates for the decision to operate in right iliac fossa pain may be as low as 50%. Although many tests have been described to increase the accuracy of diagnosis, no one method is of proved superiority. C reactive protein (CRP) is a marker for acute illness, its value in right iliac fossa pain is presented.

Sixty patients (26 men, 34 women) of median age 24 (range 3–72) were admitted with right iliac fossa pain. A full blood count and a CRP were performed. Thirty one (52%) had appendicitis, six (10%) had a negative appendicectomy, 14 (23%) settled conservatively, and nine (15%) had an alternative diagnosis. CRP had a sensitivity of 94%, specificity of 75%, and a negative predictive value of 88% in detecting appendicitis. CRP + white cell count (WCC) had a sensitivity of 93%, specificity of 93%, and a negative predictive value of 93% in detecting appendicitis.

CRP was raised more than the WCC in 70% of patients with confirmed appendicitis; this was statistically significant (p < 0.05 × 2 = 3.98). In combination, raised CRP or WCC, or both, was found in 30 (97%) of patients with a confirmed appendicitis.

While the above tests are of value in pointing to acute pathology they do not exclude appendicitis, but the performance of these tests may reduce the negative appendicectomy rate and subsequently avoid post operative complications and lower costs.

Does the irritable bowel syndrome burn out in the elderly? A random community survey

E O'KEFFE, N TALLEY, A R ZINSMEISTER, E G TANGLOS, S F PHILLIPS, AND J M JELTON (Mayo Clinic, Rochester, USA) The irritable bowel syndrome (IBS) is a common, often disabling, functional bowel disorder. There is a lack of consensus as to whether the irritable bowel syndrome (IBS) symptoms in middle aged and elderly people, to determine if these are affected by age. By mail we surveyed an age- and sex-stratified random sample of the Olmsted County, Minnesota population. All subjects completed a previously validated questionnaire that measures colonic symptoms, including the specific Manning criteria for IBS. The overall response rate was 81%; 835 were middle aged (30–64 years) and 337 were elderly (65–93 years). The proportion of middle aged subjects reporting pain relief with defecation, looser bowel habit, more frequent stools, more pain onset, abdominal distension, and mucus were 27%, 22%, 17%, 21%, and 15%; in the elderly, the proportions were 22%, 14%, 12%, 18%, and 6%, respectively. However, a feeling of incomplete evacuation was slightly more frequent in elderly than middle aged subjects (24% and 21%, respectively). Abdominal pain and the Manning symptom criteria, except distension and incomplete evacuation, significantly varied by sex interactions were detected. We conclude that symptoms compatible with IBS are common in the community. While there is little evidence that IBS burns out in elderly subjects, some symptoms are less frequent.

Is there any seasonal distribution in the exacerbations of ulcerative colitis?

D G KARAMANOLIS, K C DELIS, E KALAFATIS, D TSAMBRINOU, G PASPASIT, AND B C XOURIGIAS (Department of Gastroenterology, Tzanion General Hospital, Piraeus, Greece) The aim of the study was to determine whether there is any seasonal aggregation in the exacerbations of ulcerative colitis (UC). Between January 1980 and April 1990, 126 exacerbations in 76 patients (40 men, 36 women) with histologically proved UC were evaluated in our unit. Patients who had been followed up for 12 or 24 consecutive months were included in the study, while patients who follow up less than 12 months were excluded. The x2 goodness of fit test was used for statistical analysis. The highest frequencies were reported during March, April, and November (observed/expected 16/10–6, 14/10–6, and 14/10–6) respectively, while the lowest ones occurred during July, December, and January (6/10–6, 3/10–6, and 6/10–6 respectively) (p = 0.035). Regarding the seasonal distribution, relapses were more frequent in patients with active bowel disease (observed/ expected 48/31–8 and 39/31–8 respectively) (p = 0.0001). We conclude that there is a clear increase in the relapse rate of UC patients during Spring and Autumn. Any specific contributing factors affecting these observations should be evaluated further.

Serial observations of the mucosal changes in ileo-anal pouches

H J DE SILVA, P R MILLARD, G PRINCE, M KETTLEWELL, N MOSTARAKOU, AND P JEWELL (Departments of Gastroenterology, Pathology, Histopathology, and Surgery, John Radcliffe Hospital, Headington, Oxford) To investigate early and delayed effects of the faccial stream on ileo-anal pouch mucosa, we selected 14 pouch patients (9 men, median age 30 years (19–54)) were studied. Two pouch biopsy specimens each were obtained at the time of pouch formation (PF), ileostomy closure (IC), and three, six, and 12 months posttransplantation. Pouch biopsies were assessed for the degree of acute and chronic inflammation (grade 0–3), mucin type (HID-AB stain), degree of villous atrophy (VHT/MTM), and crypt cell proliferation (CCP)
Mitochondrial and cytoplasmic ribosomal RNAs in normal colorectal mucosa and in inflammatory bowel disease

A J S MACPHERSON, T MAYALL, K A CHESTER, G BOXER, A D MALCOLM, T J PETERS, AND J C FORBES (Departments of Clinical Biochemistry and Gastroenterology, King's College and Dulwich Hospitals, London) Expression of mitochondrial genes is essential for epithelial cell differentiation, which is known to be deranged in inflammatory bowel disease. Although most cellular genes are in the nucleus, mitochondria contain a separate chromosome which codes for mitochondrial ribosomal RNA (rRNA), transfer RNAs and some mitochondrial proteins. Mitochondrial rRNAs have distinct sizes and sequences from cytoplasmic rRNAs, and their values differ during cell growth in culture. We have studied the tissue distribution of 12S and 16S mitochondrial rRNA and compared this with 18S cytoplasmic rRNA using in situ hybridisation on sections of normal human colonic mucosa and ulcerative colitis.

Results: In normal mucosa (5 μm) were pre-treated with proteinase K and prehybridised. Hybridisation was with 32P-labelled probes from PCR amplification or plasmid inserts. Control sections were treated with ribonuclease to digest target RNA, or hybridised with IgG probes localising plasma cells. Signals were visualised by autoradiography.

Results show that mitochondrial 12S and 16S rRNA are predominantly expressed on the surface of crypts of normal mucosa (12 cases) and ulcerative colitis in remission (eight cases). However, 18S cytoplasmic rRNA is found throughout the crypts of normal epithelium and in plasma cells of the lamina propria. In ulcerative colitis in relapse, seven cases) mitochondrial rRNA is expressed uniformly in the epithelial cells. These observations suggest that the normal crypt-surface distribution of mitochondrial rRNA in the colonic mucosa is disrupted in active ulcerative colitis, and epithelial cells assume a surface phenotype.

Mepacrine in resistant collagenous colitis

J S HAYLAR, L BJARNASON, A B PRICE, AND A J LEVI (Section of Gastroenterology, MRC Clinical Research Centre, Harrow, Middlesex) Collagenous colitis remains an uncommon though increasingly recognised cause of diarrhoea. The aetiology is unknown but treatment with sulphasalazine or prednisolone, but both may be effective. We have had good results from mepacrine in resistant disease. Eleven patients with collagenous colitis have been studied, six also had autoimmune disease. Colonic biopsy specimen findings often showed patchy disease with a mean (SD) increase in thickness of the collagen plate to 31 (12) μm. Five patients responded symptomatically to sulphasalazine/prednisolone and the remaining six patients were given mepacrine 300 mg daily in divided doses for 10–14 days in the management of 11 episodes. On eight occasions symptoms abated rapidly; one patient required repeated treatments over five years. Though the mechanism of action of mepacrine is unclear, it may be a combination of immunomodulatory activity, inhibition of phospholipase A2, and inhibition of neutrophil chemotaxis. This study provides further evidence of the efficacy of mepacrine in collagenous colitis and shows that the drug reduces inflammation often with marked improvements in histological appearances, though the patchy nature of the disease may make this difficult to assess.

von Willebrand protein in inflammatory bowel disease

T R J STEVENS, J P JAMES, D A MCCARTHY, N J SIMMONDS, F J MADDISON, AND D S RAMPTON (Gastrointestinal Science Research Unit, The London Hospital Medical College, London, and The Bath Institute for Rheumatic Diseases, Bath) A chronic mesenteric vasculitis has recently been proposed in the pathogenesis of Crohn's disease (CD). von Willebrand protein (vWF) is an endothelial cell product, important for platelet adhesion to endothelium and stabilising the coagulation factor VIII molecule, whose circulating values are raised in some vascular disorders. We have sought evidence of vascular injury in inflammatory bowel disease (IBD) by measuring serum vWF levels in an enzyme linked immunosorubant assay. The vWF was raised above the normal range (≥control group 95th percentile value = 132%, median 96%, range 35–240%, n = 22) in 64% of patients with active CD, (median 202%, range 72–500%, p < 0.0062, n = 11); 54% with inactive CD (133%, 35–460%, p < 0.0005, n = 28), 61% with active ulcerative colitis (UC) (158%, 33–400%, p = 0.0051, n = 18), and 33% with inactive UC (112%, 44–296%, p = 0.044, n = 21). The vWF values were also raised in patients with confirmed bacterial diarrhoea (median 292%, range 96–420%, p < 0.0005, n = 8).

The raised values of vWF in active as well as inactive disease suggest that vascular injury is fundamental to the pathogenesis of IBD.

Serum anti-endothelial cell antibodies are present in Crohn's disease, but not ulcerative colitis

A M SAWYER, B E POTTINGER, A J WAKEFIELD, AND D PEARSON (Academic Department of Medicine, Royal Free Hospital, London and Vascular Biology Unit, MRC Clinical Research Centre, Harrow) It has been shown that vasculitis occurs in Crohn's disease. Antibodies which bind to cultured endothelial cells (AECAs) have been found in the sera of patients with other, well recognised vasculitides. We have used a serum archive to show the presence of AECAs in Crohn's disease (CD).

Sera from 10 patients with active CD, 22 patients with inactive CD, five patients with ulcerative colitis (UC), and nine healthy volunteers were analysed for the presence of AECAs by a previously published, human umbilical vein endothelial cell based ELISA technique. Sera were added at a dilution of 1/1000. Tests were designated positive if the results were greater than mean + 3 SD of the healthy control group (HC).

Positive tests for IgG AECAs were found in: HC 0 of 9, active CD 8 of 10 (p<0.01), inactive CD 8 of 22 (p<NS), and UC 0 of 5. Thus the test distinguished between normal and ulcerative colitis. Of the two patients with active CD and negative IgG AECAs, one was strongly positive for IgM AECAs. Where paired sera were studied, IgG AECAs values always fell in remission (p<0.05, Wilcoxon signed rank test).

IgG AECAs are found in patients with active CD, and, in this respect, CD is concordant with other vasculitides. IgG AECAs are not found in UC.
Effects of short chain fatty acids (SCFAs) on the motility of the rat colon in vitro

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The present study shows the differential effects on motility in the large bowel of a mixture of SCFAs, when presented as either their associated acid (pH 4.1) or their Na-salt (pH 7.4). A cocktail of 66 mM acetate, 26 mM propionate, and 8 mM butyrate was compared to a Krebs control (pH 7.4) and a Krebs solution acidified with succinic acid (pH 4.1). The large bowel was fasted intraabdominally but placed in an atmosphere in which the major gas component was 5% CO₂, 95% O₂. Serial myoelectric activity and motility were recorded for 25 minutes after treatment (p<0.01; n=6). These effects were reversed during the subsequent Krebs washout. No inhibition was observed during infusion of the acidified Krebs or the Na-salt (n=6 for each), suggesting that this effect is mediated by the associated SCFAs and not the pH or the anion. This result suggests the protective role of SCFAs in vivo may enhance colonic salvage of carbohydrate by prolonging contact with bacteria.

Arteriovenous shunting during mesorectal base regional chemotherapy for colorectal liver metastases

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The effect of chemotherapeutic drugs on microscopic arteriovenous shunting was assessed in 10 patients with colorectal liver metastases. The aim of the study was to measure the degree of shunting before and after high dose microsphere administration in patients with colorectal liver metastases. It has been suggested, however, that arteriovenous connections, or shunts, are a necessary feature of tumours. The use of microspheres allows the administration of microspheres increases shunting of intra-arterial treatment into the systemic circulation, thereby substantially reducing the therapeutic advantage of regional chemotherapy. The aim of this study was to measure the degree of shunting before and after high dose microsphere administration in patients with liver metastases, using radio-labelled albumin microspheres and hepatic artery perfusion studies.

A mathematical model was developed to improve the accuracy of base line shunting measurement using commercially available technetium labelled albumin microspheres. Also, albumin microspheres labelled with "Iodine was developed to allow measurement of the proportion of a 'therapeutic' dose of microspheres which shunts after hepatic artery perfusion.

The degree of shunting was measured in seven patients before and after arterio administra-
tion of a 'therapeutic' dose (4×10⁴) of microspheres, using imaging of abdomen and thorax by gamma camera. The mean shunt percentage before and after therapy were 2.2 (1.8%) and 3.0 (0.8%) respectively (NS).

We conclude that shunting associated with a therapeutic dose of microspheres is unlikely to

detract from their use in regional chemo-
thrapy.

Ki-67 - an immunohistochemical assessment of colonic cellular proliferation

G BARSOUm, M WINKLsT, AND M R B KEIGHELY (Academic Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH)

In man, tritiated thymidine (HTdR) studies have shown an increased mucosal labelling index in patients with polyps and colorectal cancer. No increase in crypt cell production rates (CCPR) have been identified in vitro.
The British Society of Gastroenterology

KEIGHLEY (Academic Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH) Frequency of defaecation after ileo-anal pouch construction bears a direct correlation to the ileal crypt cell production rate. Calcium supplementation, which can reduce diarrhoea post-proctocolectomy, may improve this pouch function by virtue of its anti-secretory effect, which has been demonstrated in colonic mucosa, as well as its ability to chelate fat and bile. The aim of this crossover study (with a washout period of 2 weeks) was to determine whether oral calcium supplements (1.5 g Ca gluconate/day) or placebo administered for 4 weeks, had an effect on frequency of defaecation.

Cellular proliferation in malignant and premalignant lesion of the colon

C HALL, G BARSOU, M WINSLET, and M R B KEIGHLEY (Academic Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH) Autodigestive radiographic assessment has shown an increased proliferation throughout the colon in patients with adenomas and colon cancer (CoCa). HfTDr studies, however, do not account for the crypt population and may be incorporated by a salvage pathway. A stathmokinetic technique takes account of all factors regulating proliferation and suggests the CCPR may be increased in CoCa. The aim of this study was to assess CCPR at the transitional zone (TZ) and reference point (RP) 10 cm from the anal verge in controls, villous adenoma, FAP, right and left-sided CoCa.

Redox potential measurement in the gastro-intestinal tract in man

V STIRRUP, S J LEDINGHAM, M THOMAS, G PYE, and D F EVANS (Department of Surgery, University CollegeLondon, London WC1). Colonic pH has been implicated in the pathogenesis of colorectal cancer but is influenced by short-term dietary changes. Redox potential is an expression of total metabolic and bacterial activity and may not be as sensitive to short-time dietary changes but reflect general colonic dynamics. We have measured redox potential in order to establish normal ranges in 15 healthy volunteers (age range 19–42 years) using a redox-sensitive radiotelemetry capsule and portable recording equipment during a total GI transit. Subjects were freely ambulant and had no dietary restrictions during the 48 hour study period. Mean (SD) redox potentials (mV) were –65±0.47 in the proximal small bowel (PSB), –196.5±96.8 in the distal small bowel (DSB), –415.2±72 in the right colon (RC) and –380.0±110.0 in the left colon. Significant differences were seen between PSB and DSB (p<0.01) and DSB and RC (p<0.001) but no such differences between RC and LC, a finding in conflict with previously measured pH values. Redox potentials have been successfully measured in the colon in healthy volunteers and differences that are not mirrored by pH change have been observed. Studies in patients with colorectal neoplasia are underway and may be helpful in understanding the aetiology of the disease.

Ileal pouch pH: a regulatory mechanism for evacuation

G CHATTOPADHYAY, D KUMAR, M R B KEIGHLEY, and M OYA (Department of Surgery, The Queen Elizabeth Hospital, Birmingham B15 2TH) The role of pouch pH in the regulation of pouch evacuation after a restorative proctocolectomy is not known. To investigate the mechanism of ileal pouch evacuation, we have studied pouch pH for 4 weeks in 10 patients who had restorative proctocolectomy for chronic ulcerative colitis. The pH was measured using a radiotelemetry capsule (Oxford Medical System 1000) tied to the end of a tether and positioned in the pouch. The tether was taped to the buttock. The signal was recorded continuously for 24 hours in a portable solid state pH data logger. The mean (SEM) pouch pH was 6.08±0.64. There was no difference between the day and night pH (6.10±0.64) and that during sleep (6.13±0.98). We recorded 53 episodes of pouch evacuation (mean of 5.3 per subject). The pouch pH exhibited a significant fall (p<0.05) in the 30 minutes preceding evacuation (5.71±0.68) when compared with the 30 minutes immediately afterwards (6.57±0.71). Meals, on the other hand, had the opposite effect on pouch pH. There was a significant rise (p<0.05) in pouch pH approximately two hours after a meal (5.99±0.66) t 7.08±0.74). These data suggest that pouch pH may be important in the regulation of pouch evacuation and may have important implications on pouch function after restorative proctocolectomy. The exact role of pH in the regulation of pouch emptying needs further evaluation.

Abdominal bloating in the irritable bowel syndrome (IBS)

S M CATNACH, P DEWSNAP, M HERDMAN, G LIBBY, M J G FARTHING, and P D FAIRCLOUGH (Departments of Gastroenterology and Respiratory Medicine, St Bartholomew's Hospital, London EC1A 7BE) Abdominal distension is a frequent symptom of IBS and its role in IBS remains unclear. We have examined whether bloating is due to diaphragmatic descent in 12 IBS patients (10 women, age 26–70 years) who described visible abdominal bloating in response to food. Diaphragmatic descent was measured by studying changes in functional residual capacity (FRC) by helium dilution and plethysmography. Diaphragmatic splitting was determined by measuring total capacity by helium dilution and standing the patient and remained. Bellows were also documented.

Tests were performed before and after a meal. Evidence of an affective disorder was sought by a semistructured psychiatric interview using the Schedule for Affective Disorders and Schizophrenia in nine of the 12 patients. All patients complained of bloating after the test meal and girth increase was significantly greater in IBS (2.7±1.3 cm, range) than in controls (0.9±0.5 cm; p<0.05). There was no change in lumbar lordosis or diaphragmatic position (FRC helium dilution 3.6±0.9 8v 3.0±0.9 5; plethysmography 3 0.3±0.8 4 v 2 9±0.8 4) and no evidence of splitting of the diaphragm. All nine patients tested had evidence of an affective disorder. Thus bloating is associated with increase in abdominal
girth and affective disorder but not with diaphragmatic splinting or descent. We suggest that the increase in girth in IBS patients is related to relaxation of abdominal muscles.

Ileal ecology and design of the pelvic reservoir
P M Sagar, P G R Godwin, P Quirke, P J Holdsworth, and D Johnston (The General Infirmary, Leeds) To identify differences between two designs of ileal reservoir in the bacterial content of reservoir effluent, volatile fatty acids content, efficiency of evacuation, or mucosal inflammation. Thirty patients were studied after restorative proctocolectomy for ulcerative colitis. A triplicated (S) reservoir was used in 10 patients and a quadruplicated (W) reservoir in 20. Fresh faecal samples were collected and processed promptly. Efficiency of evacuation was determined by the use of radiolabelled synthetic stool. Mucosal changes in reservoir biopsies were assessed by histology.

The effluent from S reservoirs had significantly greater numbers of bacteria (12 × 10^5 cfu/ml [0.03825-18.7 × 10^5] cfu/ml [0.0011-1.75]) (p < 0.05) and concentrations of acetate (231-7 ± 36.8 µmol/l [119-3-368.4] ± 94.9 µmol/l [33.4-211.9]) and propionic acids (60.1 ± 15.2 µmol/l [23.75-91.2] ± 16-7 µmol/l [10-2-46-2]) (p < 0.05) than effluent from W reservoirs. Efficiency of evacuation was reduced in patients with S reservoirs (59.5% [38-68-5] ± 97.4% [91-8-98]). There were no significant differences between the two groups in ratio of anaerobes to aerobes, % water content of the stool, or mucosal changes.

The ileal ecology of S and W reservoirs is different and may be related to stasis.

*Median (interquartile range).

Evaluation of current surgical management of acute inflammatory diverticular disease
S Sarin and P B Boulos (Department of Surgery, University College and Middlesex School of Medicine, The Rayne Institute, S University Street, London WC1E 6JF) Primary resection rather than non-resection has been recommended for acute diverticular disease and has extended to phlegmonous diverticulitis. Either approach is a staged procedure but the outcome at completion of treatment has not been documented. We, therefore, retrospectively examined the results of treatment in 127 patients admitted from 1980 to 1987; clinically diagnosed as diverticulitis in 86, perforation in 33, and colonic cancer in eight. Conservative treatment was effective in 73 (68%) with diverticulitis and the remaining 13 non-responders required surgery. Of 31 patients, with a clinical diagnosis of perforation, 19 (60%) had free purulent or faecal fluid at laparotomy and the rest, in common with all patients operated on, had a localised phlegmonous mass. Sigmoid resection was performed in 34 patients and non-resection in 18, with preference for the former in patients with peritonitis in the earlier period (62% ± 28%) and patients with localised disease in a later period (93% ± 90%). This significantly reduced mortality in patients with peritonitis (p < 0.01) but not in those with phlegmonous diverticulitis. However, the benefit was in the number of procedures (2.1 ± 1.5) per patient, the median total hospital stay (50.5 ± 32 days, p < 0.01) and the wound infection rate (32% ± 16%, p < 0.01) at the end of treatment. It is therefore necessary to identify patients with true peritonitis as conservative treatment is effective in the majority with phlegmonous diverticulitis. The optimum surgical approach in either case would appear to resection.

Idiopathic megacoeum and megacolon: which operation offers the best results?
G Stabile, M A Kamm, J E Lennard-Jones, and P R Hawley (St Mark's Hospital, City Road, London EC1V 2PS) Little data exist on the outcome of surgery for idiopathic megacoeum or megacolon, or both. We have reviewed the results of surgery in 60 such patients in whom Hirschsprung's disease and secondary causes had been excluded. All 60 patients had a bowel frequency of <2/week.

Twenty patients (14 men and six women, mean age 25 years, mean follow up 4.5 years) had a Duhamel procedure (D). Nineteen had abdominal pain or distension. Eighteen had dilatation of the rectosigmond only. Forty patients (17 men and 23 women, mean age 33 years, mean follow up 7.5 years) had a partial or subtotal colectomy (C). Twelve had childhood anastomosis and 37 ileostomy (-C, IRA-80%, SC-83%). Eleven had ileostomy and had resection. Of these, 40, 22 colectomy and caecocoelectomy anastomosis (CRA), 11 ileorectal anastomosis (IRA), and seven sigmoid colectomy (SC).

Bowel frequency was normalised (3/day-3/week) more by colectomy than by Duhamel (D-5.3%, CRA-80%, IRA-90%, SC-83%). Anorectal function was normal. Abdominal pain was still common after colectomy operations (D-47%, CRA-45%, IRA-90%, SC-17%). Most patients felt well or very well postoperatively (D-69%, CRA-85%, IRA-80%, SC-83%). Colectomy benefited equally left and whole colon dilatation. Pelvic sepsis was more common after Duhamel (D-15%, C-0%). Further surgery for constipation was more common after Duhamel (D-25%, C-8%). One elderly diabetic died after colectomy.

Colectomy was the option preferred to Duhamel in relation to well-being, early complications, and bowel frequency. Residual pain is common after both. Possibly the Duhamel patients had a greater rectal diameter, causing some of the differences in results.

Pyoderma gangrenosum in inflammatory bowel disease
M D Levitt, J K Ritchie, and R K S Phillipis (St Mark's Hospital, City Road, London EC1V 2PS) Since 1984, 33 patients attended this hospital with pyoderma gangrenosum (PG) in association with ulcerative colitis (UC, 21 patients) or Crohn's disease (CD, 12 patients). Lesions were multiple in 24 patients (73%), and half were below the knee. At the onset of PG, UC was clinically active in 10 patients (48%) while CD was active in nine (75%). Associated illnesses usually a seronegative arthritis affecting large joints were present in 9 (29%) patients with PG respectively. A diffuse putter rash appeared in six patients, synchronously with PG in five. In seven patients (UC, two; CD, five) the onset and course of PG appeared to be linked to non-dematological suppurations. PG resolved without the need for intestinal resection in two thirds of patients. When present at the time of surgical resection (15 procedures in 13 patients), PG healed promptly in five cases, only with additional therapy in five, and very slowly or not at all in five.

Pyoderma gangrenosum is seen in both UC and CD and healing appears unrelated to the timing and extent of intestinal resection. A purulent rash of 'pyoderma-like' lesions may also be seen. In some patients, PG may indicate the presence of occult or undrained perineal, paracolic or pelvic sepsis.

Subcutaneous rectal stump closure after emergency subtotal colectomy
R NG, A H Davies, and N J McC Mortensen (Departments of Gastroenterology and Surgery, John Radcliffe Hospital, Oxford) Subtotal colectomy with preservation of the rectum is commonly performed in patients with severe colitis requiring emergency surgery. It allows for careful assessment of colonic histology and the possibility of subsequent restorative procedures. The management of the rectal stump is controversial. If closed over in the pelvis there is a risk of perforation and it may be difficult to locate. A mucous fistula is a safer option but results in a second stoma.

We have prospectively studied the use of a transperineal approach using the sterile adhesive disc on the caudal end of the abdominal incision in the subcutaneous or fascial layer. A catheter is placed per anum to drain the rectum.

Twelve patients (seven men, five women) of mean age 32 years (range 16-76 years) with severe inflammatory bowel disease (10 ulcerative colitis, one Crohn's disease, one indeterminate colitis) have had the new procedure. Four stumps were closed with staples, four sutured, and three with both.

There were no major complications related to rectal stump closure or any other aspect of the acute colectomy. Two patients developed minor wound infections at the level of the incision. At subsequent restorative surgery the rectal stump was always readily located.

We recommend this technique as a simple and safe alternative to a mucous fistula.

Manometry before ileostomy closure predicts outcome after restorative proctocolectomy
P M Sagar, P J Holdsworth, and D Johnston (University Department of Surgery, The General Infirmary, Leeds) A diverting ileostomy is used in most patients who undergo restorative proctocolectomy (RP). It is closed two-three months later. Our hypothesis was that manometric measurements of the anal canal and ileal pouch at the time of closure would correlate with clinical outcome. The functional volume (FV), maximum tolerated volume (MTV), and compliance of the pouch and pressure profile and electromyography of the anal canal were measured in 51 patients prior to ileostomy closure. The clinical outcomes were determined by interview or questionnaire at least 12 months later.

A low resting anal pressure was associated with subsequent minor incontinence (r = 0.46, p = 0.001) and the use of a perianal pad (r = 0.37, p = 0.012). The MTV and pouch compliance at closure were 220 ml (148-340 ml, IQR range) and 9.9 ml/cmH2O (7.7-14.0) respectively in patients with a stool frequency of ≤5/day and 218 ml (170-285) and 8.9 ml/cmH2O (7.2-10.6) in patients with a stool frequency >5/day. Anal canal length,
Does rectopexy cause constipation? Results of a prospective surgical study

M V MADDEN, M A KAMM, R J NICHOLLS, A N SANTHANAM, R CABOT, AND C T M SPEAKMAN (St Mark's Hospital, City Road, London ECIV 2PS) Although patients often complain of constipation after rectopexy for prolapse, there are no prospective data. We aimed to determine (a) whether rectopexy causes constipation by careful prospective questioning and extensive physiological testing, and (b) whether the type of operation influenced the development of constipation.

Twenty three patients (mean age 52 years, 21 women and two men) with complete rectal prolapse were randomised to preservation (n = 11) or division (n = 14) of the lateral ligaments during rectopexy. They were evaluated preoperatively and three months postoperatively for symptoms: detailed questioning about bowel frequency, straining and constiuncence; for motor function anal manometry, pudendal nerve latency, perineal descent; for sensory function: rectal and anal mucosal electrical sensitivity, rectal distension.

Constipation was present preoperatively in 48% and postoperatively in 52%. Four of 11 patients were cured of constipation but 5/12 (42%) who were not constipated became so. This was not influenced by type of operation (lateral division in two, division in three) and did not correlate with changes in sensory or motor function. Continence score was improved by rectopexy (median score before 3/4, after 2/4, p <0.001) and resting anal pressure increased (before 36 cm H2O, after 49, p <0.01). There was no significant change in other motor or sensory function.

Although the proportion of patients with constipation was not changed, it was precipitated in some patients who were previously normal. This was not influenced by lateral ligament division.

Does a stoma benefit patients with severe idiopathic constipation?

J R M VAN DER SYP, M A KAMM, R EVANS, AND J E LENNARD-JONES (St Mark's Hospital, City Road, London ECIV 2PS) Colostomy for severe idiopathic constipation is variable and unpredictable in its outcome — some patients experience diarrhoea, recurrent constipation, and continuing pain. Is the formation of a stoma more successful in relieving symptoms? No data are available to answer this question.

We reviewed all patients treated with a colostomy (C) or ileostomy (I) in one hospital over a 16 year period.

Mean age of patients (mean age 38 years, two men and 35 women, mean follow up three years) had a stoma created. All had a normal diameter colon on barium enema, and a bowel frequency of less than 1/week before initial surgery. Eleven patients (C = 10, I = 1) had idiopathic constipation (IC), 16 patients (C = 16) had constipation precipitated by pelvic surgery or birth trauma (SB) and 10 patients had an ileostomy after failed colectomy with ileorectal anastomosis (IRA).

Subjective improvement was highest in IC: IC-82%, SB-25%, IRA-50%. In all patients after a stoma pain was still present in 61%, bloating in 46%, and lack of faecal incontinence in 37%. Further surgery was required in: IC-18%, SB-38%, IRA-70%.

Patients who had a colostomy for idiopathic constipation as a primary procedure fare the best with the greatest symptom relief and are the lowest need for further surgery. Patients with an ileostomy after failed ileorectal anastomosis fare the worst; these patients may be at the most severe end of the constipation spectrum. Pain and other symptoms often persist despite stoma formation.

ANORECTAL POSTERS

Faecal mucin sulphatase activity is increased in ulcerative colitis.

H H TSAI AND J M RHODES (Department of Medicine, University of Liverpool, PO Box 147, Liverpool) Colonic mucin is heavily sulphated and this is likely to be important in determining its resistance to enzymatic attack. In previous studies using a non-specific substrate, faeces have been shown to contain sulphatase activity.

We have recently developed an assay that is specific for mucin sulphatases and have used this to quantify faecal mucin sulphatase in inflammatory bowel disease and control subjects.

Radio labelled mucin was synthesised by colonic biopsy specimens cultivated in the presence of 35S sulphate and purified by high performance gel filtration. Faecal sulphatase activity was assayed by incubating bacteria-free faecal homogenates in the substrate, and reactants were separated by desalting, and the released radio labelled sulphate precipitated by barium chloride and scintillation counted. Stool samples (22 ulcerative colitis (UC), 14 Crohn's disease (CD), and 17 normal subjects) were studied. Detectable mucin sulphatase activity was present in 10/17 controls, 11/14 CD, and 21/22 UC. Faecal sulphatase activity was increased in UC (median 80-2 range 0-1063 U/mg) compared with controls (median 11 range 0-53 U/mg) (p <0.001, Wilcoxon's rank sum test).

Patients with active UC (n=13, median 38-4 range 0-249 U/mg) had higher sulphatase activity than inactive UC (n=10, median 105-9 range 22-5-1063 U/mg) (p<0.05). Mucin sulphatase activity was not significantly increased in CD (median 36-5 range 0-106-6 U/mg). This finding may have significant implications for the pathogenesis of UC.

Cerebral evoked potentials — are they of value in anorectal disease?

C T M SPEAKMAN, M A KAMM, C SPENCE-JONES, AND M SWASH (Physiology Unit, St Mark's Hospital, City Road, London) Although motor abnormalities are well characterised in constipation and incontinence, sensory pathways have received little attention. To determine whether abnormalities of sensory conduction are important, we have assessed peripheral sensory perception and cerebral evoked potentials (CEPs) produced by anorectal stimulation.

Nine healthy controls (four M, five F) and 13 patients (11 F, 2 M) with either severe constipation (nine) or idiopathic faecal incontinence (four) were studied. (a) Recordings were obtained 2 cm behind the vertex (C2) with a surface electrode. CEPs were averaged from 200 sweeps. Using a bipolar ring, electrode stimulations were performed in the mid-anal canal and 10 and 15 cm into the rectum (3 Hz, 200 usec). Recordings were also made from posterior tibial (PT) and bilateral genial nerve (DGN) stimulation for comparison. (b) Rectal sensation was also assessed using balloon distension and electrical stimulation (10 Hz, 500 usec).

To CEPs from DGN and DGN, subjects were able to tolerate three times threshold stimulus, but for anorectal potentials they were only able to tolerate two to two and a half times the threshold. Reproducible recordings were possible in only three of nine controls and six of 13 patients after rectal stimulation and only two of 22 after anal stimulation. In all cases recordings from DGN and PT were easily reproducible. The mean latencies were 37 ms (range 34–40) for DGN, 38 ms (32–42) for PT. There was no difference in the CEP latencies after DGN stimulation between the groups. From rectal stimulation the latencies ranged from 35–73 ms. In the constipated group there was a significant difference in balloon distension threshold and urge volumes (p<0.05) and rectal electrical sensation (p<0.05) from controls.

Peripheral sensory testing shows abnormality in severe constipation. However, CEPs cannot be reliably produced by anal or rectal stimulation, and when evident are of too broad a range to discriminate between health and disease. This probably relates to the difference between somatic and visceral pathways.

Prevalence of the irritable bowel syndrome in a random sample of the British population

L J D’O’DONNELL, K W HEATON, R A MOUNTFORD, AND T E BRADDON (University Department of Medicine, Bristol Royal Infirmary, and BS2 8HW) Irritable bowel syndrome (IBS) symptoms are known to be common in apparently healthy individuals but population based epidemiological data are non-existent. To investigate whether IBS symptoms and how many complain to doctors about them, we interviewed a stratified random sample of 1896 urban residents using a questionnaire incorporating the six diagnostic criteria of Manning et al (1978) — that is, recurrent abdominal pain relieved by defaecation or associated with more numerous or looser stools, frequent bloating, frequent incomplete evacuation, and passage of mucus. Altogether 1058 women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample.

At least one of the six symptoms was admitted to by 36% (33% women) and more by 19-5% and 8% respectively (women>men, p<0.01). The classic IBS symptom of recurrent pain relieved by defaecation or associated with more numerous or looser stools, frequent bloating, frequent incomplete evacuation, and passage of mucus. Altogether 1058 women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample. Although 36% women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample. Although 36% women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample. Although 36% women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample. Although 36% women (25–69 years, 838 men (40–69 years) were interviewed, comprising 72% of the targeted sample.
valent in the population especially in women, with no clear relation to age. Women also
complain more to doctors.

Reduction of rectal sensitivity and postprandial motility by granisetron, a 5HT3
receptor antagonist, in patients with irritable bowel syndrome (IBS)

A PRIOR AND N W READ (Royal Hallamshire Hospital, Sheffield). It is thought that 5HT3
receptors play a role in visceral nociception. Many patients with IBS have visceral hyper-
sensitivity and a drug which reduces sensitivity might become therapeutic. We have been
placebo controlled study on the effect of intra-
venous granisetron (160 μg/kg), a specific 5HT3 antagonist, on the anorectal response to
rectal distension and a 1000 calorie meal was therefore performed in 12 patients with IBS.

Granisetron caused a significant increase in the mean (SEM) threshold volumes (ml) for
the perception of gas (placebo 17.2, granisetron 34 (6) p<0.05), stool (placebo 43 (5), granis-
tram 58 (7) p<0.03), and discomfort (placebo 84 (10), granisetron 113 (13) p<0.01.

No significant changes in basal anal pressures (placebo 123 (12), granisetron 125 (9)
mmHg, rectal compliance (placebo 5-3 (9-8), granisetron 6-5 (1-1) ml/cmH2O) or motility index
during distension (placebo 254 (71), granisetron 213 (64)) were noted.

Granisetron also caused a highly significant reduction in postprandial motility (0-60
minutes motility index; placebo 5263 (1669), granisetron 1675 (527) p<0.005.

The results suggest that the 5HT3 receptor antagonists may have a potential therapeutic
role in patients with IBS.

Diversion colitis and involution of the defunctioned anorectum

A M ROE, B F WARREN, A J M BRODIRRIB, AND C BROWN (Department of Surgery, Derriford
Hospital, Plymouth and Department of Histopathology, Bristol Royal Infirmary).
The defunctioned anorectum may be affected by diversion colitis and involution leading to
difficulties with surgical reanastomosis. These changes are not well documented and this
was the aim of the study. Patients were five men and three women, aged 63 (45-81)
years. All had Hartmann's procedure; five for complicated diverticular disease and three for
carcinoma. Physiological changes were measured by anal sphincter manometry and
proctometrygrams at one and three months postoperatively. Diversion colitis was assessed
by endoscopic index and by histology of mucosal biopsy specimens at three months.
Results showed no changes in anal sphincter length, maximum resting pressure, or maxi-
mum squeeze pressure. Proctometrygrams showed no change in 1st sensation of rectal
filling, maximum tolerable pressure, or rectal compliance. However, there was a marked
reduction in maximum tolerable volume (p<0.01). Endoscopic index of colitis (0 absent, 1 mild, 2 severe) was erythema (0-2); oedema (1-0); friability 0 (0-1); granularity 1 (0-2); and erosions 0 (0-1). Seven of eight patients showed changes of diversion colitis but
these remained mild at three months. Diversion colitis has no effect on the anal
sphincters or rectal sensation but rectal volume has reduced by a mean of 34% and this predates
the severe changes of diversion colitis.

Results of Delorme's operation for rectal prolapse

A SENAPATI, R J NICHOLLS, R K S PHILLIPS, AND J P THOMSON (St Mark's Hospital, London). The
Delorme's operation is a perineal operation for rectal prolapse, which can be performed on
unfit patients with possible advantages over recropexy.

Thirty two patients (24 men and eight
women mean age 69±6 years) underwent Delorme's operation between 1978 and 1990
following symptoms lasting between 10 years and two weeks. Thirteen patients had had 21
previous operations for prolapse.

The mean total operation time was 64-6 minutes. No blood transfusions were needed, there was
no operative mortality, and two patients had complications. Over a mean follow up of 24
months, nine patients died of unrelated conditions with whom had had two previous procedures.

Incontinence improved in 46%. No patient became constipated and 50% of those consti-
ipated improved. In 1 patient abdominal rectal sensitivity is low with a rectal sensation but rectal volume
in good bowel function, and has a low recurrence rate and perhaps should be used more readily.

Predictive value of the funnel deformity in idiopathic faecal incontinence

JORTZS, M OYA, C CHATTAPADHYAY, D KUMAR, AND M R B KEIGHLEY (Department of Surgery, Queen
Elizabeth Hospital, Birmingham B15 2TH). A funnel shaped defect at the anorectal junction
may be seen on videoproctography among patients with neuropathic faecal incontinence.

We identified this defect in 75 of 103 patients with neuropathic faecal incontinence com-
pared with only one of 23 controls (p<0.001).

The deformity is associated with impaired sensations in the upper anal canal, an obtuse
anorectal angle, and low anal canal pressures.

We have examined the relation between this defect and functional outcome in 25 patients
in a longitudinal study. Functional outcome was scored in the last six months of the study,
in the 2 years after, and after 5 years. We compared patients with follow up and those who
had no follow up.

The funnel defect was observed in 18 (72%) before post anal repair. Preoperative evidence of this
defect predicted persistent incontinence to solids in 14 of 18 patients compared with only two
of seven where the deformity was absent (p<0.05).

The funnel defect was present in 14 (70%) before total pelvic floor repair. Since
only one patient had persistent incontinence to solids after a total pelvic floor repair,
the presence of the defect before operation was of no predictive value.

We conclude that a funnel defect is common in neuropathic faecal incontinence. The defect
predicts a group of patients who are likely to have persistent faecal incontinence after post
anal repair but not after total pelvic floor repair.

STOMACH POSTERS

Effect of inhibition of Helicobacter pylori urease activity with acetohydroxamic acid on
plasma gastrin in subjects with duodenal ulcer

A M EL NJUMI, C A DORIAN, AND K E L MCCOLL (University Departments of Medicine and Therap-
etics, and Pathological Biochemistry, Western
Infermary, Glasgow) Plasma gastrin concentrations are raised in patients with Helicobacter
pylori infection. This may be due to the ammonia produced by the bacterium's urease
stimulating gastrin release directly or via its effect on antral surface pH. We have examined
the effect of competitively inhibiting H pylori
urease activity, with acetohydroxamic acid
(AHA) on plasma gastrin in six duodenal ulcer
(=DU) patients. On day 1 the fasted patients
received placebo tablets at 08:00 hours, an
'OXO' meal at 10:00 hours and a 'C-urea'
breath test at 10:00 hours. On the following
day the following day but 750 mg AHA
was administered orally in place of placebo. A third
breath test was performed 10 days later.

The median (range) 20 minute breath test value
with placebo was 90 (15-17) ppm. with placebo/placebo (74 (16-136)) and with AHA
(40 (1.5)) after 10 days. The median (range) 20 minute breath test value
with AHA/placebo was 14 (10-17) ppm. The breath
value with AHA/placebo was 14 (10-17) ppm.

It is possible that with AHA the urease
activity of Helicobacter pylori was suppressed
with AHA/placebo breath test values were comparable to the pretreatment.

The results of this study showed that AHA/helicobacter gastrin concentration in patients
with H pylori infection is not directly related to the organism's urease activity. It also
shows that suppression of H pylori urease activity does not eradicate the infection.

Study of gastric juice factors implicated in gastric carcinogenesis in members of a
gastric cancer family

G M SOBALA, B PIGNATELLI, C J SCHORAH, H BARTSCH, S H SHURES, N SCOTT, P QUERE,
M LANDOWSON, I MARTIN, A TR AXON, AND M MCAHON (Gastroenterology Unit, University
Departments of Chemical Pathology and Pathology, and the Professorial Surgical Unit,
General Infirmary, Leeds, and the Institute of Environmental Carcinogens and Host Factors,
IARC, Lyon, France) A study of factors implicated in gastric carcinogenesis was made
in a family in which two siblings have died of gastrointestinal cancer. A third individual
has had a gastrectomy for dysplasia and three of the children have chronic gastritis
and intestinal metaplasia before age 35 years. Fasting gastric
juice was obtained from four of the children
with Helicobacter associated chronic gastritis,
three also have intestinal metaplasia. The
gastric juice was acid (pH 1.8-2.1) and
nitrile (5.0-17.9 μmol/l) and nitrosocom pound (0-28 μmol/l) levels. Fasting gastric
conzenttrations were not different from those found in gastric juice from normal subjects.

Previous published studies have shown that secretion of ascorbic acid (a putative protective factor)
into gastric juice is impaired in chronic gastritis. However, in this family gastric ascorbic acid
concentration ranged between 76 and 366 μmol/l, much
higher than that in 20 age and pH matched controls with chronic gastritis (median 24 μmol/l,
95% confidence limits 10-100 μmol/l). Also, fasting gastric juice levels of vitamin C concentrations
did not differ from controls. Thus in this cancer family (a) intestinal metaplasia has occurred earlier than
documented by the Correa hypothesis (b) gastric carcinogenesis and must be due to factors other
than nitrite and nitrosocomound exposure, and
(b) chronic gastritis has unexpectedly
failed to impair gastric ascorbic acid secretion.
Is Helicobacter pylori-associated hypergastrinaemia due to the bacterium's urease activity or the antral gastritis?

R S CHITTALLU, C A DORIAN, AND K E L MCCOLL

(University Department of Medicine and Therapeutics, Department of Pathological Biochemistry, Western Infirmary, Glasgow)

Eradiation of Helicobacter pylori is associated with a fall in serum gastrin but the mechanism by which the infection raises serum gastrin is not clear. It may be related to the ammonia produced by the bacterium's urease stimulating gastrin release by the antral G cells.

Alternatively, the antral gastritis induced by the infection may modify the regulation of gastrin release. To determine which of these mechanisms may be responsible for the hypergastrinaemia we have studied eight patients before and 24 hours after commencing triple therapy consisting of trimetoprim, diclofenac sodium (120 mg qid), metronidazole (400 mg tid), and amoxicillin (500 mg tid). The urease activity assessed by the 20 minute value of the pH-urea breath fell from a median of 176 (range 116–504) at baseline to CO×100 pretreatment to 4 (2–13) at 24 hours (p<0.01).

The median antral gastrite score was 6 (4–6) pretreatment and fell to 3 (2–5) at 24 hours (p<0.02). Despite this complete suppression of basal gastrin activity and partial neutralisation of antral gastritis the median basal gastrin concentration remained unchanged being 60 ng/l (50–77) pretreatment and 59 (47–80) at 24 hours.

In conclusion, these findings do not support a causal association between H pylori urease activity and hypergastrinaemia. In addition our results demonstrate that there is rapid improvement of antral gastritis following commencement of anti-H pylori therapy.

Simultaneous measurement of ascorbic acid, nitrate, nitrite, total nitroso compounds and total bile acids in gastric juice: relevance to gastric carcinogenesis

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To determine the relevance of gastric juice factors to gastric carcinogenesis, 56 patients with unoperated stomachs undergoing endoscopy for dyspepsia had gastric juice analysed for pH, ascorbic acid, total bile acids, nitrite, nitrate, and total nitroso compounds. Plasma was obtained for vitamin C estimation. Antral and biopsy specimens were assessed for gastritis, Helicobacter pylori, atrophy, and intestinal metaplasia. Patients with chronic gastritis (n=35) had lower juice ascorbic acid (p<0.001), higher pH (p<0.05) and higher incidence of H pylori (p<0.001). Patients with reflex gastritis (n=9) had higher total bile acids (p<0.01). Patients with chronic gastritis and intestinal metaplasia (n=11) had higher juice pH (p<0.01) and total bile acids (p<0.05), and lower juice ascorbic acid (p<0.01) than those with only chronic gastritis (n=24). In chronic gastritis high nitrite was associated with high pH (p<0.01). There were no differences in plasma vitamin C, gastric nitrite, nitrate, or total nitroso compounds in relation to gastric histology. Thus, intestinal metaplasia is associated with H pylori, low gastric ascorbic acid, and elevated total bile acids, but contrary to the Correa hypothesis of gastric carcinogenesis no elevation in nitrite or total nitroso compounds in fasting gastric juice.

A prospective evaluation of psychiatric morbidity and personality trait in non-ulcer dyspepsia

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The importance of stress and disordered personality on the aetiology of non-ulcer dyspepsia (NUD) is unknown. In this prospective study, the incidence of psychiatric morbidity and disordered personality trait was sought in 33 NUD patients, after exclusion of peptic ulcer, gall stones, and gastro-oesophageal reflux. Psychiatric morbidity was evaluated by the General Health Questionnaire (GHQ) and a score >12 was regarded as positive for psychiatric illness. Personality of the trait assessed by the Eysenck Personality Inventory (EPI) which contrasts levels of extraversion and neuroticism. Results were validated against 20 healthy volunteers and 20 non-dyspeptic surgical inpatients. Both groups were age and sex matched.

On the basis of the GHQ, there was no difference in the incidence of psychiatric morbidity in the NUD patients (eight positive) against the healthy control group (five positive) and non-dyspeptic surgical inpatients (six positive). In relation to the EPI, the mean scores for extraversion and neuroticism were 11/11 in NUD patients, 14/12 in healthy controls, and 13/13 in patient surgical controls. Thus there was no evidence of disordered personality trait in NUD.

Psychiatric morbidity or disordered personality do not seem to be an important factor in the aetiology of NUD.

Carcinoma of the gastric cardia – a five year audit

A J JEWKES, A PRIOR, C SMALLPIECE, AND J B ELDER (Department of Thoracic and General Surgery, North Staffordshire Hospital Centre, Stoke-on-Trent)

Survival in the incidence of gastric cancer, the proportion of tumours affecting the cardia seems to be increasing. Surgery still offers the only prospect of long term survival. To assess an aggressive surgical approach we have audited the outcome of patients in one hospital centre.

From 1984 to 1989, 52 patients (mean age 64-6 years; M:F=-3:2) underwent operation for proven, localized cancer of the cardia. Radical resection was possible in 69-2%. Total gastrectomy was undertaken in 42-3% with the remainder having an oesophagogastrectomy.

Hospital mortality was 9-6%, with a further two patients dying within 30 days of operation (30 days mortality=15-3%). Significant complications occurred in nearly one third of patients (30-5%), including five clinical leaks (mortality 60%) and five anastomotic strictures. Median survival was 11 months with a four year survival of 19-2%. The type of reconstruction and the use of staples had no significant effect on operative mortality or long term survival.

Surgery of carcinoma of the cardia seems relatively safe with mortality and morbidity comparable to specialised centres. All patients with this condition should be considered for surgery as long term survival is possible in a significant number of cases. Despite a policy of laparotomy in all cases without obvious metastatic disease, the high proportion of stage II and III disease (67-3%) suggests patient selection was occurring.

Omeprazole v sulcrate in the treatment of NSAID-induced gastric and duodenal ulcer

G BIANCHI PORRO, F SANTALUCIA, AND M PETRILLO (Gastrointestinal Unit, L Sacco Hospital, Milan, Italy)

Both anti-inflammatory drugs and cytoprotective agents are helpful in promoting healing of NSAID-induced gastroduodenal lesions. As no studies as yet have directly compared omeprazole (OM) with sulcrate (SC), we investigated 30 rheumatoid patients (four men, 26 women, mean age 56-3 years) with NSAID-induced gastric (n=17), duodenal (n=10), and gastric and duodenal ulcer (n=3). Patients were randomised to receive 20 mg of OM (UG=4, UD+UD=2) or 4 mg daily of SC (UG=8, UD=6, UG+UD=1). NSAID therapy was not stopped during the antulcer treatment. Endoscopic control was performed after four weeks and eight weeks in those not healed. After four weeks 13 of 13 patients (100%) treated with OM were healed compared with nine of 14 patients (64-2%) on SC (p<0.05). Two patients treated with OM and one with SC withdrew for reasons unrelated to the therapy. Another patient (one of four, 25%) on SC healed after a further four weeks. One patient withdrew for reasons unrelated to the treatment.

This preliminary data shows that OM is more effective than SC in promoting the healing of NSAID-induced gastric duodenal lesions in rheumatic patients who do not interrupt their NSAID treatment for arthritis.

A randomised trial of diazemuls v midazolam in monitoring patients undergoing gastroscopy

I FARQUHAR AND J D HARRISON (Departments of Anaesthesia and Surgery, University Hospital, Nottingham, NG7 2UH)

Gastroscopy is associated with arterial oxygen desaturation, however no data exists comparing the two most commonly used agents, diazemuls and midazolam. This prospective randomised study compared the effects of these drugs on blood pressure (BP) and oxygen saturation in 81 patients presenting for gastroscopy. Patients received either midazolam (0-7 mg/kg) or Diazemuls (0-21 mg/kg). In a double blind study patients were randomized to one of two groups, diazemuls and midazolam randomized groups were matched for age and sex. The RPP was significantly higher during sedation with midazolam compared with diazemuls during the induction of sedation (p=0.001); endoscopy (p=0.0004), and recovery (p=0.001), implying a higher myocardial workload in the midazolam group. There was also a significantly greater fall in the OS during endoscopy with midazolam (p=0.001). There...
was a significant negative correlation between RPP and OS during endoscopy. We conclude that diazemosul has a superior cardiovascular profile for use in sedating patients for gastroscopy.

### Risk factors for gastrointestinal injury: prospective multicentre study on 497 rheumatic patients

W Biewer, B Buschmeier, and W Bolen (introduced by R P WALT) (Klinik für Rheumatologie, Bad Kreuznach, Rheumaklinikin, Bad Reichenau, W Germany) This study investigates the damaging effect of acetylsalicylic acid, other NSAID and corticosteroids on gastroduodenal mucosa. Risk factors were evaluated comparing patients with Lanza score greater than 4 and with duodenal ulcer disease (without ulcer protecting agents for at least two weeks) were endoscopically controlled. The incidence of Lanza score 3 or 4 (>10 erosions/duodenal or gastric ulcer) was 18/8% for the stomach and duodenum. Gastric lesions (score 3 and 4) were frequent both in symptomatic (20%) and asymptomatic patients (15%).

There was a significantly higher incidence of gastric injury for patients with ulcer history (28-7%), age over 60 years (24-0%), sedimentation of blood >40 mm/h (28-3%), and concurrent diseases (23%). Duodenal damage was significantly higher in patients with ulcer history (12-2%), acute dyspeptic symptoms (11-3%), and smokers (12-1%). A high proportion of patients taking ASS (n=15) had mucosal lesions in patients taking corticosteroids alone or in combination with a NSAID had no increased risk.

As indicated by previous studies, rheumatic patients with ulcer history are at high risk for gastric and duodenal damage. The data show also a clear relation between prevalence of gastric damage and age over 60 and sedimentation of blood >40 mm/h.

### Double bite endoscopic biopsy specimens increase the number of sampling sites and increase tissue weight by 58%

C Stone, B Norton, A M Mackay, and G R Youngs (Chester Royal Infirmary, Chester CH1 2AZ) Repeated passage of biopsy forceps at endoscopy is time consuming and the target lesion may disappear from view. This study assesses whether multiple bite biopsies increase tissue yield while retaining quality for histology. Altogether 90 patients (61 gastroscopy (94.7%), 26 flexible sigmoidoscopy (FS)) seen to have a pathological lesion had biopsy specimens taken by two methods: a single bite on each of the three consecutive passages of the forceps, and a triple bite on one passage of the forceps. Spikey forceps were used. The specimens were submitted to the pathologist in coded bottles and judged adequate or inadequate for histology. Eighty-eight of the 90 repeat single samples and 86 of the 90 triple bite samples were considered adequate for histological diagnosis. Biopsy specimens from 53 further patients (25 OGD, 28 FS) were taken by two methods: a double bite on two consecutive passages of the forceps, and a single bite on two consecutive passages. The weights of these specimens were recorded after blotting. The mean percentage increase in weight of tissue obtained per patient with the double bite technique was 58% (OGD 65%, FS 53%). This study shows that a double bite biopsy technique increases tissue yield without loss of quality, increases the number of sampling sites, and reduces endoscopy time.

### Validation of a commercial ELISA for serodiagnosis of Helicobacter pylori infection

J E Crabtree, T M Smallcress, J J Wyatt, and R V Heatley (Departments of Medicine and Pathology, St James's University Hospital, Leeds LS9 7TF) It is well established that serology is an accurate means of diagnosing Helicobacter pylori infection. Currently serodiagnosis is based on in house ELISAs and there has been no universal attempt to standardise assays, each laboratory having its own individual protocol. This study was collected from 242 patients undergoing routine endoscopy. Antral biopsy specimens were taken for histology and identification of H pylori by the modified Giemsa stain.

Altogether 150 of the 160 patients colonised with H pylori, all of whom had antral gastritis, were seropositive for H pylori. Sixty five of the 82 patients who were histologically negative for H pylori with normal antral mucosa were seronegative for H pylori. The Bio-Rad ELISA was significantly higher than the ELISA for H pylori, the Bio-Rad ELISA was therefore comparable with that of other reported ELISAs. Analysis of the data to include only patients under the age of 61 years (n=139) improved the sensitivity of the commercial ELISA to 97-6% and the specificity to 85-4%.

This study shows that a commercially available ELISA would be suitable for use in clinical practice.

### Cytological brushing urea broth test (CBBT) as a sensitive alternative for detecting antral Helicobacter pylori colonisation

C K Ching, C Buxton, C Holgate, J G Freeman, and G K T Holmes (Derbyshire Royal Infirmary, London Road, Derby DE1 2QY) Helicobacter pylori are located underneath the mucus layer and are predominantly in the antrum. We aimed to assess antral cytological brushings combined with urea broth test as an alternative approach for diagnosis of H pylori colonisation.

Patients with endoscopic appearance compatible with antral gastritis (n=28) have been studied. Pinch biopsy specimens were obtained for urea broth test and histochimistry followed by antral brushings. Brushings were then smeared on glass slides and each incubated in 0.5 ml modified Christensen urea broth. The time required for the colour change for cytological brushings (CBBT) and pinch biopsy specimens (BBT) were recorded. Histo logical examination reported by an independent experienced pathologist. Paired t test was used to compare the efficiency of CBBT and BBT.

Thirteen of the 28 cases lacked H pylori histologically and none of these was positive for CBBT or BBT. H pylori were shown histologically in the remaining 15 patients. Some 15 of 15 were CBBT+ but only 13 of 15 were BTT+. CBBT gave a significantly faster confirmation (mean time=7-36 minutes (range 1-15 minutes)) than BBT (mean time=30-45 minutes (range 5-60 minutes)) (p<0.0000) in the 13 cases that were both CBBT+ and BTT+. Furthermore, the speed of CBBT positivity correlated well with the density of H pylori observed in Giemsa stained specimens. CBBT is a highly sensitive, cheap, and simple test for detecting H pylori infection.

### Validation studies with a portable bile reflux detector

D L Stoker, J G Williams, M A Macleod, and D G Colin-Jones (introduced by J G Williams) (Royal Naval Hospital, Haslar, Gosport, Hampshire PO14 2AA) Gastric bile reflux has been studied in two units, with difficulty to monitor in ambulatory patients. This study aims to validate a newly developed intragastric probe for measuring duodenogastric bile reflux in humans.

Two patients (A and B) with bile reflux, and three normal volunteers (C, D, and E) underwent monitoring. The probe was passed nasally, to a position 5 cm below the cardia. Each subject was placed supine under a gamma camera, centred on the upper part of the stomach. The 99mTc-HIDA were administered intravenously, and simultaneous internal/external scanning was performed for between 45 and 90 minutes. Gamma camera counts from a region of interest over the fundus of the stomach were then correlated with counts from the internal probe (linear regression analysis).

Radionucleated bile refluxed into the stomach during HIDA scanning in three of the four units (one patient and two volunteers). There was a strong correlation between internal and external gamma counts (A, r=+0.79, C, r=+0.53, E, r=+0.54 p<0.01). In the other two subjects, where difficulty reflux, there was still significant correlation between internal and external gamma counts (B, r=+0.89, D, r=+0.75 p<0.01).

We conclude that the newly developed portable probe is capable of measuring the reflux of radionucleated bile into the human stomach.

### Randomised comparison of video vs conventional UGI endoscopy

S E Stock, J Watson, and C W Venables (Department of Surgery, Freeman Hospital, Newcastle upon Tyne) Video endoscopy offers distinct mechanical and use characteristic advantages over standard fibroptic endoscopy. To date, however, no comparative trial in the same subjects has been reported.

For the past 18 months a Fujinon EVF system has been in use in our unit and 97 patients have entered a direct comparative trial of this instrument against a standard endoscope (C2T). The order of usage was randomised and findings were recorded before the second examination.

Identical findings were made in 68 patients but discrepancies occurred in 29. Most differences related to minor mucosal changes but in seven the differences were major. These included three positive diagnoses (early cancer, polyps, hiatus hernia) and four negative diagnoses (cancer, gastric ulcer, duodenal ulcer) when the findings with EVF were compared with the C2T. Two discrepancies occurred with the first examination, whichever instrument was used.
Problems encountered during use and endoscopy’s views on the system will be reported. This study emphasises the need for meticulous and unhurried UGI endoscopy whichever instrument is used. Further comparative studies are required to confirm whether video endoscopy is suitable for routine diagnostic use.

Intrafamilial transmission of Helicobacter pylori

R COLLINS, S PATCHETT, B DRUMM, C T KEANE, and C O’MORAIN (Department of Gastroenterology, Adelaide and Meath Hospitals, Tallaght, Dublin, Ireland) The association between Helicobacter pylori, primary gastritis, and duodenal ulcer (DU) is well recognised. The mode of infection, however, is yet undetermined. We have studied 50 patients with proven DU and H pylori infection, in whom infection was eradicated and the ulcer healed, and followed for one year. Twelve of these were reinfected with H pylori. Ten had previous recurrence of gastritis and five had recurrence of DU. The reason for their reinfection remains unclear.

Accordingly, we sought evidence of intrafamilial spread by serological testing in families of H pylori positive and negative patients. We developed an ELISA assay to detect IgG antibodies to H pylori. A dilution giving 95% confidence intervals of infection with H pylori was established by comparing Ab titres in patients with biopsy specimen proven infection with those in normal controls. The family members of eight H pylori positive patients (n=42) and eight H pylori negative patients (n=37) were screened serologically. Thirty eight family members (90-5%) of the H pylori positive patients had significant titres. In the H pylori negative group, only three patients (8-1%) had significant titres (10-16%).

Therefore, it would seem that intrafamilial clustering of H pylori infection occurs and person to person spread of the organism may account for the reinfection rate encountered in our study.

Accurate determination of Helicobacter pylori status at endoscopy by measurement of the urea/ammonium ratio in gastric juice

W D NEITHERCUT, A MILNE, R S CHITTAJALLU, A M E. NUJUMI, and K E L. MCCOLL (University Department of Medicine and Therapeutics, and Department of Pathological Biochemistry, Western Infirmary, Glasgow) Helicobacter pylori possesses unusually high urease activity which lowers the urea concentration and raises the ammonium concentration of the gastric juice in infected individuals. We have assessed the value of measuring urea and ammonium concentrations in gastric juice obtained during endoscopy for diagnosis of gastritis, presence and eradication of the infection. Twenty four individuals with the infection and 14 in whom it had been eradicated were examined. H pylori status was confirmed by antral biopsy and the C14-urea breath test. The median (range) gastric juice urea concentration in those infected was 8-0 mmol/l (0-5-2.9 mmol/l) and 2-1 mmol/l (0-3-7 mmol/l) in non-infected patients (p=0.001). The median ammonium concentration in the infected subjects was 3-4 mmol/l (1-0-13-0 mmol/l) compared with 0-64 mmol/l (0-02-1-4 mmol/l) in non-infected patients. Though there was considerable overlap of the two groups with respect to their urea and ammonium concentrations, there was complete separation of them when their urea/ammonium ratios were calculated. In infected subjects this ratio ranged from 0-04-0-7 (median 0-26) and in non-infected subjects from 1-11-13 (median 3-4) (p=0.001). In conclusion, measurement of the urea/ammonium ratio in gastric juice obtained at endoscopy allows rapid and accurate determination of H pylori status.

Evaluation of European standard C14 carbon urea breath test for the detection of Helicobacter pylori

R P H LOGAN, S DILL, M M WALKER, F E BAUER, R P RATHBONE, P JOHNSON, J H BARON, and J J MISIEWICZ (Departments of Gastroenterology, Central Middlesex, St Mary’s Hospital, Leeds General Infirmary, UK, University Hospital, Basel, Department of Clinical Pharmacology, Gottingen, and Dukes Infirmary, London NW3) There are no agreed standard methods for the detection of Helicobacter pylori, a standardised protocol for the C14-urea breath (C14-UBT) was proposed by a European group. Novel features include a 100 mmol/l liquid test meal, C14 urea 100 mg and analysis of a single pooled sample. The results were compared with those from ELISA serology, CLO-test®, histology, and culture. To minimise sampling error, the ‘gold standard’ was taken as any two of the three biopsy specimen based tests being positive.

Ninety four patients (61 men, mean age 41 years, range 18-75 years) undergoing routine upper GI endoscopy were studied. Indications for endoscopy included epigastric pain (53%), previous DU (22%), abdominal pain (15%), with the most frequent endoscopic findings being DU (33%), normal (29%), and ‘gastriis’ (25%). H pylori was detected by the ‘gold standard’ in 70 of the 94 patients (74%). For the C14-UBT the specificity was 100%, with a sensitivity of 96%, compared with ELISA serology (98%/94%), CLO-test® (96%/97%), histology (96%/91%), and culture (96%/94%). The new European standard C14-UBT is as good as, and possibly better, than other methods for the detection of H pylori; as it is a non-invasive, safe, and low cost method it is ideal for epidemiological and clinical studies.

Self selection for endoscopic surveys in patients on NSAIDs

N HUDSON, S J EVERITT, A S TAH, R I RUSELL, R D STURROCK, and C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham and Centre for Rheumatic Diseases, Glanfield (Royal Infirmary) Peptic ulceration and gastropathy are claimed to be common in asymptomatic patients on non-steroidal anti-inflammatory drugs (NSAID). Previous studies have hypothesised the possibility of self selection by patients with low levels of dyspepsia. We therefore compared symptoms elicited by a sensitive diary questionnaire in patients starting or declining surveillance endoscopy. Altogether 106 patients with rheumatoid arthritis on NSAID were recruited to record symptoms over four weeks. Eighty eight patients returned completed diaries and were invited to undergo surveillance endoscopy.

Of 41 patients who declined, 61% were asymptomatic, compared with 33% of 47 patients who accepted (x2=p<0.02). Patients agreeing to endoscopy had significantly more frequent episodes of heartburn (p<0.04), dyspepsia (p<0.01), and abdominal pain of all types (p<0.004). There was no correlation between symptoms and age, smoking status, or length of NSAID usage. At endoscopy, mucosal damage (ulceration, erosions, or submucosal haemorrhage) was present in 66% of asymptomatic patients (n=15 ulcers=3), and 63% of symptomatic ones (n=32 ulcers=7).

Symptomatic patients are more likely to volunteer for surveillance endoscopy confirming estimates of prevalence. However, gastric lesions readily occur in patients without symptoms so that many patients with ulcers and gastropathy remain undetected by this approach.

Does Helicobacter pylori potentiate the damaging effect of non-steroidal anti-inflammatory drugs (NSAID)?

P M GOGGIN, D A COLLINS, J M MARRERO, R P JAZRAWI, B E BOURKE, and T C NORTHFIELD (Department of Medicine, St George’s Hospital Medical School, Cranmer Terrace, Tooting, London SW17 0RE) NSAID and Helicobacter pylori infection are both associated with an increased risk of peptic ulceration and gastropathy, but it is not known whether there is an interaction between these two agents, and thus whether or not screening for H pylori before NSAID treatment is of value. The aim of this study was to determine whether H pylori potentiates the damaging effects on NSAID. We studied 43 patients with rheumatoid arthritis requiring long-term NSAID therapy. Gastric biopsy was performed following one a week washout period during which NSAID were stopped. Gastric mucosa was graded endoscopically according to the Lanza classification, and H pylori identified by biopsy specimens urease (CLO) test and by histology. Investigations were repeated after one month’s treatment with indomethacin or lornoxicam.

After the washout period, the Lanza score was higher in H pylori positive (n=17) than in negative patients (n=26, Z=−2.74 p<0.01, Mann-Whitney U). One patient with duodenal ulcer H pylori positive and two with Lanza scores of 3 or more (both positive) were excluded from further study. Following treatment there was a rise in Lanza score both in the H pylori positive (p<0.05) and negative (p<0.01) groups. There was no difference in the extent of increase in grade (Z=0.9, NS) or the final grade at the end of the treatment period (Z=−0.247, NS) between the H pylori positive and negative patients. We conclude that H pylori infection, although associated with the presence of gastric erosions, does not potentiate the damaging effects of NSAID.

Helicobacter pylori increases the pH of the gastric mucosa in vivo

S M KELLY, J CRAMPTON, and J O HUNTER (Department of Gastroenterology, Addenbrooke’s Hospital, Hills Road, Cambridge) There is a strong association between Helicobacter pylori, gastritis, and duodenal ulceration. The exact pathogenic mechanism is unknown but it has been shown that the infection leads to increased gastrin release. Bacterial urease is postulated to increase gastrin release by converting urea to ammonia, so raising antral mucosal pH and impairing the normal
negative feedback of intraluminal acid. We assessed the effect of *H pylori* on antral intramucosal pH in vivo.

Measurements were made during endoscopy by means of a flexible pH microelectrode which could be passed down the biopsy channel of an endoscope. The electrode was connected to a pH meter and chart recorder. Studies were performed on patients attending for routine gastroscopy. Antral mucosal pH was measured at all sites. Biopsy samples were taken from these sites for histology and a CLO test for urease. The antral mucosal pH of 23 patients negative for *H pylori* was 6.4±3.0±0.6 compared with 6.9±5.0±0.16 in 13 positive patients (p<0.001). This study confirmed that *H pylori* increases antral mucosal pH. This could be a factor in the mechanism by which *H pylori* increases gastrin release.

Prevention of gastric mucosal damage by enteric coating (Nuseals) despite inhibition of prostaglandin synthesis

A B HAWTHORNE, S M HURST, Y R MARIDA, A T O’MORAIN (Department of Gastroenterology, Rowland Hill Street, London) and C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) Aspirin in low dose cardiovascular prophylaxis increases risks of melena substantially (US physicians study). We therefore investigated whether enteric coating (EC) could prevent gastric injury induced by low dose aspirin.

Twenty volunteers each received five days’ treatment with: placebo, aspirin (300 mg daily), Nuseals (300 mg daily), aspirin (300 mg qid), and NuSeals (600 mg qid). We assessed gastric mucosal injury endoscopically, bleeding by orthotolidine method, ex vivo gastric mucosal prostaglandin (PG)E2 synthesis, serum thromboxane and serum calcylate after each period.

All regimens inhibited mucosal PG2 synthesis by ≥90% (p<0.01). Plain aspirin (300 mg daily) caused significant gastric injury (blood spots): median 2 IQR (0–5), bleeding: 2:8 (1:6–4:8) μl/10 minutes, both p<0.01), which was abolished to placebo levels with NuSeals (erosions: 0 (0–1), bleeding: 0–0 (0–1), both p<0.01 compared with aspirin). With plain aspirin, bleeding increased in proportion to serum calcylate (regression slope = bleeding 4 μl/10 minutes, for each mg/I, calcylates RS=0.42, both p<0.01). With NuSeals the regression slope was flat consistent with topical protection. Both preparations reduced serum thromboxane by ≥99%.

Gastric injury from low dose aspirin is predominantly topical. It can be eliminated by enteric coated Seals, a suitable formulation for cardiovascular prophylaxis.

A randomised controlled trial of eradication of Helicobacter pylori on the symptoms of non-ulcer dyspepsia

S PATCHETT, S BEATTIE, E LEEN, C KEANE, and C MOWAN (Department of Gastroenterology, Meath/Adelaide Hospitals, Dublin, Ireland) The higher prevalence of *Helicobacter pylori* infection in patients with non-ulcer dyspepsia, and the strong association of *H pylori* with chronic active gastritis suggests that the organism may be causally associated with non-ulcer dyspepsia. This prospective study was carried out to assess the effect of *H pylori* eradication on the symptoms of non-ulcer dyspepsia. Altogether 84 patients with non-ulcer dyspepsia, who were positive for *H pylori* infection and had histologically proved gastritis were randomised to receive: (1) colloidal bismuth subcitrate (CBS) (1 g qid x 4 weeks (n=29), (2) amoxicillin (500 mg qid x 1 week) plus metronidazole (400 mg tid x 1 week) (n=28); or (3) amoxicillin (500 mg qid x 1 week) plus metronidazole (400 mg tid x 1 week) (n=29). All patients were endoscoped at entry and four weeks after cessation of treatment. At each endoscopy two antral biopsy specimens were taken and assessed histologically and microscopically for *Helicobacter pylori* infection. Symptoms were assessed before and after four weeks after completion of treatment using a standardised dyspepsia score. *H pylori* was eradicated in 44 (51%) of the 86 treated patients. In this group significant improvement of mean symptom scores was noted (6.82–2.23 p<0.01). However, of the 42 patients in whom infection persisted, a similar improvement in mean symptom scores was noted (6.98–2.95 p<0.01). Similar results were obtained for the three treatment subgroups, showed no significant correlation between eradication of infection and improvement of symptom scores regardless of treatment regimen. This suggests that the response rate observed in this study occurs by a mechanism other than *H pylori* eradication, and that an infection with *H pylori* does not play an important aetiological role in the symptoms of non-ulcer dyspepsia.

Transmucosal penetration of bismuth in the human stomach

C U NWOROKOLO, J F LEWIN, M HUDSON, and R E FOUNDER (Academic Department of Medicine, Royal Free Hospital School of Medicine, Rowland Hill Street, London NW3) Twelve patients attending routine upper GI endoscopy swallowed De-NolTab (2 (n=5) or Pepto-Bismol 30 ml (n=5), washed down with 50 ml of water. Endoscopy was performed 30–60 minutes after dosing. Single biopsy specimens were taken from five sites in each patient: 1st and 2nd parts of the duodenum, stomach, pyloric antrum, and oesophagus. Biopsy specimens fixed in glutaraldehyde were processed for transmission electron microscopy. The microscopist was blind to the dosing regimen. The presence of bismuth (Bi) was confirmed by x-ray microanalysis.

In all five patients dosed with De-NolTab, Bi was seen traversing intercellular spaces deep to damaged antral mucosa. Bi particles surrounded porphyrin blood vessels, and endothelial cells were seen to contain Bi particles in their intracellular channels. Bi particles were also seen within multivesicular bodies of antral mucosal cells. In the duodenum, particles were seen within mucosal and submucosal endovessels. Patients dosed with Pepto-Bismol showed negligible mucosal penetration by Bi. Intragastric bismuth particle size: De-NolTab=4–85 nm (diameter); Pepto-Bismol=123 nm×174 nm.

Colloidal bismuth formulated as De-NolTab (tri-potassium dichrato-bismuthate) penetrates gastric antral mucosa. This corresponds with the rapid absorption of bismuth observed with De-NolTab. The small particle size of colloidal bismuth may account for this phenomenon.

What length of treatment with tripotassium dichrato-bismuthate (TDB) for Helicobacter pylori?

R P H LOGAN, P A GUMMETT, R J POLSON, J H BARON, and J M MISIEWICZ (Departments of Gastroenterology, Central Middlesex and St Mary’s Hospital, London) There is no ideal treatment for *Helicobacter pylori* infection. Bismuth compounds have a direct toxic effect on *H pylori*, but the optimal length of treatment is not known. This study determines the effects of one, two, and four weeks’ treatment with TDB on *H pylori*.

Thirty five patients (18 men, median age 43 years) were randomised to receive four weeks’ treatment with a bismuth component as NuSeal (positive stool test) for four weeks. Histology, culture, and a modified 13C-urea breath test (13C-UBT), were treated with either one, two, or four weeks TDB (De-Nol) (1 tablet qds). Patients comprised active (n=20), or previous (n=3) DU, or dyspepsia (n=8).

Follow up 13C-UBTs were performed within 24 hours of finishing treatment and subsequently on day three and day five and then twice weekly until positive (active DU were endoscoped at follow up).

Of 15 patients treated for one week, five (33%) failed to clear *H pylori*, and *H pylori* recurred in the remaining 10 within one week of the end of therapy. With two (n=12) and four (n=20) weeks TDB treatment, 6 weeks of treatment became negative post treatment in eight (75%) and 17 (83%) respectively. However, *H pylori* recurred in all but one of the patients within one week of stopping either treatment regimen. *H pylori* was eradicated in one patient only after four weeks’ treatment (‘C-UBT negative after four weeks).

TDB generally does not eradicate *H pylori* regardless of length of treatment. However, ulcer healing occurs despite failure of eradication.

Gastric cancer is not associated with KI ras mutations or abnormal p53 expression

I G MARTIN, N S SCOTT, S BELL, A PICKLES, V MURPHY, M F DEANS, D JOHNSTON, and A QUIRK (University Department of Surgery and Pathology, The General Infirmary, Leeds) It has been suggested by several authors that because of similarities in morphology, and in particular colorectal cancer, it is likely that the molecular pathology of the two tumours is different and this has implications for both further research and applications of adjuvant therapy.
Human glutathione S-transferases: a case control study of the incidence of the GST0 phenotype in patients with adenocarcinoma

M DEARIN, B MATHAROO, R C STRANGE, G C PAULDER, P JONES, W COTTON, AND J B ELDER (School of Postgraduate Medicine and Biological Sciences, Thornburrow Drive, Harshill, Stoke on Trent, ST4 8QB) Detoxifying enzymes are often polymorphic. For example, the human glutathione S-transferase (GST) family of enzymes includes the mu group of isoenzymes which are encoded by the GSTT1 locus. Three alleles (GSTT1*0, GSTT1*1, and GSTT1*2) have been identified at this locus with homoyzogotes for GSTT1*0 apparently producing no active protein. In view of suggestions that GSTs are critical for the detoxification of geno- and cytotoxic electrophiles it has been hypothesised that these homoyzogotes are particularly susceptible to carcinogens.

In this study the frequency of the various GSTT1 alleles in liver samples from patients with cancers of the stomach (n=19) and colon (n=26) was determined. Using a starch-gel zymography approach we found that the GSTT1 0 phenotype (GSTT1*0 GSTT1*0) was significantly more common in the patients with adenocarcinoma than in matched local controls (p<0.05). Comparison with a larger multicentre control group with gastric cancers showed similar results (p<0.05) and an odds ratio analysis indicated that the homoyzogotes had a three-fold increased risk of developing carcinoma.

Expression of somatostatin receptors in human gastrointestinal cancer

G V MILLER, J P WOODHOUSE, S M FARMERY, AND J N PRIMROSE (University Department of Surgery, St James’s University Hospital, Leeds LS9 7TF) Somatostatin receptors (SR) have been identified in a number of malignancies including gut neuroendocrine tumours. The aim of this study was to evaluate SR expression in human non-neuroendocrine gastrointestinal malignancy. A competitive displacement assay was applied to the plasma membrane fraction of 40 consecu- tive primary and secondary human gastrointestinal cancers, 15 expressed SR, 14 of these exhibiting low affinity, high capacity binding sites (Kd=100 nM, Bmax=82 pmol/mg protein). One tumour exhibited high affinity receptors (Kd=4 nM, Bmax=229 pmol/mg protein). Of 24 colorectal cancers, 22 showed specific somatostatin binding at abundant, low affinity sites (Kd=158 nM, Bmax=2-9 pmol/mg protein). One of these patients had SR positive liver metastases but SR negative normal adjacent liver.

Low affinity, high capacity binding is an ubiquitous property of human gastrointestinal cancer SR which is occasionally, high affinity receptors are shown. Somatostatin analogues may be a therapeutic option in advanced gastrointestinal malignant disease.

Preparation and characterisation of a monoclonal antibody to human sulphomucin

J D MILTON, D EECLESTON, N PARKER, H-H TSAI, S D RYDER, J COX-SINGH, AND J M RHODES (Department of Medicine, University of Liverpool and Walton Hospital, Liverpool) Changes in mucin sulphation have been reported in gastric metaplasia (increased) and colonic cancer (reduced). These changes are usually detected using toxic histochemical stains with indifferent reproducibility so there is a need for a sulphomucin-specific antibody. A BALB/c mouse was immunised with human colonic sulphomucin purified by high performance gel filtration (Superose 6) from the homogenate of the macroscopically normal portion of a colon used for carcinogenesis. An IgG MAb was prepared using standard techni- ques. This has been characterised by (a) immunohistochemistry on 150 sections from a wide range of formalin fixed normal and neo- plastic tissues, (b) immunohistochemistry as colon of patients with known ABO/Le blood group, (c) dot blotting on purified mucin with or without pretreatment of the mucin by a purified faecal mucin sulphatase, (d) agglutination of a blood group specific antibody. The MAb binds intensely and with high specificity to normal colon goblet cells. Binding to mucin was markedly reduced by sulphatase treatment and no anti-blood group activity was shown.

Preliminary studies show selective positive in gastric metaplasia and loss of binding in colonic cancer. This antibody should prove very useful for studying mucin sulphation in neoplastic and inflammatory conditions.

Hypnorn cytoprotection against indometha- cin is mediated through acid suppression by fentanyl

R J PLAYFORD, D A VESEY, M ALISON, S HALDANE, T FREEMAN, AND J CALM (Departments of Medicine and Histophatology, RPMs, Hammsmier Smith, Du Cane Road, London W12 (DN)) Suppression of Hypnorn unexpectedly pro- voked the rat stomach from damage by indomethacin. Hypnorn contains the opiate bupivacaine and the butyrophenone flunisone which has a blocker and weak antiinhibitory effect. We have previously reported that the rat stomach is protected by indomethacin 20 mg/kg sc. Animals were killed after three hours, gastric damage was assessed macroscopically, and gastric juice was analysed for pH.

Animals given indomethacin alone had a mean (SEM) ulcer score of 10 (3) mm'. Drugs with significant cytoprotective effect (p<0.01) were Hypnorn; (1), atropine; (3); fentanyl 180 μg/kg; (2); and fentanyl 90 μg/kg; (2); but there was no effect from low doses of fentanyl 18 μg/kg; (5) and fentanyl 3.6 μg/kg; (8) or from phenoxbenzamine; 13 (2) or haloperidol; 12 (2).

Cytotoxic doses of fentanyl significantly (p<0.01) raised gastric pH: indometha- cin alone: pH 2.7 (0-6), fentanyl 180 μg/kg; pH 5 (0-8) and 90 μg/kg; pH 5 (1-0). Lower doses did not: 18 μg/kg; pH 2.8 (0-3) and 3-6 μg/kg; pH 2.1 (0-2). Naloxone (2.5 mg/kg sc) prevented the cytoprotective effect of fentanyl 180 μg/kg; ulcer score 14 (5) mm' and pH 1.8 (0-5).

Fentanyl inhibits gastric acid secretion via opiate receptors. Hypnorn is widely used in studies of rats but may alter the results of gastric studies.

Histamine receptors in canine gastric and colonic muscularis mucosae
Inhibition of gastric mucosal cyclic AMP (cAMP) by Helicobacter pylori protein

A S TAHIA, W D FRASER, R W KELLY, C G GEMMELL

(Manuscript)

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A S TAHIA, W D FRASER, R W KELLY, C G GEMMELL

(Manuscript)
Prolonged monitoring of gastric pH by radiotelemetry capsule attached by an endoscopic sewing machine

D F EVANS, G BROWN, A KALABAKAS, E YASAKI, M SCOTT, T MILLS, AND P SWAIN (Academic Department of Gastroenterology, The London Hospital and Department of Medical Physics, University College, London) Measurements of gastric pH of >24 hours are rare due to subject intolerance, catheter and catheter-related difficulty in securing sensors. We have succeeded in making long term recordings of intragastric pH by sewing radiotelemetry capsules (RTC) to the gastric fundus of four beagle dogs for up to 21 days. The sewing technique was performed by an endoscopic overtube and the RTC secured to the stomach wall by a transmural tilt switch under endoscopic control. Recent developments allowed deeper stitching and payload capacity without an increase in machine size. Recordings were made during normal feeding and ambulation using a belt aerial and solid state recorder worn in a jacket.

Considerable variations in gastric pH were observed under normal feeding conditions with substantial periods of alkalisation. Daytime gastric pH>7 was found for median 39% (range 10-45) and night-time 29% (range 0-39) of recording periods. pH was buffered after feeding for up to 12 hours.

We conclude that the period of alkaline shift and day to day variation in pH are considerable. This study shows the feasibility of prolonged minimally invasive monitoring of gastric pH. The technique could easily be applied to extend monitoring of physiological parameters at other GI sites in man.

THERAPEUTIC ENDOSCOPY

Techniques for dilating difficult oesophageal strictures

N VAN SOMEREN, Y MELBOSE, D CORBY, AND C P SWAIN (Academic Department of Gastroenterology, The London Hospital, Whitechapel, London E1 1BB) From a consecutive series of 576 dilations of oesophageal strictures under endoscopic control, patents for oesophageal stricture, 1987 and 1990, we examined techniques used when a standard Eder-Puestow flexible tip guide wires failed to cross stricture (n=87) and when a 13 mm OD plastic dilator (Celestin) could not pass (n=69). Small diameter 0.35 mm guide wire passed strictures (n=35) too tight for a 1.4 mm OD max standard flexible tip guide wire. Food debris obscured the lumen above malignant strictures (n=20); overtube, washing, and suction allowed dilatation (20/20 at second attempt). Guide wire coiling/jutting above the diaphragm gave worrying appearances (n=19); passing a 2.5 mm OD, 1.5 mm ID tubing over the guide wire and contrast injection showed biliary hernia (18) and mediastinal abscess (1). A new lumen seeking evertion balloon catheter (Baxter) 2-4 mm OD ×10 cm crossed tortuous strictures (n=13) enabling passage of a 0.35 mm guide-wire. Small diameter dilators (such as Savary) often succeeded when a 13 mm stepped dilator failed (n=54). Overtube and temperature adjustment of plastic flexibility bore when dilator butting caused failure (n=8). Backloading the endoscope over guide wire allowed the endoscope to cross strictures (n=6). Thus, guide wires crossed all 87/87 difficult strictures and only one could not be dilated to 13 mm. No perforations occurred with these techniques/patients. These results suggest that cautious use of simple techniques, especially use of thin guide wires, dilators, and narrow bore balloon allowing safe dilatation of almost all difficult oesophageal strictures when standard methods fail.

A randomised controlled comparison of injection of adrenaline, polidocanol, alcohol, hypertonic saline, normal saline and bipolar electrocoagulation in treatment of standard experimental bleeding ulcers and bleeding mesenteric vessels

A KALABAKAS, R XOURGIAS, N VAN SOMEREN, AND C P SWAIN (Academic Unit of Gastroenterology, The London Hospital, Whitechapel, London E1 1BB) There are few data comparing thermographic and injection methods in models of ulcer bleeding. Efficacy of injection of adrenaline (1:10000) (AD), polidocanol (1%) (PO), absolute alcohol (20%) and normal saline (HS), bipolar electrocoagulation (10F, Bicap, 50W, 5-5 setting, 1 s) (BE), and control treatment were compared in a canine standard experimental bleeding ulcer model and in two experimental bleeding standard ulcer terminals, BE stopped bleeding in all 32/32 ulcers (mean pulse no 5) while no injection method (AD, PO, AL, AD+PO, HS) in recommended volumes (5-10 ml AD, 3-5 ml PO, HS, 0.8-1 ml AL) or much larger volumes could stop bleeding from these ulcers (0/96) (p<0.0001). Injection of AD, PO, and AL but not HS or NS significantly reduced bleeding rates (p<0.05) when compared to lab controls. BE stops bleeding from severe mesenteric vessels of 0.5-2 mm (10/10) while injection stopped bleeding in one of 10 (p<0.05), although flow rates were reduced (p<0.05) with AD, PW+AL and AD+PO but not HS or NS when compared with controls. In conclusion, injection methods did not stop bleeding from experimental ulcers. Some injection methods reduced bleeding rates from ulcers and vessels by improved the best (AL and AD+PO) caused severe tissue damage. The thermal method of bipolar electrocoagulation was far superior to all injection methods in these models of endoscopic ulcer haemostasis.

Optimum injection therapy in experimental bleeding peptic ulcer

C RAGOPAL, A M LESLIES, AND K R PALMER (GI Unit and Department of Pathology, Western General Hospital, Edinburgh EH4 2XU) The prognosis of patients presenting with bleeding peptic ulcer is improved by endoscopic injection therapy but the optimum injection combination is unclear. Although dilute adrenaline stops acute bleeding, this could be due to local tamponade rather than a pharmacologically significant effect. Oesophageal ulcers may cause acute septicaemia. Sclerosants prevent rebleeding by inducing an inflammatory response but may not stop acute bleeding.

Bleeding gastric ulcers were created in harnessed rabbits by performing a gastroscopy and excising standard mucosal patches. Mean (SD) blood loss was 2.3 (4.0) ml/min (n=27). Injection of 1 ml, 1:100,000 adrenaline around the ulcer stopped bleeding, mean blood loss 0.2 (0.02) ml/min, increasing after five minutes to 0.35 (0.02) ml/min (n=9). Injection of 1 ml of isotonic saline had no effect upon bleeding, mean blood loss 1.69 (0.4) ml/min (n=9), showing that the effect of adrenaline was pharmacological rather than due to tamponade. Injection of 1 ml, 5% ethanolamine significantly increasing bleeding, mean blood loss 4 (0.6) ml/min, p<0.05, this return- ing to basal values, 2.1 (0.3) ml/min, after five minutes (n=9). Both in these acute experiments and in chronic experiments in which endoscopic injections were made into the rabbit stomach, ethanolamine but not adrenaline or saline caused endarteritis at the injection site.

Is surgery a safe option after failed endoscopic sclerotherapy for bile duct calculi?

M LAVELLE-JONES, M L LAVELLE, R LENDRUM, AND C W VENABLES (Freeman Hospital, Freeman Road, High Heaton, Newcastle upon Tyne NE7 7DN) Endoscopic sclerotherapy (ES) is now the preferred therapy for bile duct stones in elderly patients. Many are referred as " unfit" for surgical therapy, and are considered as candidates for surgical treatment. We have assessed the outcome of biliary surgery carried out between 1978 and 1990 in 65 patients after failed ES (median age 71 years, range 31-97). The reasons for surgery were: failed biliary cannulation (10); unsuitable for ES (6); failed ES (12); complications after ES (9); problems after successful ES (28). In the latter group, the stones were too large to remove in 26 patients and two had persistent symptoms.

In 33 patients, urgent surgery was required (<48 hours); 13 had an operation on the next list (two to five days) and 19 had semielective operations (>5 days). Supraduodenal examination of the bile duct was undertaken in 58, the remaining seven required transduodenal control of bleeding at the ES site. Choledochoduodenostomy was performed in 33 patients. There were nine major postoperative complications (13.5%) and two required reoperation (bleeding; bile leak). There were two deaths, one from septicemia and another after an unsuspected cholangiocarcinoma was found at laparotomy.

In conclusion, surgical treatment should always be considered if ES is unsuccessful as the outcome may be better than anticipated.

Total hospital stay (THS) and endoscopic stent replacement in primary malignant bile duct obstruction

A C SMITH, J F DOWSETT, R G RUSSELL, AND A R W HATFIELD (Departments of Gastroenterology and Surgery, The Middlesex Hospital, Mortimer Street, London W1N 8AA) The endoscopic management of obstruction of the biliary tract is controversial in women; median age 70 years (range 46-84) with primary malignant low bile duct obstruction randomised to the stenting arm of a prospective trial was examined to determine immediate and long term results.

Technical success was achieved in 95 patients (1st attempt 67% (median THS=22 days), 2nd attempt 23% (median THS=20 days) and 3rd attempt 10% (median THS=29 days)) with successful drainage in 94. Major complications occurred in eight patients (sepsis, four; acute renal failure, four; GI obstruction, three; variceal bleeding, two).

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bleeding, two; acute liver failure, one; and pulmonary oedema, one) while minor complications were documented in 20. There were three procedure related deaths (failed drainage, one; sepsis and GI bleeding, one; acute renal failure, one) and a further five patients died within the I year. Of the 33 patients needing a stent change, 24 required a single stent replacement and only nine multiple changes. The median time to the 1st stent change was 21 weeks (range 1-73), 2nd replacement - 41 weeks (range 22-137), and 3rd change - 65 weeks (51-75). Of the 91 patients who had died, the median survival was 21.5 weeks (range 1-127) and median total hospital stay from randomisation (32 days (range 4-107).

(1) 67% of patients do not require reaspiration for stent replacement. (2) ThS is significantly prolonged with multiple stent changes (p=0.01). (3) Multiple attempts at initial bilateral drainage are not associated with prolonged ThS.

Endoscopic management of primary sclerosing cholangitis (PSC)

P C Craig, S J Williams, A R W Hatfield, M Ng, AND P B Cotton (Department of Gastroenterology, The Middlesex Hospital, London) Twenty oesophageal biopsy specimens were assessed for Barrett's oesophagus. One of us (DH) graded all biopsy specimens according to severity of histological abnormality (Jarvis criteria). Thirty two specimens were reported as normal and 23 as having inflammation of squamous mucosa and eight with Barrett's. Immediately adjacent to the sample taken for histological examination, another was taken and processed to show epithelial growth factor receptor (EGF-R) immunochemically.

Positive staining showed a peripheral membranous pattern and was predominantly confined to the basal cells in all of the first group of patients. None of the patients with Barrett's oesophagus had any staining. A computerised planimeter was used to determine the proportion of stained areas of squamous cells as the results were expressed as a percentage of the total area examined.

The differences in the area of cells stained for EGF-R present between normal and inflamed oesophageal mucosa (29-5% and 43-1% respectively) were significant (p<0.001). In conclusion, this EGFR receptor, as assessed by monoclonal antibody, provides valuable diagnostic information in benign oesophageal reflux disease.

Epithelial growth factor receptors in the oesophageal diseases

JANKOWSKI, S MURPHY, G COGHILL, A GRANT, K G WORMLEY, AND D HOPWOOD (University Departments of Clinical Pharmacology and Pathology, Ninewells Hospital and Medical School, Dundee) Twenty five consecutive patients attending for oesophagoscopy had biopsy specimens taken from different levels of oesophagus. In addition, eight patients with proved Barrett's oesophagitis had a biopsy specimen taken from the columnar lined oesophagus. One of us (DH) graded all biopsy specimens according to severity of histological abnormality (Jarvis criteria). Thirty two specimens were reported as normal and 23 as having inflammation of squamous mucosa and eight with Barrett's. Immediately adjacent to the sample taken for histological examination, another was taken and processed to show epithelial growth factor receptor (EGF-R) immunochemically.

Positive staining showed a peripheral membranous pattern and was predominantly confined to the basal cells in all of the first group of patients. None of the patients with Barrett's oesophagus had any staining. A computerised planimeter was used to determine the proportion of stained areas of squamous cells as the results were expressed as a percentage of the total area examined.

The differences in the area of cells stained for EGF-R present between normal and inflamed oesophageal mucosa (29-5% and 43-1% respectively) were significant (p<0.001). In conclusion, this EGFR receptor, as assessed by monoclonal antibody, provides valuable diagnostic information in benign oesophageal reflux disease.

pS2 and hsp (spasmolytic polypeptide) are coproduced in abundance in ulcerative gastrointestinal diseases and associated exclusively with epithelial growth factor (EGF/FGFR) secreting cell lines

N A WRIGHT, G STAMP, P POUSSON, P HALL, M C RIO, AND P CHAMON (Diabetes Research Institute, London and INSERM, Strasbourg) We have recently described a novel cell lineage in the human gut, induced by ulceration, which secretes EGF/EGF-URO in the lumen, where it is available to aid healing. We now report that these cells express other secretory proteins of considerable interest: pS2 is a 60 amino acid polypeptide originally identified by screening a cDNA library of the breast carcinoma cell line MCF-7. It is highly homologous with pancreatic spasmolytic polypeptide (originally found in porcine pancreas), a 108 amino acid peptide which inhibits gastric acid secretion and intestinal motility, and stimulates cell proliferation in several cell lines. The 5' end of the pS2 gene contains a DNA enhancer sequence responsive to EGF. Using immunocytochemistry to localise pS2 and riboprobes in situ hybridisation for hsp and pS2 mRNA, we report that the superficial cells of the EGF/FGFR secreting cell lineage coexpress abundant pS2 and hSP; enterocytes and endocrine cells in the adjacent mucosa also express pS2. Furthermore, we have also shown the association between EGF/FGFR secretion and expression in pancreatic ducts and pancreatitis, and in gastric foveolae in gastritis. We conclude that pS2 and hsp secretion in the gut are controlled by EGF/FGFR; also that, in addition to EGF/FGFR, these molecules are produced by this cell lineage in large amounts, particularly in Crohn's disease, to assist mucosal healing after ulceration.

Monocyte activity in relation to disease activity in patients with Crohn's disease

C J OBRIEN, P BRUMWELL, A CLARK, AND C D HOLDWORTH (Gastroenterology Unit and Department of Clinical and Experimental Microbiology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF) Crohn's disease is a destructive granulomatous disease running a chronic relapsing course. Monocytes may play an important role in pathogenesis by promoting inflammation and tissue damage. We have examined the production by peripheral blood mononuclear cells of toxic oxygen radicals and lytic enzymes in patients with active (n=15) and non-inactive (n=10) Crohn's disease in relation to concurrently studied controls (data expressed as percentage difference, mean (SEM). As assessed by reduction of cytochrome C, superoxide anion (O2) generation was found to be similar in patients with active (n=15) and inactive (n=20) disease and increased compared with normal controls (p<0.01). Further assessment of the O2 dependent pathway's potential to produce highly toxic radicals, was mucosal ileostomy. A recent study has shown an increase in patients with active (121 (40), but not inactive (3 (21)), disease over normal controls (p<0.05). Lysosome, released from disrupted monocytes was also included in patients with active (n=15) and inactive (n=20) disease activity is present in Crohn's disease independent of disease activity (p=0.057); but the increased disease activity is associated with the further production of redox agents and lytic enzymes. The results suggest an important role for the monocyte/macrophage in Crohn's disease pathogenesis.

Reduced antigen-specific suppression in peripheral blood mononuclear cells (PBMC) in inflammatory bowel disease (IBD)

H R DALT ON AND D P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Woodstock Rd, Oxford) Studies on suppressor cell function in Crohn's disease (CD) and ulcerative colitis (UC) have reported variable results, possibly because the assays have been non-specific. The aim of this study was to investigate antigen-specific suppressor cell function after stimulation with a range of mycobacterial antigens, including M. paratuberculosis, and common enterobacterial antigen (Kunin). PBMC were isolated from peripheral blood (n=15) and the inactive CD (n=16), and inactive CD (n=6). No patient was receiving steroids or immunosuppressive therapy. PBMC were incubated with antigen for seven days, irradiated (2500 rad), and then cocultured with fresh autologous PBMC and con A (2.5 μg/ml). After 48 hours the cultures were pulsed with 1 μCi of [3H] thymidine and harvested after a further 16 hours. Suppression indices (SI) were calculated: positive values indicating antigen-specific, negative values indicating lack of suppression.

Compared with normal subjects, patients with CD and UC had significantly reduced suppression. The mean SI's to the antigens M. paratuberculosis, M. avium, M. fortuitum, M. kansasii, PV2, PPD and M. intracellulare were 3.5, 11±5±12.2, 5±8±11±5; PPD (normal: 16±7±3±7, CD: 22±0±17, UC: 22±9±10±5); M avion (normal: 13±6±8, 9, CD: 18±5±17, UC: 19±5±10±5); M fortuitum II (normal: 13±5±8, 6, CD: 23±8±9, 3, UC: 10±7±5±2); and Kunin (normal: 21±2±2, 7, CD: 10±5±11, UC: 40±5±9±6). In patients with CD there was reduced suppression to M. avion, and in UC to M. fortuitum (p<0.05). There was no significant difference in suppression between patients with CD and UC; except to the Kunin antigen where there was less...
suppression in UC (p<0.05). These data show impaired suppression to specific antigens and may have significance for the immune regulatory control of the immune response in IBD.

Mucosal oxygen free radical (OFR) production in duodenal ulcer disease

G R DAVIES, N J SIMMONDS, C LOVEKIN, P REVELL, D S RAMPTON, and D R BLAKE (Departments of Gastroenterology and Histopathology, The London Hospital, Whitechapel, London E1 1BB) OFR have been implicated in the pathogenesis of many inflammatory conditions. However, their role in human duodenal ulcer disease is unknown. We have used 75 Mmoluminol-dependent chemiluminescence (CL) to assess OFR production by duodenal biopsy specimens in vitro. Disease activity was assessed both macroscopically, using a modified Lanza grading, and microscopically. Biopsy specimens from patients with macroscopically severe duodenitis or ulceration, or both, had a mean CL (median 150; range 10-1000; 95% confidence intervals, 2.5 to 299) n=16) than those with mild duodenitis (5 -6 to 16) n=15, p<0.005) or control patients (n=12-0 to 4) n=20, p=0.001). CL in duodenitis was positively correlated with disease activity assessed histologically (Spearman’s R=0.8, p<0.001). There was no apparent relation between CL and smoking, alcohol intake, or treatment with NSAIDs or H₂ blockers. Superoxide dismutase (SOD) was added to the control to superoxide-derived hydrogen peroxide to CL. The median change in CL induced by addition of SOD was +15% (7 to 66) (n=7).

Their disease activity related production supports a role for OFR in the pathogenesis of duodenal ulcer disease. The measurement of CL provides a simple method for assessing potential antioxidant treatment.

Circulating free radicals and peptic ulcer disease

J JANKOWSKI, A BRIDGES, N SCOTT, J BROWN, and J J BELCH (INTRODUCTED BY G K WORMLEY) (University Departments of Clinical Pharmacology and Medicine, St Bartholomew’s Hospital Medical School, Dundee) Seventeen patients who had duodenal ulcers (>0.3 cm diameter) proved on upper gastrointestinal endoscopy had a plasma sample analysed for thioldisulphide (PHS) and glutathione (GSH) and a product of free radical consumption malondialdehyde (MDA). The mean age for the group was 57-5 years (range 23-80) and 10 were men and 7 women. A sex, age, and smoking matched control group was selected from preoperative patients admitted for minor surgery, mean age 55 years (range 21-77). None had illnesses or were taking drugs known to cause altered free radical values.

The circulating thiold values were lower in the ulcer group: PSH 419; GSH 1578 compared with PSH 466; GSH 1927 in the control group (analysis of variance p<0.005). Consistently the MDA values were increased in the ulcer group: 9-14 compared with 6-67 in the control group (analysis of variance p<0.05). In addition, the older the patient with ulcer disease, the lower the PSH value and the higher the MDA value (regression p<0.05). In conclusion this study confirms previous work which suggests that abnormal free radical production may play a role in the pathogenesis of peptic ulcer disease. It may also be that advancing age predisposes to increased production or decreased scavenging of free radicals. Moreover the abnormalities can be shown in the plasma.

Effect of SMS 201-995 on portal pressure and porta-systemic shunting following haemorrhagic shock and volume restitution in portal hypertenion

J D GREIG and D C CARTER (University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW) Previous work in this department has shown significant increases in mean portal pressure (MPP) following resuscitation of shocked portal hypertensive rats. We hypothesise that if this pertains in the clinical situation, variceal bleeding may continue. The aim of the study was to assess the effect of SMS 201-995 (SMS) on MPP after haemorrhagic shock and retransfusion. Four male rats were bled 14 days after graded portal vein ligation. Under halothane anaesthesia, animals were subjected to haemorrhagic shock by maintaining mean arterial pressure (MAP) >35 mmHg for 30 minutes. Five minutes after the onset of hypotension, a saline infusion was commenced in the control group and an SMS infusion (1 μg, 2 μg, or 4 μg/kg/hour) in the other three groups respectively. Portal-systemic shunting (PSS) was measured prior to shock and following retransfusion using labelled microspheres.

There were no significant changes in PSS in any group. In the saline and SMS (1 μg/kg/hour) groups, MPP increased from 12-1 to 13-7 mmHg (p<0.01) respectively. SMS 201-995 at doses of 2 and 4 μg/kg/hour prevented a rise in MPP following blood volume restitution: 12-9 to 12-9 mmHg (NS) and 12-2 to 11-7 mmHg (NS) respectively. This indicates the clinical observation that SMS 201-995 is an effective agent in arresting variceal haemorrhage.

Circulating anti-glutathione antibodies in patients with primary sclerosing cholangitis

P MACATHURNA, M FARRANT, D KELLEHER, D B HOURIHANE, P DONALDSON, M LOMBARD, D WESTABY, C FEIGHERY, D W GEER, and ROGER WILLIAMS (Lister Unit, King’s College Hospital and School of Medicine and Dentistry, London SE5 9PG) and Departments of Clinical Medicine and Pathology, Trinity Medical School, St James’ Hospital, Dublin) Coeliadisease (CD) has recently been recognised as the cause of steatorrhoea and weight loss in a number of patients with primary sclerosing cholangitis (PSC). However, the prevalence of latent CD in PSC and other chronic liver diseases (CLD) is not known. In 69 patients with PSC (MNW: 44/25, aged 13-79 years), we tested serum for IgG antigliadin antibody (AGA), an immunological marker for coeliac disease. Control groups comprised patients with chronic active hepatitis (CAH, n=36), primary biliary cirrhosis (PBC, n=33), and extrahepatic biliary obstruction (EHBO, n=27). AGA was detected in 55% of patients with PSC (p<0.001 ears EHBO), 35% with CAH, 33% with PBC, and 9% in the EHBO group. Small bowel biopsy specimens performed in a cohort of patients with PSC (n=26) and disease controls (n=19) did not show features characteristic of CD. In the PSC group, AGA was associated with the presence of HLA DR2 antigen, and a high AGA titre advanced to clinical presentation. However, the presence and titre of AGA did not correlate with age, sex, associated colorectal, auto-antibodies, serum bilirubin, or IgG values. The results indicate that AGA is commonly present in patients with PSC and to a lesser extent in CAH and PBC without concomitant morphological changes in the small bowel. This suggests that latent gluten sensitivity may be more common than pre-existing CD in patients with PSC and associated biliary disease.
admission values of FV were 28% (range 9–57%; p<0.001 v control: 10%, range 45–118%) and of FVII 163% (range 91–369%; p<0.001 v control: 107%, range 72–144%). Median trough FV values in four patients who died (11% range 6–5–14–4%) were significantly lower than in the 17 who survived (median 26–9%, range 14–6–57%; p<0.01). In the first 48 hours after OLT, FV and FVII values increased in all but two patients, one with primary graft non-function and one who died on the third postoperative day, both with FV values falling below 16%. During episodes of acute graft rejection (n=8), FVII results (median 278%, range 218–369%) increased relative to values at 10 days in 14 non-rejectors (median 135%, range 102–266%; p<0.005) with a corresponding rise in FVIII/FV ratios (median 4:8 ± 1.62; p<0.005). In FHF, the ratio of peak FVIII/trough FV results in 11 patients who survived POD (median 24:4, range 8–54–9) was significantly lower than in 11 patients who died after POD (median 68:5, range 35–128; p<0.005) and five NAB patients and the control group (range 16–7). Measurements of factors V and VIII are simple to perform and may have diagnostic and prognostic value in ALH, OLT, and FHF.

F protein: a new serological marker of liver cell damage

C P DAY, D B G OLEINVEIRA, M K BENNETT, O F W JAMES, AND M F BASSENDEJNE (Departments of Medicine, Cambridge and University of Newcastle Upon Tyne) F protein is a 44 kD cytoplasmic protein of unknown function found in high concentrations only in the liver. Its release into serum during liver cell damage suggests it may be a sensitive marker of hepatocellular necrosis.

To examine this hypothesis we have measured serum F protein concentration by radioimmunoassay in 52 patients with liver disease at the time of liver biopsy. Biopsy specimens were assessed blind, and inflammation who all died (median 218, range 80–302). Measurements of factors V and VIII are simple to perform and may have diagnostic and prognostic value in ALH, OLT, and FHF.

Poor prognostication for survival of individual patients with PBC using Cox models

M R BIAGNI, M GUARDASCIONE, C RASKINO, N MCINTYRE, C SURRENTI, AND K A BURRERGHS (Academic Department of Medicine, Royal Free Hospital School of Medicine; Departments of Epidemiology and Population Science, School of Hygiene and Tropical Medicine, London; Department of Physiology of University of Firenze, Italy) Cox models have been used to show benefit of liver transplantation and its optimal timing in PBC. However, Cox models only reflect average prognosis whereas precise estimation is crucial for decision making in individual patients. We have examined a model derived from 370 PBC patients (199 deaths) at first biopsy which had very good validation in a separate group of 65 patients (predicted and actual survival curves p=0.5). Bilirubin, age, hepatomegaly, varices, albumin, ascites, and biopsy stage 3 or 4, were independently predictive for mortality (all p<0.05). The median prognostic index (PI) was 2.64 (range 0.08–6.1), with a PI >2.5 signifying a 50% chance of death within three months. However, for a similar PI, the intervals to death were very wide—e.g for example PI 2.9 to 3.1, 14 patients died between 1.4 and 14 years (median 9.5); PI 5.2 to 6.1, 12 patients died between 0.2 and 5.6 years (median 1.6). Our Cox model has similar variables and good average predictive power to three other models published in the period (Springer, Mayo, and Groningen). However, it shows a wide variation in individual prognostics, even with the worst prognostic indices when the expected average survival is short. This means that other statistical tools must be used to assess timing of liver transplantation in individual patients with PBC.

A double blind placebo controlled study of antioxidants in primary biliary cirrhosis (PBC)

H L SMART, P A CANN, P J THULUVATH, AND D R TRAVIS (University of Sheffield, Department of Medicine and Pharmacology, Royal Hallamshire Hospital, Sheffield S10 2FF) As free radical mediated tissue damage might be important in PBC we have conducted a study of antioxidant therapy in this condition. Twenty patients (median age 39–81 years) with biopsy specimen confirmed PBC were randomly allocated to receive either an antioxidant cocktail of vitamin E (100 mg daily), selenium (100 μg daily), and zinc (25 mg daily) or matching placebo for 6 months. Patients had clinical, haematological, and biochemical assessments at one, three, and six months, including estimation of urinary and serum zinc, serum selenium, and vitamin E values. Free radical activity was assessed by measuring serum lipid peroxide and diene conjugate values. At trial entry both treatment groups were comparable for demographic data, haematology, and biochemistry. Three patients on active therapy and one on placebo were withdrawn due to side effects. In the remainder neither therapy was associated with any significant change in symptomatology, haematological or biochemical indices. Any antioxidant therapy, but not placebo, produced significant (p<0.05) elevation in urinary and serum zinc and vitamin E values throughout the study period, evident from month one. Selenium values were not changed. There was significant change in serum lipid peroxide and diene conjugate values despite antioxidant supplementation. We conclude that antioxidant therapy is unlikely to benefit patients with PBC.

Effect of ursodeoxycholic acid (UDCA) on hepatic bile acid handling in primary biliary cirrhosis (PBC)

R P JAZRAWI, J DE CAEDESTCKER, A BRITTAIN, P M GOGGIN, G GALATOLA, A E JOSEPH, J D MAXWELL, AND T C NORTHFIELD (Departments of Medicine and Nuclear Medicine, St George’s Hospital Medical School, Crammer Terrace, Tooting, London SW17 0RE) The mechanism underlying the beneficial effect of UDCA in PBC is not known. Our aim was to test the hypothesis that UDCA, being a hydrophobic bile acid, improves the hepatic handling of other bile acids. We studied 12 patients with biopsy specimen proved PBC before and during UDCA (10 mg/kg day given for three months). Following an intravenous bolus of [3H]UDCA, we carried out simultaneous γ-camera scanning the seriality of excreting for 90 minutes as previously described (Gastroenterology 1988; 94: 771–8). We measured initial plasma disappearance, hepatic uptake, transit time, and net excretory rate for [3H]UDCA. Mean plasma disappearance was similar in PBC and controls (16±7±9%/dose minute, MS), as was hepatic uptake (9·5±12·1%/dose minute, NS). By contrast, net excretory rate was markedly reduced in PBC (2·2±3·7%/dose minute, p<0.01), and hepatic transit time prolonged (16·9±9·7 minute, p<0.01). UDCA improved hepatic excretory rate and transit time in all patients (from 2·2±3·7%/dose minute to 3·9±6·5%/dose minute) but had no effect on plasma disappearance or hepatic uptake (17·9±16·5±11·6±9·5%/dose minute respectively, NS). We conclude that in PBC hepatic bile acid excretion but not uptake is abnormal; and that UDCA improves this defect in hepatic bile acid handling.

GASTRIC FUNCTION

Interleukin-1 is a potent inhibitor of gastric acid secretion

M CUGALA, K MUGRIEG, L PARENTE, AND J L WALLACE (Gastrointestinal Research Group, University of Calgary, Calgary, Alberta, Canada and Schlo Research Laboratories, Siena, Italy) In addition to being a mediator of inflammation, interleukin-1 (IL-1) has recently been shown to reduce the severity of experimental gastroduodenal ulceration. The mechanism through which IL-1 exerts these actions may involve inhibition of gastric acid secretion. This study examined the effects of IL-1 on pentagastrin stimulated acid secretion in rats an in vivo perfused rat stomach preparation.

Anaesthetised rats (n=4 per group) were pretreated with IL-1g at doses of 1–10 μg/kg. Thirty minutes to four hours later, pentagastrin was given iv as a bolus (20 μg/kg) followed by an infusion (20 μg/kg/hour) for two hours. The stomach was continuously perfused with 37°C isotonic saline and the perfusate collected and titrated to determine acid secretion. Each group of rats was pretreated with indomethacin (5 mg/kg sc) one hour prior to IL-1 (5 μg/kg) administration. In control rats, pentagastrin stimulated acid secretion over the two hour period to approximately 400 μEq. Pretreatment with IL-1 one hour prior to pentagastrin resulted in a dose dependent reduction of acid secretion. At doses of 1, 5, and 10 μg/kg, acid secretion was inhibited by 32%, 60%, and 62%, respectively (p<0.05 for the latter two doses). In the same model, cimetidine (100 mg/kg ip) inhibited acid secretion by 87% (p<0.05). Significant inhibition of
acid secretion by IL-1 (5 μg/kg) was also observed if the rats were pretreated with indomethacin (60%); a single baseline prolactin value, buspirone was given orally and serial samples obtained for prolactin, estimation (HPLC). The response was determined by measuring the difference between the baseline and peak values. Furthermore, DGE was determined by isotopic (C-139) scintigraphy of a standard solid meal. 

Symptoms and function in non-ulcer dyspepsia (NUD): a hypothesis rejected

B WALDRON, P T CULLEN, D SMITH, R KUMAR, and F C CAMPBELL (Department of Surgery, Ninewells Hospital and Medical School, Dunbarton DD1 5SY, UK) suggested a causative relation between symptoms and abnormalities of gastrointestinal function in NUD, but evidence is lacking. This prospective study has sought a relation between symptoms and objective abnormalities in 70 patients with NUD.

Dyspeptic symptoms were evaluated by a linear analogue scale questionnaire. Objective tests included (1) solid meal gastric emptying (GE), (2) pepsin output (PAO), (3) gastrointestinal transit time (SBBO) and evidence of small bowel bacterial overgrowth (SBBO).

Patients were categorised by symptoms (1) dysmotility-like dyspepsia (n=33), gastrooesophageal reflux-like dyspepsia (n=14), ulcers (n=7), and essential dyspepsia (n=20). Solid meal GE was delayed in NUD patients (T50 mean (SEM) 101.6 minutes (NUD) v 64.6 minutes (controls); p<0.01). A high incidence of gastritis (n=28) and Helicobacter infection (n=20) was observed. Hypochlorhydria was found in 11 patients. OCGT was delayed (OCGT mean (SEM) 290.12 minutes (NUD) v 244.12 minutes (controls); p<0.05) and 10 patients had SBBO. Multivariate analysis showed an inverse association between GE and PAO (r=−0.45; p<0.01) but no relation between symptoms and any abnormality of gastrointestinal function. In conclusion, NUD has multifactorial aetiology and symptoms are unrelated to any objective disorder.

Abnormal central 5HT receptors functioning in patients with delayed gastric emptying

A CHUA, D HAMILTON, T DINAN, and P W N KEELING (Departments of Gastroenterology, Radiology, and Pharmacology, St. James’s Hospital, Dublin) Abnormalities of gastric emptying may present with symptoms of functional dyspepsia. The pathophysiology of this common problem remains unclear. Serotonin, a monoamine, is both a neurotransmitter and a transmitter in the gut – it regulates peristalsis and intestinal tone. Furthermore, recent animal studies have implicated central 5HT receptors in the control of GE. We examined the involvement of central 5HT receptors in a group of patients with normal GE by measuring serum prolactin response to buspirone. Buspirone stimulates central 5HT receptors, and the extent of prolactin release is an indicator of the sensitivity of central 5HT receptors. Prolactin response was studied in 12 (seven W, five M) dyspeptic patients with DGE, four (two W, two M) dyspeptic patients with normal GE, and 20 (nine W, 11 M) healthy controls. After a single baseline prolactin value, buspirone was given orally and serial samples obtained for prolactin, estimation (HPLC). The response was determined by measuring the difference between the baseline and peak values. Furthermore, DGE was determined by isotopic (C-139) scintigraphy of a standard solid meal. 

Increased nutrient ‘sensitivity’ in a subgroup of patients with non-ulcer dyspepsia (NUD)

A Houghton, Y F Mangnall, A Dwyer, and N W Read (Department of Surgery and Sub-department of Gastroenterological Physiology and Nutrition, London Hospital, Whitechapel, London). The pathophysiology of NUD is not well understood, but there is evidence to suggest that disturbed gastric motility may play an important role, though no clear consensus exists. The problem is that different investigators have used different test meals to evaluate gastric emptying and have consequently been investigating different mechanisms. We have investigated the nature of any gastric emptying disturbance by comparing the emptying of different meals, rich in nutrients (RNL), with one low in nutrients (LNL) (300 ml radiolabelled beef consoomé with 227 kcal and without (12 kcal) 30 g marigarine). Randomised, paired genome studies were carried out in 17 healthy volunteers (aged 20–58 years) and 26 patients (aged 17–64 years) diagnosed as NUD without gastrointestinal pathology. Disordered gastric emptying was diagnosed if t½ > 2 SD above or below the mean for controls. The RNL emptied more slowly than the LNL in both the volunteers (t½ 85 (26) minutes v 24 (12) minutes (mean SD); p<0.001) and patients (t½ 117 (54) minutes v 33 (37) minutes; p<0.001). However, eight of the 26 (31%) patients had disordered gastric emptying: three patients showing delayed emptying of only the RNL. There was no correlation between symptoms and the different categories of gastric emptying. 

The data suggests that a subgroup of patients with NUD exist, that empty bland foods normally and rich nutrient foods abnormally slowly. These patients may have a duodenal receptor mechanism which is ‘over-sensitive’ to nutrients.

Identification of gastric motor abnormalities in functional dyspepsia using real time ultrasound

N K Ahluwalia, D G Thompson, H Mamota, and M Clenton (Departments of Medicine and Radiology, University of Manchester School of Medicine, Hope Hospital, Salford M6 8HD) Gastric antral motility was studied in 15 healthy volunteers and 18 patients with functional dyspepsia (FD) using percutaneous real time ultrasound. Antral circumference, anterior to the aorta was serially measured (every 15 minutes for 90 minutes) after ingestion of a standard meal both during relaxation (R) and during peristaltic contraction (C) to assess peristaltic contraction amplitude in addition to gastric emptying. 

Normal subjects – immediate post meal antral circumference (R) was mean (SD) 138 (12) mm and progressively declined with eating to 72 (10) mm at 90 minutes (slope=−7.2 (1/0.9/10) minutes. Change in circumference with peristaltic contraction (R−C) decreased linearly with eating from 33 (15) mm at 0 minutes to 13 (6) mm at 90 minutes. There was a consistent linear relationship (correlation coefficient=0.98; p<0.001) between antral circumference (R) and peristaltic amplitude (R−C) throughout emptying in all normal volunteers (mean R−C/R ratio=0.22 (0.07)). 

The consistently greater peristaltic contraction amplitudes despite delayed gastric emptying indicated that the existence of an dissociation between the ‘antral pump’ and nutrient efflux in patients with FD which appears pathophysiologically relevant.

Role of the vasoactive intestinal polypeptide (VIP) in the postoperative suppression of gastric motility

D Grundy, M K Gharib Naseri, and D Hutson (Department of Biomedical Science, The University, Sheffield S10 2TN) We have used auto-antibodies to neutralised endogenous VIP as a means of investigating the role of vagal non-adrenergic non-cholinergic (NANC) neurons in the recovery of gastric motility following acute surgical procedures. Six ferrets were immunised over a period of two months with VIP and killed by an adjuvant, the equivalent of VIP, in Freund's complete adjuvant, sc. The presence of circulating antibodies was confirmed by binding radiolabelled VIP to plasma diluted 1:200 (18.7±7.2% binding). These animals and eight controls were anaesthetised with urethane 1.5 g/kg and at laparotomy the greater splanchic nerves were sectioned, the corpus separated from the antrum, and intubated for manometric studies. Following closure, spontaneous corpus motility was followed for 40 minutes. In control animals the mean amplitude of phasic corpus contraction was 0.43±2.0 CmH2O and increased over the 40 minutes to a level of 0.86±0.6 CmH2O. In immunized animals the corpus motility was higher at the onset (7.07±1.97 CmH2O, P<0.02) and continued throughout the recovery period. These data suggest the involvement of NANC inhibitory nerves in the post-operative suppression of gastric motility.

GALL STONES

Natural history of recurrent gall stones: implications for treatment
Does the cholecystokinin provocation test (CCK-PT) identify gall bladder related symptoms?

J S BAILEY, A E GENT, AND D FINNIS (Salisbury General Infirmary, Fisherton Street, Salisbury) Patients who present with typical biliary symptoms but without stones pose a therapeutic challenge. The cholecystokinin provocation test (CCK-PT) has been reported to identify patients who will benefit from cholecystectomy. We report the results of 72 patients treated after a CCK-PT test.

A double blind CCK-PT was performed by one clinician. Thirty one tests were CCK-PT positive and 41 negative. Twenty one CCK-PT positive patients underwent cholecystectomy. One had a bile duct stone. At review of the acalculous patients (one to seven years), eight (40%) had no benefit from surgery, six (30%) were improved, and six (30%) were symptomatically cured. All gall bladders showed changes of mild to moderate chronic cholecystitis. Ten CCK-PT positive patients were treated conservatively. Five (50%) improved without therapy, three (30%) remained symptomatic and declined surgery, and two (20%) received an alternative diagnosis. One CCK-PT negative patient had cholecystectomy and was improved. Of the other 40 CCK-PT negative patients, 15 (37.5%) were better without a diagnosis, 17 (42.5%) had been treated for an alternative diagnosis, and eight (20%) remained symptomatic and undiagnosed.

Forty per cent of our patients were not helped by cholecystectomy despite a positive CCK-PT and histologically abnormal gall bladders.

Gall stone disease in diabetic population

When is the diagnosis gall stone disease and treatment of asymptomatic gall stones necessary?

J M PETRONI, P J ZARZAR, P M GOGGIN, A LANZINI, D FACCHINETTI, K W HEATON, AND T C NORTHFIELD (St George’s Hospital, London, UK, Spedali Civili, Brescia, Italy, and Royal Infirmary, Bristol, UK) Gall stone recurrence is the biggest problem in patients with a history of non-surgical treatment. As for primary stones, a knowledge of the natural history of recurrent stones is essential to determine whether and how these should be retreated, but there is little information on this subject. We analysed results from 100 patients (84 W, 16 M) with confirmed gall stone dissolution during bile acid therapy, followed up for over 13 years. Actuarial recurrence rate was 46% at six years and remained constant thereafter. Recurrent stones were radiolucent and in functioning and functioning gall bladders in 90% of patients. Some 84% of primary and 91% of recurrent stones were multiple; and those who had multiple primary stones were likely to have multiple recurrent stones (p<0.05). The diameter of 83% of the recurrent stones was <6 mm at diagnosis, by comparison with 50% of the primary stones (p<0.05). In 11 of 39 patients, recurrence was accompanied by symptoms despite early retreatment, and in seven of these the symptoms occurred within six months of the diagnosis of recurrence. We conclude that recurrent stones require early retreatment because a high proportion develop symptoms at an early stage; that 90% are suitable for non-surgical retreatment; and that bile acid therapy alone is the most suitable treatment, without the need for lithotripsy, because the majority are multiple and small.

Gall stone dissolution in 512 pregnant women

L BASSO, P T MCCOLLUM, M R N DARLING, AND W A TANNER (Department of Clinical Surgery, Meath/Adelaide Hospitals, Dublin and Mater Misericordiae, Rotunda Hospital, Dublin) We prospectively studied 512 pregnant women (mean age: 26.6 years; range 15–43 years) attending an antenatal clinic to assess the true prevalence of gall stones in a pregnant population in Ireland. Gall stones were found in 23 women (4.5%). We found no significant difference in the parity of those women found to be gall stone positive compared with the control population. Also early pregnancies, breast feeding, age at menarche, oral contraception, family history of cholelithiasis, coffee/tea and sucrose consumption, smoking, alcohol, physical activity, dietary fats, intake of fried food, education, arterial blood pressure, and blood group did not show statistically significant differences between the two groups. However, there was an increased incidence of cholelithiasis in women complaining of dysmenorrhea (χ^2= 3.93; p<0.05), in women who had diated (χ^2= 5.84; p<0.05), and in asymptomatic women with a history of non-specific abdominal pain (χ^2= 4.15; p<0.05). This study suggests that conditions such as menarche, oral contraception, and diet do not actually increase the risk of developing cholelithiasis. Apparently unrelated factors, such as dysmenorrhea or non-specific abdominal pain, increase the likelihood of finding unsuspected gall stones.

Obesity influences gall stone disease (GS) targeting, fragmentation, and clearance after extra-corporeal shock wave lithotripsy (ESWL)

P C HAYES, A PATRICK, J N PLEVRS, J MURCHISON, P ALLAN, J ROULSTON, B F CLARKE, AND I D A BOUCHER (Departments of Medicine, Diabetics, Radiology and Clinical Chemistry, Royal Infirmary, Edinburgh) Gall stones (GS) are reputed to be common in diabetics but the evidence for this is poor. We have investigated the prevalence of GS in diabetics along with a number of biochemical predisposing factors. Altogether 120 patients (40–70 age group, 57 M, 63 W, mean age 57.0±8.5, 50 IDDM, seven NIDDM) were studied. All had abdominal ultrasound and various clinical and biochemical parameters measured. The results were compared with a control population of similar age undergoing ultrasonography for non-GI reasons.

24-2% of diabetics v 15% of controls (p<0.05) had GS and this increase was most obvious at the 61–70 age group (41% of diabetics v 18% of controls, p<0.05). No difference was found between NIDDM and IDDM patients. Diabetics with GS compared with those without were older (62.1±1.2 v 55.5±9.9, p<0.01), female (7/122 W v 50/54 M, p<0.01), with higher serum apolipoprotein (Apo) A1 (128.0±0.7 v 111.0±0.4, p<0.003) and lower ratio Apo B/A1 (0.9±0.05 v 1.0±0.04, p<0.02), and a tendency for higher HbA1, body mass index, and LDL. No differences in LFTs or presence of diabetic complications were found between those with or without GS.

We conclude that diabetics have a higher incidence of GS. Risk factors include sex, ApoA1 values, and diabetic control.

and adversely affects the outcome of ESWL

J P M ELLUL, J R F WALTERS, K HOOD, A KEIGHTLEY, AND R H DOWLING (Gastroenterology Unit, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals and the Department of Diagnostic Radiology, Guy’s Hospital, London SE1 9RT) We and others find that GS size, number, and CT score significantly affect GS fragmentation which, in turn, affects GS clearance with adjuvant UDCA+CDCA. Since diuretic-waves attenuates shock waves in vitro, we studied the influence of body weight (BW) (an index of obesity) on GS targeting, fragmentation, and clearance in 69 patients with one or three symptomatic cholesterol gall stones, and CT GS in opacifying gall bladders treated with piezoceramic (Wolf) ESWL, and adjuvant bile acids.

In five patients whose GS could not be targeted, the mean (SEM) BW of 98.4±6.4 kg was greater than that of the remainder (78.7±2.3). Of the 64 patients whose GS were successfully targeted, 49 (77%) achieved GS fragmentation but the mean BW in ‘fragments’ was again less than (71.0±2.0 kg) than that in the non-fragments (88.0±4.0 kg; p<0.005).

Overall GS clearance at 27 months (84±13% by LTA) was influenced both by BW (68.3±3.7 kg in the GS-free v 79.3±3.2 in those not yet GS-free; p<0.005) and by fragment size (77±18% for fragments ≤5 mm v 53±21% for fragments >5 mm at 18 months by LTA; p<0.02).

Obesity adversely affects the outcome of ESWL

Dissolution of cholesterol gall stones with methyl tert-butyl ether (MTBE) – technique, efficacy, and recurrence

J KEATING, A CHUA, S AH-KION, J MCNULTY, AND P W N KEELING (Departments of Gastroenterology and Radiology, St James’ Hospital, Dublin, Ireland) In vitro studies show that choline esters are more rapidly dissolved by MTBE in one hour. Furthermore, surgically implanted gall stones in the dog gall bladder dissolved within four hours when MTBE was infused via a persitistic pump. In 21 patients with symptomatic cholesterol gall stones, a percutaneous transhepatic catheter was inserted (modified Thistle technique). Placement of the catheter was successful in 20 patients, one patient requiring cholecystectomy for bile peritonitis. MTBE was infused and aspirated continuously (4-6 cycles per min) resulting in rapid stone dissolution (median 7 hours; range 4–30 hours). In 16 patients, four (25%) had recurrent stones within six–18 months. Three patients had residual debris which failed to clear completely despite bile acid therapy. One patient with incomplete rim calcium in a large stone did not respond to MTBE therapy. Only one patient required cholecystectomy for symptomatic recurrence. There were no serious side effects observed; one patient required a sphincterotomy to remove a stone fragment impacted at the ampulla; a second patient developed a transient episode of painless jaundice and had a negative ERCP. MTBE therapy is a rapid, safe, and effective therapy for patients who refuse surgery or who for medical reasons cannot undergo ERCP. The results of this study confirm that complete dissolution of all fragments is essential and may prevent recurrence.
Non-operative gall bladder destruction: intraluminal bipolar electrocoagulation or scleroserum?

A V DILLEY, D DY, T A COOK, AND D L MORRIS (University Department of Surgery, The St George Hospital, Sydney, Australia) Non-operative gall bladder destruction is clearly an attractive concept which may be approached in several ways. We have studied the effect of bipolar-argon coagulation with the Nd-YAG cervical 3-2-mm Bicap probe; generator setting 7; for 10, 15, 20, or 60 seconds in eight rabbits by making a small cholecystostomy at operation. All rabbits survived with no evidence of complications. All animals were sacrificed and their gall bladder or gall bladder bed was excised en bloc. Peritoneal adhesions were the only complication noted at necropsy. In five rabbits no evidence of gall bladder tissue could be found (60 s, 10 x 4). In the remaining three rabbits, two fibrosed and contracted gall bladders were found but these contained no residual mucosa (20 s, 10 s) and in the last animal the probe appeared to have pierced the liver and inadequately treated the gall bladder. No evidence of residual mucosa was found in any other animal other than this single operative failure.

Six rabbits received an intraluminal injection of 1 ml sodium tetradecyl sulphate (STD Hereford). This was left in situ (n=4) or reaspirated (n=2). Gall bladders were recognisable at necropsy in all cases and exhibited thickened walls and small amounts of intraluminal fluid. Histological examination showed markedly normal gall bladders in all STD treated rabbits.

Bipolar electrocoagulation may be an effective method of non-operative gall bladder destruction and would seem superior to the scleroserum tested.

Readmission and mortality rates in the assessment of outcome following cholecystectomy

R SUTTON, M QUGLEY, AND M J GOLDMERE (Introduced by M W L GEAR) (Nuffield Department of Surgery, and Unit of Clinical Epidemiology, University of Oxford) Readmission and death are the only outcome measures collected routinely by IHDs (hospital activity analysis), but the use of these measures as performance indicators remains largely unexplored. We examined readmission and death during the first year after cholecystectomy in 15,000 patients between 1975 and 1985 in a single NHS region, using linked admission data. Emergency readmission was significantly more frequent than elective readmission after elective cholecystectomy (920 v 99 of 12,600, p<0.01) as after emergency cholecystectomy (96 v 46 of 2400, p<0.05). Readmission was more frequent during the first 28 days than thereafter, and was significantly associated with patient illness, length of stay, but not sex, time of operation (1975–1980 v 1981–1985), or numbers done by individual surgeons. Mortality after elective cholecystectomy at 28 days was 0.4%, and at 36 days 1.8%; and after emergency cholecystectomy at 28 days 3.1% and 36 days 10.1%. Mortality was significantly associated with age; concurrent illness; male sex; and whether emergency surgery was done. These results quantify the prognosis of patients undergoing cholecystectomy, providing some guide as to acceptable outcome, although the structure and process of care was not analysed.

Inflammatory bowel disease

Definition of remission in Crohn's disease using a computer controlled scanner; total count of bowel uptake of Tc-99m hexamethyl propylene amine oxime (HMPAO) leucocyte bowel scanning

M H GIFFEY, C D HOLDSWORTH, W B TINDALE, AND D C BARBER (Departments of Gastroenterology and Medical Physics, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2FF) A computer based method for the quantitation of bowel uptake of Tc-99m HMPAO for IBD. Quantitative bowel scanning has been shown to provide an objective indicator of disease activity in Crohn's disease. We applied this method to monitor the therapeutic effect of elemental diet (Vivonex) in 10 patients with Crohn's disease.

Five patients achieved remission. Their Crohn's disease activity index (CDAI) fell from a mean (SE) of 280 (32) before treatment to 91 (14) after four weeks on Vivonex. Their scan score decreased from 130 (60) to 31 (10) (p<0.05, Wilcoxon test). Associated with the changes in the CDAI and scan score was a reduction in the C reactive protein (CRP) and alpha acid glycoprotein (AGP) values. The remaining five patients either failed to respond (3) or responded as assessed by CDAI but relapsed within two months (2). Their scan score increased from 105 (50) to 154 (67). Reliable increases in the CRP (from 28 (11) to 55 (23) (p<0.05) and AGP (from 1.5 (9.2) to 1.9 (0.5)) were obtained. The two patients with early relapses had persistently raised scan score despite apparent clinical improvement. We conclude that the quantitation of bowel uptake after Tc-99m HMPAO bowel scanning can provide an objective measure for monitoring therapeutic intervention in Crohn's disease, and usefully complements a clinically acceptable assessment such as the CDAI.

Quantitative assessment of the inflammatory cell infiltrate in ulcerative colitis

D J LYONS, J M GILVARRY, AND J F FIELDING (Departments of Medicine, Beaumont Hospital, Dublin and Royal College of Surgeons in Ireland) Variations in the expression of cell markers have been shown to affect the outcome and cell processing impair knowledge of the cellular infiltrate in inflammatory colitis. We evaluated a quantitative method of studying cell populations in colonoscopic biopsy specimens. Ten patients with ulcerative colitis (UC) and 10 controls with irritable bowel syndrome (IBS) were studied. Intraepithelial and lamina propria lymphocyte densities were measured in situ by two observers. Correlation coefficients for intraepithelial lymphocytes (IELs) were r=0.91 for area, R=0.99 for total lymphocyte count, and R=0.97 for lymphocytes staining positive for T and B cell markers. For UC the lamina propria cell density (cells/mm2) was: total lymphocytes 3344 (1792) c/mm2 (cells/mm2); T cells 1248 (800) c/mm2 and B cells 448 (400) c/mm2. Corresponding figures for IBS were: 1520 (976) c/mm2, 912 (544) c/mm2, and 192 (384) c/mm2. Total lymphocyte density and proportion of non-staining cells were significantly increased in UC (p<0.01) but F1B were significantly increased in UC (p<0.01) but different from those in IBS. Intraepithelial T cells were present significantly more frequently in luminal than in crypt epithelium (p<0.004) for both UC and IBS. Quantitative measurement of cell populations in the colon is accurate, reproducible and informative.

Detection of inflammation in inflammatory bowel disease using Tc-99m labelled monoclonal anti-granulocyte antibody

Y R MAHIDA, A C PERKINS, M FRIER, M L WASTIE, AND C J HAWKLEY (Department of Therapeutics and Medical Physics, University Hospital, Nottingham NG7 2UH) In vivo labelling of circulating granulocytes with labelled monoclonal antibody may provide a convenient way of assessing the severity and extent of inflammation in inflammatory bowel disease (IBD). We have studied the use of Tc-99m labelled monoclonal anti-granulocyte antibody, BW 250/183, in six patients with ulcerative colitis and six with Crohn's disease. Twenty-four hours after intravenous injection of Tc-99m labelled antibody was injected slowly intravenously. Planar images were recorded for four, six, and 24 hours. There were no adverse reactions. Positive uptake was seen in the images of five out of six patients with active ulcerative colitis and five (out of six) with Crohn's disease. Perianal abscesses in two patients with Crohn's disease gave strongly positive scans. For most of the positive cases, sites of increased uptake were visualised at four to 24 hours. Radioactivity was also measured in faecal samples obtained from three patients. In one whose samples were collected for 48 hours, peak activity occurred 11 hours after injection of the IBD.

Use of intravenous Tc-99m monoclonal anti-granulocyte antibody is a simple technique capable of detecting inflammation in IBD without the need for labelling after cell isolation.

Salicylates used in inflammatory bowel disease (IBD) impair IFN-γ induced HLA-DR expression

B CROTTY, P HOANG, AND P JEWELL (Gastroenterology Unit, Radcliffe Infirmary, Oxford) Colonic epithelial cells express HLA-DR antigen in inflammatory bowel disease (IBD). We have investigated the effect of drugs used in the treatment of IBD on interferon-γ (IFN-γ) induced DR expression. HT-29 cells were cultured in 25 cm² flasks. At 48 hours IFN-γ (0, 50, or 100 μg/ml)±2 drug were added. At 120 hours the cells were stained with biotinylated HLA-DR antibody and streptavidin-peroxidase. For assay 5ASA, N-acetyl 5ASA, salolazine, 4ASA, and N-acetyl 4ASA were incubated at concentrations of 0.1 mM, 1.0 mM and 10.0 mM. The 0.1 mM 5ASA reduced DR expression induced by 50 μg/ml of IFN-γ from mean (SEM) 62 (6%) of cells to 29 (9%) (p<0.005 – one way analysis of variance). Corresponding figures for 10 mM N-acetyl 5ASA were 68 (7%) to 39 (8%) (p<0.05); for 1 mM salolazine, 66 (7%) to 35 (13%) (0.05<p<0.01); for 10 mM salolazine, 78 (3%) to 2 (0.2%) (p<0.001); for 10 mM 4ASA, 61 (2%) to 57 (2%) (p=0.6); and for 10 mM N-acetyl 4ASA, 61 (6%) to 35 (6%) (p<0.05). Similar results were obtained with 5ASA reduced by induced by 100 μg/ml of IFN-γ, except with 10 mM 4ASA, which reduced expression from 77 (2%) to 68 (1%) (p<0.05). Sulphasalazine, prednisolone, indomethacin and cyclosporine A had no effect. Concurrent staining with propidium iodide showed that these results were unchanged when only viable cells were analysed. Prior incubation of cells with drug, followed by washing, had no effect on IFN-γ induced HLA-DR expression. In IBD these com-
Is a defunctioning ileostomy necessary in restorative proctocolectomy? A pilot study

P M Sagar, P J Holdsworth, and D Johnston

A temporary ileostomy has been employed routinely by most centres to defunction the ileal reservoir after restorative proctocolectomy. The aim of this pilot study was to compare the early postoperative results in patients undergoing restorative proctocolectomy with and without the use of a temporary stoma.

A consecutive series of 26 patients were studied. Each patient underwent restorative proctocolectomy with quadruplicated ileal reservoir; 13 with a defunctioning ileostomy, 13 without. The two groups of patients were similar in age and sex distribution.

There was a reduced incidence of pelvic sepsis (0% v 23%) and intestinal obstruction (8% v 38%) (NS) in patients without an ileostomy compared with patients with an ileostomy. The overall complication rate (23% v 69%, p<0.05) and the total length of stay in hospital after operation (median 28 days (IQ range 23–31) v 14 days (12–17), p<0.01) were both significantly reduced in the group of patients without an ileostomy.

The avoidance of a defunctioning ileostomy was associated with a reduced length of stay in hospital and a reduced incidence of postoperative complications.

Reoperation rates after restorative proctocolectomy

A H Davies, J E de Silva, T C B Dehn, M Kettlewell, and N J McC Morstensen (Departments of Gastroenterology and Surgery, John Radcliffe Hospital, Oxford) Restorative proctocolectomy has become the surgical choice in patients with ulcerative colitis, and it has an increasing place in family polyposis coli and a controversial role in constipation. We have looked at the reoperation rate before and after ileostomy closure. Seventy three consecutive patients (52 men and 21 women) of median age 51 years (range 19–55) have had an ileal pouch formed. Sixty eight patients (93%) had ulcerative colitis, four (6%) had familial polyposis coli, and one (1%) had idiopathic constipation.

Overall 26 patients (36%) have required reoperation excluding closure of the ileostomy. There have been 32 reoperations and eight patients (11%) have required three or more reoperations. Twenty three reoperations (44%) were performed prior to closure of the ileostomy and 34 reoperations (65%) were performed with the first year after formation of the reservoir. Nine pouches (12%) have been removed (four ischaemia, two sepsis, one pouchitis, one Crohn’s disease, one vaginal fistula), four have been revised (three sepsis, one pouchitis, one vaginal fistula). Of the nine patients with small bowel obstruction, four have required a further laparotomy. Three patients have had local surgery for ano-vaginal fistula and four patients have had a simple dilatation (10) for anastomotic stenosis.

Restorative proctocolectomy has a high reoperation rate especially in the first year after surgery and this needs to be clearly explained to potential candidates for the operation.

Longitudinal study of growth, diarrhoea, and small intestinal permeability in rural Gambian infants

R M Downes, C A Northrop-Clews, L T Weaver, and P G Lunn (Dunn Nutrition Unit, Keneba, The Gambia and Cambridge, UK) The interrelation of growth, diarrhoea, and small intestinal (SI) permeability was measured prospectively in a cohort of 100 rural Gambian infants aged 2–15 months. Growth was measured monthly from birth and morbidity weekly. Intestinal permeability was measured monthly by the differential uptake and urinary recovery of orally ingested lactulose (L) and mannitol (M). All children were breastfed throughout and supplementary weaning foods were introduced at a median age of 3 months. There was a steady decline in SD score (NCHS standards) from birth to 1.2–13.2% at 12–15 months. L:M ratios in Gambian infants before the introduction of weaning foods were similar to those in the UK with a mean (SEM) of 0.36 (0.03). Thereafter the L:M ratios rose to a peak of 0.79 (0.04) at 9–12 months (p<0.001). This was due largely to a decreasing uptake/excretion of mannitol which may reflect a decrease in SI mucosal surface area. These changes were paralleled by an increased period of time with diarrhoea for a mean of 2.5 (0.7)% at 0.3 months, to 10.4 (1.3)% at 9–12 months (p<0.001). Out findings support the hypothesis that damage of the SI mucosa, leading to loss in absorptive area, may be an important factor contributing to the growth failure of Gambian infants during early life.

Small intestinal dysmotility and recurrent symptoms in children with malrotation

R C Coombs, R G Buick, P J Gornall, J J Corkery, and M J Booth (Institute of Child Health, Birmingham and Birmingham Children’s Hospital) The natural history of malrotation and the likelihood of an associated disorder of intestinal motility are poorly defined. We have therefore joined together with the children with malrotation undergoing surgery at the children’s hospital between 1977 and 1989 (n=93). Patients were divided into three groups according to age at operation: (a) <1 month; (b) 1–12 months; (c) >12 months. Group (a) (n=50) all presented with obstructive symptoms; associated major abnormalities were common (n=12). Four died, usually because of the associated anomalies. Only three had continuing mild symptoms post surgery. Group (b) (n=22) presented with recurrent vomiting (11), acute obstruction (5), poor feeding/distension (2); five had other abnormalities. Response to surgery was good in 16, but two had continuing severe symptoms, both fatal: diarrhoea (1); intestinal pseudoobstruction (1). Two others died: biliary atresia (1); septicaemia (1). Of the late presenters in group (c) (n=21); median age 79 months; eight had symptoms of less than 2 months. In eight of the group with long standing symptoms, surgery failed to relieve their symptoms (continuing pain (4), diarrhoea (4), vomiting (1)). Small bowel motility was normal or minimally disturbed in four of these subjects, one pre- and three post surgery. All four were abnormal; non-propagation of phase III (4); long periods of non-propagated phasic activity (2); random disorganised activity (2); tonic increases in baseline pressure during phase III (1). These findings suggest that small intestinal dysmotility may be a not uncommon cause of recurrent preoperative and persistent postoperative symptoms in subjects with a malrotation.

Raised secretory IgA in the urine of children with chronic diarrhoea and malnutrition

P B Sullivan, A Prentice, D M Stirling, C Northrop, and G Neale (MRC Dunn Nutrition Unit, Cambridge) Secretory IgA outputs in the urine were measured, using an ELISA method which can distinguish between secretory IgA, serum IgA and breakdown products, in 24 Gambian children with chronic diarrhoea and infection. Secretory IgA secretion was significantly higher in secretory IgA outputs in the urine of children of similar age who had no diarrhoea. Of the chronic diarrhoea subjects (11 boys, 13 girls; age range 10–31 months) 16 had marasmus, seven marasmic-kwashiorkor, and one kwashiorkor. String in children with chronic diarrhoea malnutrition and infection subjects showed that 15 were infected with Giardia lamblia, two with Strongylodes stercoralis, two with Ascaris lumbricoides, three had Shigella sp, three had E coli and one Campylobacter. Some biopsy specimens showed an enteroatopy in all children with chronic diarrhoea. Among the controls, those who were malnourished (74% weight for age), had secretory IgA outputs significantly lower, by a factor of three (p<0.01), than those who were well nourished. Children with chronic diarrhoea, irrespective of the severity of associated malnutrition, had secretory IgA outputs that were 6–8 times higher than malnourished controls (p<0.001) and 2–3 times higher than well nourished controls (p<0.01). These results show that secretory IgA production in the urinary tract can be stimulated by intestinal disease suggesting that malnourished children are able to mount a response to mucosal infection and supporting the hypothesis of a common secretory immune system.

Chronic inflammatory bowel disease in the children of Indian subcontinent immigrants living in Britain

A F M Salim, C M Evans, and J A Walker-Smith (Academic Department of Paediatric Gastroenterology, St Bartholomew’s Hospital, London EC1A) Chronic inflammatory bowel disease (CIBD) is reported to be very uncommon among the indigenous population of the Indian subcontinent (ISC). To study the occurrence and nature of CIBD in the children of ISC immigrants now living in Britain, we took a study of all patients referred to a paediatric CIBD clinic between 1978 and 1990. During this period, 272 children had either Crohn’s disease (CD, n=184) or ulcerative colitis (UC, n=88). Twenty seven of these (9-9%) were of ISC origin, of whom 19 were born in Britain and the remainder had lived here for at least five years. Ten had CD (5-4% of CD cases) and 17 had UC (19-3% of UC cases).

The ratio of UC:CD was significantly higher among these children (1:0-6) than among the indigenous cases (0:4;1). p<0.001. The clinicopathological features of both disorders were not dissimilar to those of the indigenous population. However, mean follow up of 3·1 years showed that bowel resection was required in 60% of CD cases and 47-1% of UC cases among the ISC children.
Oesophageal Pforters

An oesophageal reflux patient support group: the first year’s experience

J. Jankowski, P. von Eichhorst, L. Strachan, J. Mayet, R. Jankowski, and R. Harden (Department of Clinical Pharmacology and Centre for Medical Education, University of Dundee, Ninewells Hospital & Medical School, Dundee)

Two hundred and five patients with endoscopically proven oesophagitis were given a questionnaire with regard to their views in joining a support group; 146 responded. Of those, 48% expressed a strong desire for the formation of a group, 21% were unsure and 31% had no interest at all. Sixty-eight patients were invited to the support group meetings nine months ago. The meetings are held on a three monthly basis and 80 attended the most recent meeting. The format of the meeting consists of three short lectures about medical, psychological, and self help strategies concerning oesophagitis. Time was allowed for audience questions, and patients were encouraged to discuss their problems more intimately with the speakers during tea: 97% found the meeting helpful, 90% felt that the meetings helped them cope much better with oesophagitis, and 95% expressed a strong wish to attend future meetings; 60% concluded that they had attended their general practitioner less often and 47% thought they would require less frequent hospital clinic appointments (if they could choose intervals between clinics). Ninety seven per cent of 100 general practitioners contacted, strongly supported the group and felt it helped their patients. In conclusion, we have identified a demand for patient support groups from both patients and doctors. We also show that these groups can have a very high degree of patient satisfaction and success.

Prospective evaluation of Ndg-YAG laser palliation for malignant dysphagia

R. Carter, C. G. Morran, J. S. Smith, and J. R. Anderson (University Department of Surgery, Royal Infirmary, Glasgow, and Department of Surgery, Stobhill Hospital, Glasgow) One hundred and forty one patients with biopsy proven malignant dysphagia palliated with the Ndg-YAG laser since 1985 have been prospectively evaluated. Patients treated since November 1988 have not been included to allow a minimum follow up of 18 months. The principal reasons for palliation were evidence of metastases at presentation (43.9%), recurrent or inoperable disease (29%), serious concomitant medical disease (18.4%), severe dementia (6.3%), and refusal of alternative therapy (2.1%). Seventy six patients were men and 65 women. Eighty one patients had an adenocarcinoma and 61 squamous carcinoma. Sixty six were oesophageal lesions, 36 oesophagogastric, and 39 primarily gastric carcinomas. Six two had proven metastatic disease and 74 loco-regional disease. The dysphagia grade, inpatient stay, survival, and complications were studied. Tumour histology, length, or site did not influence the overall outcome. Only the presence of metastatic disease had a significantly adverse effect on survival (p<0.01). Five patients are still alive and swallowing normally. Mean survival of those that have died (n=136) was 21.5 weeks (±7.1). Two year survival rate was 3.5%.

Ninety two per cent of patients swallowed at least a semisolid diet during their treatment. There were 11 treatment failures (7.4%); seven proved impossible to recanalise and four refused to swallow more than liquids despite adequate recanalisation. The perforation rate was 6-4% and the overall complication rate 12%. Laser recanalisation provides effective palliation of malignant dysphagia.

The timed swallow in achalasia

Z. M. Jussa, R. H. R. Park, and J. F. Mackenzie (Gastrointestinal Investigation Unit, Royal Infirmary, Glasgow G31 2ER) Twenty five patients consecutively referred to a specialist unit for the investigation of dysphagia were found to have achalasia on oesophageal manometry. Before referral, this diagnosis had been suspected in 14 patients (28%) and confirmed by routine barium swallow and in only three patients (12%) by endoscopy. The emptying of the oesophagus after a standardised swallow of low density contrast medium (Gastrografin or Nipom) was measured radiologically in the 25 patients and in 26 normal controls: the ‘timed swallow.’ Twenty five of the 26 control subjects emptied in seven seconds or less, whereas 24 of the 25 patients with achalasia took eight seconds or more to empty the oesophagus.

These findings suggest that routine barium swallow and, more particularly, endoscopy commonly fail to detect a motility disturbance in a significant number of patients with achalasia. We suggest that the addition of this simple quantitative measure of oesophageal emptying to the routine barium swallow examination using a low density contrast medium may considerably increase its sensitivity in the detection of motility disturbance in patients with this type with dysphagia.

Omeprazole or ranitidine at standard or doubled doses in the treatment of patients with refluxary reflux oesophagitis

G. Bianchi Porro, F. Pace, O. Sangalletti, A. Peracchia, L. Bonavina, S. Vignieri, and F. Muratore (Gastrointestinal Unit, L. Sacco Hospital, Milan, Italy, Clinica Chirurgica I, Padova, and Clinica Medica II, Palermo, Italy) Sixty two patients with refluxary reflux oesophagitis were randomised to receive a four to eight week treatment with omeprazole (OM) 20 mg od or ranitidine (RA) 150 mg bd. Patients not healed after treatment were randomised to receive double dose of the same drug as doubled doses for a second period of equal duration. Patients still unhealed after this were openly treated with OM 20 mg bd for a third period of four to eight weeks. Endoscopic assessment and clinical and laboratory evaluation were performed every four weeks until complete oesophageal mucosal repair. After four weeks, complete healing was observed in 50% of patients on OM 20 compared to 20-7% on RA 300 (p<0.01). After eight weeks the figures were 79-3% vs 34-5% (p<0.05). With doubled doses, after four weeks’ treatment complete healing was achieved in 96-6% of patients on OM 40, compared to 64-2% on RA 600 (p<0.05), after four weeks more, the figures were 96-6% and 75% (p<0.05). The eight still ‘refractory’ patients (1 ex OM 40, 7 ex RA 600) healed completely with eight more weeks of OM 40. Most symptoms disappeared in both groups after four weeks. This study confirms that omeprazole, even at a low dosage, is the choice for refractory reflux oesophagitis.

Lansoprazole, a new proton-pump inhibitor, vs ranitidine in the treatment of reflux oesophagitis

K. D. Bardhan, R. Long, C. J. Hawkey, K. G. Wormsley, D. Brocklebank, and I. Moules (For the Lansoprazole Clinical Research Group, District General Hospital, West Bromwich, and Queen Elizabeth Hospital, Birmingham) Lansoprazole is a benzimidazole parricidal cell H KATPase inhibitor; 30 mg daily reduces day time reflux by up to 85%, whilst maintaining a minimal effect on gastric acid by approximately 80% and therefore seems of potential benefit in oesophagitis. One hundred and seventy four patients (five centres) with endoscopy proven oesophagitis, stratified by grades (1, 2, & 3) were randomly assigned to receive double blind treatment for up to eight weeks with either: ranitidine 150 mg bd (R) (n=57); lansoprazole 30 mg (L) (n=60), or 60 mg daily (L) (n=57). The demographic characteristics of patients in the three groups were comparable.

Healing, defined as disappearance of
Smoking and cancer risk in Barrett’s columnar lined esophagus

M R GRAY and A N KINGSNORTH (University of Liverpool, Department of Surgery, PO Box 147, Liverpool L69 3BX) Patients with Barrett’s columnar lined esophagus (CLO) are a high risk group for adenocarcinoma of the oesophagus. All these tumours can be shown to arise in pre-existing CLO; however, the population with CLO is large (12% of those presenting with acid reflux), and in prospective screening programmes 40–450 patients are required to detect one case of adenocarcinoma at an estimated case detection cost of £60 000. Tumours arising from Barrett’s metaplasia can be differentiated from other causes of incurable oesophageal disease.

Current efforts are aimed at defining a high risk subgroup for intensive screening in order to detect malignant change early and reduce cancer mortality.

We interviewed 20 patients with Barrett’s tumours and 60 age and sex matched patients with biopsy proven CLO at least 4 cm above the gastro-oesophageal junction. Patients with Barrett’s tumours had a mean lifetime smoking history of 40.3 (6.9) pack years, which was 10 times greater than those with benign CLO – 4.6 (1.6) (p<0.01 Mann Whitney U test).

Patients with CLO should be strongly discouraged from smoking and together with those patients with established dysplasia heavy smokers represent a high risk subgroup for the development of adenocarcinoma and thus warrant regular follow up and rebiopsy.

Postprandial oesophageal bile reflux in patients symptomatic of gastro-oesophageal reflux disease and in postgastrectomy patients

S M SHMI, A D REID, D W EAST, AND A CUNNINGH (Department of Surgery, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland) A new method to quantify individual bile salts in the upper digestive tract has been developed. This method was used to quantify postprandial bile salts in the duodenum, stomach, and oesophagus in 14 asymptomatic volunteers, patients symptomatic of gastro-oesophageal reflux disease (n=9), and posttotal gastrectomy patients (n=6).

Most sections were taken of columnar epithelium, however, sections showing transitional epithelium were present.

DNA quantification of squamous cell carcinoma of the oesophagus: a comparison of flow cytometry and image analysis

T N WALSH, T DORMAN, B CURRAN, O DROOGAN, D HOURIHANE, T P J HENNESSY, AND M LEADER (Departments of Histopathology, Royal College of Surgeons in Ireland and Department of Surgery, St James’s Hospital, Dublin & Ireland) Flow cytometry (FC) determined DNA aneuploidy indicates a poor prognosis in many solid tumours but its application is limited by lack of control cells and poor discrimination. Cyto-photometric image analysis (IA) overcomes these limitations. Two groups of patients with stage 2A invasive, well or moderately differentiated squamous cell carcinoma of the oesophagus were studied. Group 1 (n=11) were patients who succumbed to tumours within one–30 mm of group 2 (n=17) were patients who were tumour free more than one year since operation. Ploidy was determined by both FC and IA of formalin fixed paraffin embedded tissue. The percentage of cells within the diploid and aneuploid (5C exceeding rate) was determined by IA. Acceptable histograms were derived from 100% of samples using IA compared to 83% using FC. IA was more sensitive in identifying aneuploid stem lines. The incidence of aneuploidy in well and moderately differentiated squamous carcinomas was higher than suspected. IA successfully identified the low ploidy cases. The data suggests that IA is a more sensitive technique for detecting cellular DNA abnormalities and should replace FC if correlation between ploidy and outcome is to be established.

An alternative method of positioning the pH probe for oesophageal pH monitoring

A ANGGANASH, M MCCULLAGH, N BRIGHT, AND W J OWEN (Department of Surgery, Guy’s Hospital, London SE1 9RT) The most reliable method of positioning a pH probe for oesophageal pH monitoring is to place it 5 cm above the upper margin of the lower oesophageal sphincter (LOS) as determined by oesophageal manometry. Manometry, however, is expensive and requires special equipment and training. We have looked at an alternative, economical means of determining the site of the LOS. A fine bore nasogastric tube with a latex balloon at its tip was inserted transanally into the stomach in 30 patients. The balloon was inflated with 10 ml of air. The tube was withdrawn, until resistance was met. The distance from the nose, in centimetres, was noted and compared with the upper margin of the LOS as determined by oesophageal manometry. When the manometric distance was compared statistically with the balloon distance minus 1 cm, the correlation was highly significant (p=0.017; r=0.902).

We recommend that, where manometry is unavailable, the upper margin of LOS can be determined using this method. The pH sensor can be placed 6 cm above this level for satisfactory pH recording.

Epidermal growth factor: the role in oesophagitis?

JANKOWSKI, B TREASKIRK, C COUGILL, A GRANT, D HOWARD, AND G W MURRAY (University Department of Clinical Pharmacology and Pathology, Ninewells Hospital & Medical School, Dundee) Forty patients who attended an oesophagoscropy clinic had an oesophageal biopsy specimen taken from between 20 and 40 cm from the incisors which was assessed histologically for the presence of oesophagitis by a consultant pathologist. An immediately adjacent biopsy specimen was taken for immunohistochemical analysis of epidermal growth factor (EGF).

Thirteen sections were graded as having oesophagitis and 27 as being normal histologically. Most sections had positive staining for EGF and this was confined to the endothelial cells in the papillae. The number of EGF positive papillae was expressed as a percentage of the total number of papillae. The normal mucosa had more positive papillae than inflamed mucosa, 81% and 42% respectively (analysis of variance <0.001).

This is the first report to describe EGF in the oesophagus. Moreover, the finding of reduced EGF in inflamed mucosa corroborates previous work indicating decreased salivary EGF in those with oesophagitis. Whether the low EGF levels are primary or secondary to the inflammatory change is not yet clear. It may be that EGF is transported from an extra-oesophageal site to the capillary endothelial cells and then exerts its trophic action on the basal cells of the oesophagus.

Regression of columnar epithelium in Barrett’s oesophagus with omeprazole

S GORE, R SUTTON, I A HYDE-BROOK, M W L GEAR, N A SHEPHERD, AND S P WILKINSON (Gloucestershire Royal Hospital, Gloucester GL1 3NN) Fourteen adult patients with a columnar lined lower oesophagus of at least 3 cm extent, were entered into a longterm study of the effects of omeprazole. An endoscopy was carried out six months before treatment, immediately before treatment, and six months later. Biopsy specimens were taken every 3 cm, starting at the gastro-oesophageal junction up...
to 3 cm above the squamocolumnar junction (SCJ).

There was no statistically significant change in the extent of columnar epithelium during the six months before treatment, but this fell from 7-21 cm (SD 2-30) to 3-1 cm (SD 1-8) at 6 months of omeprazole (p<0.005). None of the patients had macroscopically evident islands of squamous epithelium within the columnar epithelium pretreatment, yet these were present in six patients after six months. Only two patients had microscopic squamous islands pretreatment and these were present in seven patients after six months of taking omeprazole. Also after six months of treatment in the majority of treated in from the SCJ there was encroachment of squamous epithelium over the glandular columnar epithelium.

These preliminary findings suggest that omeprazole induces a regression of the metaplastic epithelium of Barrett’s oesophagus.

Combined gastric and oesophageal 24 hour pH monitoring and oesophageal manometry in patients with reflux disease, resistant to treatment with omeprazole (OME)

E C KLINENBERG-KNOL AND S G M MEUWISSEN (Department of Gastroenterology, Free University Hospital, Amsterdam) Combined oesophageal and gastric 24 hour pH monitoring and oesophageal manometry were performed in 19 patients with reflux disease (RD) resistant to short term treatment with OME (40 to 60 mg daily) for 12 weeks or with recurrence of RD during maintenance treatment with OME (20–80 mg daily). The degree of efficacy of OME was analysed as well as the possible influence of oesophageal motility factors.

In 27 of 29 measurements an intragastric pH<4 was present during considerable periods of time, particular during the night. As a consequence, pathological gastro-oesophageal reflux occurred, particularly in the supine period. In 25 of 29 registrations (86%) intragastric pH reached values below 2 and in six cases (21%) pH was even less than 1. Lower oesophageal sphincter insufficiency was present in all but one patient; decreased or virtually absent motility of the oesophagus was found in 63% of the patients.

The present study emphasises the need to investigate all patients with refractory RD. In particular, dividing into a morning and an evening dose or switching to a single evening dose instead of a morning dose has to be considered.

Investigation of symptoms in achalasia after pneumatic dilatation: ambulatory pH or motility studies?

R STUART, J MCDONAGH, J ADAMS, A TANNER, A READER, A DELLIPIANI, AND T P J HENNESSY (North Tyneside District Hospital, Stockton-On-Tees and St James’s Hospital,† Dublin, Ireland) Symptoms after treatment in achalasia may be due to recurrent achalasia or reflux. We aim to obtain information about the investigation of patients after pneumatic dilatation. Of 72 achalasia patients treated by pneumatic dilatation (1973 to 1989), 20 with symptoms were reassessed. Symptoms were scored and ambulatory pH monitoring, manometry, ambulatory pH, scintigraphy, and endoscopy were performed. Six reported dysphagia alone, six had reflux symptoms alone, and eight had combined dysphagia and reflux symptoms. Eight of the 14 with reflux symptoms and two of the six with dysphagia alone had abnormal pH studies (% time pH>4.0-5.0). Median % time pH <4.0 in patients with reflux symptoms was 11.6 (range 0.1–45.9) compared to 2.2 (range 0.1–8.5) for the remaining subjects. Seven of 10 patients with abnormal pH studies and two with normal pH studies had oesphagitis. Ten of 14 subjects with dysphagia had mild and eight of these had abnormal pH studies (median 14.1%, range 0.1–45.9). The four patients with moderate dysphagia had normal pH studies (median 0.6, range 0–1–9) and ambulatory manometry was abnormal in all four. Scintigraphy and stationary manometry failed to distinguish between patient groups.

Ambulatory oesophageal pH is the most useful initial investigation, regardless of the patients symptoms. Reflux was the most common cause of symptoms (10/20). Few had symptoms attributable to recurrent achalasia (4/20) and ambulatory manometry identified these patients. No clear cause was identified in the remaining patients (6/20).

Palliation of oesophageal carcinoma with YAG laser and endoluminal cesium radiation

D G MORGAN, M CASTELLI, R H HUNT, V BASRUR, AND G T MENON (Departments of Gastroenterology and Surgery, McMaster University, Hamilton, and Hamilton Regional Cancer Centre, Hamilton, Canada) We have reviewed treatment with endoluminal cesium radiation, YAG laser photocoagulation, and a combination of the two treatments in patients with at least stage II oesophageal carcinoma. Since 1989, 19 patients have received endoluminal cesium radiation to deliver localised high dose radiation to reduce tumour bulk and to spare surrounding normal tissue. A Selectron catheter is endoscopically inserted and cesium pellets are delivered to the oesophagus by the application tube. Over 2.5 hours, 1500–2000 cGy are delivered. This is a lower dose than has been reported. Using the YAG laser 29 patients received 82 treatments. Forty-four of these received both laser and endoluminal radiation. In the laser+radiation group, there is a significant difference between the total number of laser treatments and the mean number of treatments after radiation. There is a significant difference between the mean total number of laser treatments in the laser only group and the mean number of treatments after radiation in the laser+radiation group.

Interluminal radiation is a useful adjunct to YAG laser treatment and reduces the number of palliative laser treatments required to maintain oesophageal patency. A RCT is warranted to further evaluate this treatment.

Relationship between labelling indices of tritiated thymidine ([3H]TdT) and Ki 67 immunohistochemistry in the oesophagus

J JANKOWSKI, W AUSTIN, S MURPHY, G COGHILL, D KENNY, AND K G WORMLEY (Departments of Clinical Pharmacology and Pathology, University of Dundee, Ninewells Hospital & Medical School, Dundee) The relationship between labelling indices of Ki 67 reactive epithelial biopsy specimens and [3H]TdT incorporated into S-phase cells was investigated in 30 patients with either a normal or inflamed oesophagus. Patients underwent oesophagoscopy and had one oesophageal biopsy specimen immediately incubated in medium with [3H]TdT and another biopsy specimen from an adjacent site was 'snap frozen' for subsequent Ki 67 immunohistochemistry. Ki 67 labelling index was determined by counting at least 150 epithelial cells. The [3H]TdT labelling index was determined by counting at least 500 basal epithelial cells. Positive staining with [3H]TdT was confined to the basal layers while Ki 67 labelling was also evident in the middle and suprabasal layers. Both of the labelling indices varied greatly from patient to patient; the labelling index of Ki 67 mean was 1.2% (range 28–4%), and [3H]TdT mean 9.7% (range 24–2%). The correlation between Ki 67 and [3H]TdT labelling index was significant (p<0.01).

We conclude that the Ki 67 labelling is an alternative to autoradiography in assessing cellular proliferation in the oesophagus. Ki 67 immunohistochemistry may also supply additional information regarding the cell cycling population.

Human oesophageal bacillary infection – a factor in oesophageal acid clearance?

C M BROWN, D BOTHAM, AND W D W REES (Hope Hospital, University of Manchester School of Medicine, Salford) Luminal neutralisation by bacitracin may be important in protecting oesophageal mucosa against refluxed acid. A negative pH is a significant correlate of acid reflux. If luminal neutralisation of acid reflux does provide a protective effect then bacitracin may be a useful agent in acid oesophageal reflux.

Eighteen patients with esophageal erosions were divided into two groups: treated with bacitracin (n=8) and controls (n=7) (the latter treated with placebo daily). The mean basal and postprandial oesophageal acid clearance was 9.4 ml/minute in the treated group versus 2.5 ml/minute in the control group. The mean acid clearance during acid reflux was 12.2 ml/minute in the bacitracin group versus 3.4 ml/minute in the control group. The inhibitor was effective in decreasing acid clearance and neutralising acid reflux.

Chylorhaphos complicating oesophageal resection

C BOLGER, H SANFEE, T N WALSH, P KEELING, A TANNER, AND T P J HENNESSY (Departments of Surgery, St James’s Hospital, Dublin, and the University College Hospital, Galway, Ireland) Chylorhaphos – intrathoracic leakage of chyle from an injured thoracic duct – was not seen by us during oesophageal resection, with few surgeons having large experience in its management. A multicentre retrospective study was carried out to examine the cause, management, and outcome in
patients with thoracic duct injury after oesophageal resection. Ten patients were identified. Chylothorax occurred in nine of 91 (10%) after transhiatal oesophagectomy but only one case followed 489 cases of oesophagectomy at open thoracotomy. Management was conservative in seven cases with nil by mouth, total parenteral nutrition, and chest drainage, and operative in three cases with ligation of the thoracic duct at open thoracotomy. Of the seven operated conservatively three survived, while of those three who underwent thoracotomy, two survived. Chylothorax is a serious complication of oesophagectomy associated with a mortality of 50%. The incidence of oesophagectomy. Its management presents a particular dilemma since conservative approaches are protracted requiring at least two to four weeks for effect in an already nutritionally depleted population, while the alternative is to perform a second major operation in a group of patients in whom thoracotomy was originally contraindicated.

Effect of the smoking habit on operation rates for Crohn's disease

Y R MAHIDA, R F A LOGAN, M EDMOND, AND C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham NG7 2UH) A case-control study from this unit in 1984 first identified a relationship between smoking and Crohn's disease. This raises the possibility that continued smoking worsens the natural history of this disease. We therefore examined the relation between smoking and surgical resections for Crohn's disease in patients from the 1984 study. Patients were questioned about their smoking habit in 1989 and operation rates of those who replied were determined from the clinical records.

Of the original group of smokers, never-smokers, and ex-smokers (who stopped before 1984), 73%, 72%, and 59% respectively replied. Eleven out of 45 (24%) of the original smokers had stopped by 1989. Surgery (at least one operation) was performed in 8/13 (62%) more patients who continued to smoke (85%) compared to those who continued to be non-smokers (never-smokers plus ex-smokers; 56%, \( \chi^2 = 3.3, p = 0.07 \)). These differences seemed more pronounced for patients who had required two or more operations by 1989: 45% of smokers compared to 10-3% of non-smokers (\( \chi^2 = 7.8, p = 0.01 \)) or 8-7% of non-smokers (\( \chi^2 = 5.6, p = 0.02 \)).

This study suggests that patients with Crohn's disease who continue to smoke are more likely to require surgery.

Rectal examination is of no value in the diagnosis of right lower quadrant abdominal pain

J M DIXON, R A ELTON, J B RAINNEY, AND D A MACLEOD (INTRODUCED BY D. C. CARTER) (University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh, EH3 9YW) This study set out to determine whether rectal examination performed in a series of 1204 patients admitted to hospital with right lower quadrant pain provided useful diagnostic information. Rectal tenderness, if present, was recorded as right or left sided or generalised; masses were noted separately; 37-3% of the group had proven acute appendicitis, 38-5% non-specific abdominal pain, and 3-7% gynaecological disorders. To assess the diagnostic value of symptoms and signs, odds ratios (OR), which are indicators of the diagnostic value of a test, were calculated for each diagnostic group. For appendicitis multiple logistic regression analysis was also performed.

Neither left sided nor generalised rectal tenderness was associated with any diagnostic group, but right sided tenderness was more common in those with appendicitis, OR 1-41, \( p = 0.05 \). This is significant only rela-
tive than for other signs: right lower quadrant tenderness OR 4-11, guarding OR 2-88, rebound tenderness OR 3-36, and abdominal rigidity OR 5-14, each \( p < 0.001 \). When allowance was made for rebound, rectal tenderness to the right lost its significance in the regression analysis. Of the six patients with rectal masses, three had signs of appendicitis and in the other three masses were palpable on abdominal examination.

Rectal examination may not provide any useful diagnostic information in patients with right lower quadrant abdominal pain.

Intraepithelial T cell clones from the small intestinal mucosa of coeliac and control patients

C J SMART, P D HOWDLE, H W BOYSTON, AND L K TREDEOSIEWICZ (Departments of Medicine and Pathology, University of Leeds) Intraepithelial lymphocytes (IEL) constitute a substantial proportion of all immunocytes of the human intestinal mucosa, although little is known of their function. Due to problems of cell yield, heterogeneity, and the difficult procedures required to isolate IEL, the establishment of IEL clones would be invaluable for functional studies. To these ends, IEL were isolated from six coeliac and nine control mucosae and cultured with irradiated peripheral blood lymphocyte 'feeder' and phytohaemagglutinin. After four days cells were transferred to medium containing interleukin-2 and restimulated one to two weeks later. Clones were isolated by limiting dilution after one to two stimulation cycles. In total, 19 clones were isolated.

Freshly isolated IEL were >95% CD3+ T cells, predominantly of the CD8+ CD4- phenotype, from both coeliac (75-0% (15-9)) and control (63-1% (10-8)) patients. The majority of clones were CD8+ CD5- , the phenotype characteristic of IEL but very rare in the periphery. In addition, >85% of isolated IEL expressed the mucosal lymphocyte-associated HLA-1 antigens. These data imply that the clones are indeed of IEL origin and can be used for the investigation of IEL function in normal and coeliac patients.

Azathioprine and levamisole in Crohn's disease: a double blind controlled trial of one year's treatment with long-term follow-up

J M T WILLOUGHBY, J M THOMAS, AND D M SUDWICKS (Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW) In a population based retrospective study of coeliac disease among ethnic groups of the Asian community in Leicester, cases diagnosed between 1975 and 1990 were identified from hospital diagnostic codes, pathological records, dietetic files, and a survey of family practitioners throughout the city. All young people were reviewed using the ESPGAN criteria. Of the

**Epidemiology of coeliac disease in the Asian community**

K SHERR AND J M MAYBERRY (Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW) In a population based retrospective study of coeliac disease among ethnic groups of the Asian community in Leicester, cases diagnosed between 1975 and 1990 were identified from hospital diagnostic codes, pathological records, dietetic files, and a survey of family practitioners throughout the city. All young people were reviewed using the ESPGAN criteria. Of the
Significance of small bowel bacterial overgrowth in the elderly

N Y HABOUBI, R D MONTGOMERY, P ASQUITH, and G SLEE (Wrexham Maelor Hospital and East Birmingham Hospital) Duodenoejejunal bacterial overgrowth is increasingly recognised in older people, but its clinical significance is not defined. Eleven elderly subjects (12 women, 4 men; mean age 78 years) were selected for study on the basis of an abnormal hydrogen breath test. In 12 cases the small bowel was radiologically normal, and in 14 pentagastrin tests showed normal gastric acid secretion. Nutritional assessment, anthropometric measurements, culture of small bowel aspirates, C14 volatile breath tests, and corrected one hour blood xylose tests were performed before and after three to six months of cyclical antibiotic treatment. After this treatment alone, weight gain was noted in 13 patients (p<0.01) and mean haemoglobin concentration rose from 10-74 to 12-31 (p<0.01). Blood xylose test levels increased in 14 cases (p<0.01) and mean exhaled C14 rose from 164-3 to 240-06 (p<0.01). The breath hydrogen test reverted to normal in all cases and bacterial overgrowth (>10^10 organisms per cm) was eliminated in 10/11 cases. The mouth-to-caecum transit time was prolonged initially (mean 190-4 min) and was unaffected by treatment (mean 196-2 min). This suggests that extended bowel transit time in the elderly may cause appreciable malabsorption and under-nutrition, both correctable by antibiotic treatment. Impaired peristalsis seems to be more important than gastric hyposecretion in the pathogenesis of this syndrome.

Twelve controls, 17 patients with Crohn's disease, and 25 of their first degree relatives were studied. After an overnight fast subjects drank a 100 ml solution containing 5 g of PEG 400 with subsequent five hour urine. After a millet starch meal (380 g) of the dose which did not differ significantly from that of the first degree relatives, 24-1 (4-9%) (p<0.05). Patients with small bowel involvement excreted 18.3 (5-9%) (n=11, p<0.01) and patients with Crohn's colitis were normal 25.5-5 (3-8%) (n=6, p=0.05). This study shows normal permeation of PEG 400 in first degree relatives of patients with Crohn's disease and reduced permeation in patients with Crohn's disease. These patients seem genetically determined abnormality of intestinal permeability does not seem to be an important aetiological determinant in Crohn's disease.

Effect of non-steroidal anti-inflammatory drugs on human jejunal morphology

J D ARNOLD, G T WILLIAMS, F M KHAN, W E WILKINS, J S MORRIS, and J RHODES (University Hospital of Wales, Cardiff) NSAIDs Modulation of jejunal morphology on inflammation in the small intestine has previously been assessed indirectly by radio-labelled leucocyte scanning and sugar permeability tests. We have examined changes in jejunal morphology of patients taking NSAID in the long term compared with normal volunteers. Jejunual biopsy specimens were taken from 11 patients (eight women, mean age 46 years) on NSAIDs and eight healthy volunteers (five women, 51 years). In the NSAID group five had rheumatoid disease and six oesooarthritids; clodafenac and indomethacin were most commonly used. Upper gastrointestinal endoscopy was performed on all the subjects and a modified Crosby biopsy capsule was mounted on the endoscope and passed beyond the liga-

tment of Treitz. Well oriented biopsy specimens stained by haematoxylin and eosin were assayed by a histopathologist who was unaware of the treatment received by subjects. The following parameters were assessed: (a) mucosal thickness, (b) villous height, (c) crypt depth, (d) villous enterocyte height, (e) intraepithelial lymphocytes, (f) epithelial atrophy, and (g) acute and chronic inflammation in the lamina propria. None of the biopsy specimens from NSAID subjects showed appreciable abnor-

mality. Chronic NSAID ingestion does not seem to cause appreciable change in jejunal morphology in man.

Intestinal permeation of polyethylene glycol 400 (PEG 400) in patients with Crohn's disease and their first degree relatives

K TEAHON, J M RIDOUT, A J LEVI, and I BJARNASON (Department of Gastroenterology, MRC Clinical Research Centre and Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ) Most patients with Crohn's disease have increased intestinal permeability to oligosaccharides and CR EDTA. It has recently been suggested that the permeation of PEG 400 is increased in first degree relatives of patients with Crohn's disease, indicating a genetically determined predisposition to the disease or exposure to a common environmental agent (Ann Intern Med 1986; 105: 883-5). A parallel study has been performed because of the implication of these findings.

After elemental diet, disease activity improved (HBI 8:5 (1:2) to 3-9 (0:6), mean (SEM), p<0.01 and faecal excretion of [11]indium (44.1 (1.5%) to 8.2 (1.5%), p<0.02), but there was no significant change in serum sIL-2R, T (1121 (181) units/ml to 789 (79-6) units/ml, p<0.05) or the nutritional indices. Serum sIL-2R did correlate with nutritional indices, PA (r=0-661), CH (r=0-537) and TBK (r=0-499), but not with disease activity. Elemental diet, therefore, reduces intestinal inflammation but not chronic T cell activation in Crohn's disease. Nutrition may have some bearing on T cell activation but not in clearing up acute inflammation.

Plasma interleukin-6 in inflammatory bowel disease

A J LOBO, S C JONES, S W EVANS,* R BANKS,* B J RATHBONE, AND A R RAXON (Gastroenterology Unit, Leeds General Infirmary, and University Department of Chemical Pathology, University of Leeds, Leeds, UK) The effect of dietary intervention on serum interleukin-6 (IL-6) is thought to be the major cytokine responsible for the production of an acute phase response. Using a double antibody ELISA assay, plasma concentrations were measured in 20 patients with severe inflammatory bowel disease (55 Crohn's disease, 65 ulcerative colitis). Plasma IL-6 in healthy volunteers was 12-5 pg/ml. Significantly higher concentrations of IL-6 were found in both ulcerative colitis (CDAI>150) Crohn's (mean (SE) 43-6 (5-5) pg/ml) compared to inactive disease (mean 5-2 (2-27) pg/ml; p=0.0005). These values correlated with CDAI (Spearman R=0-52; p<0-05) and erythrocyte sedimentation rate (R=0-28; p<0-04), CRP (R=0-27; p=0-03) and platelets (R=0-27; p<0-04) and were inversely correlated with haemoglobin (R=0-36; p=0-005) and albumin (R=0-54; p<0-002). There was no difference between concentrations of IL-6 in active ulcerative colitis (stool frequency of at least three a day with rectal bleeding) compared with inactive disease, although individual raised values were seen in both groups. Significantly higher concentrations were seen in active Crohn's disease compared with active ulcerative colitis (p<0-02). This suggests that IL-6 is an important mediator of the acute phase response in Crohn's disease and therefore may be a useful additional marker of disease activity.

Transmission electron microscopy of the vascular changes in the intestinal wall of patients with Crohn's disease

R M PITTOLO, A J WAKEFIELD, A M SAWYERR, A P DILLON, P M ROWLES, M HUSDSON, E A SANKEY, L MORE, R SIM, A A M LEWIS, and R E FOUNDER (Inflammatory Bowel Disease Study Group, Department of Histopathology, University College and Middlesex School of Medicine and the Royal Free Hospital School of Medicine, London NW3, England) We have examined, by trans-
mision electron microscopy, the vasculature of rectal biopsies from 15 patients with Crohn's disease. Tissues were obtained from areas of macroscopic vascular abnormality in glutaraldehyde perfusion-fixed specimens. Vascular abnormalities were identified by plastic casting of the vasculature, and targeted biopsy of methyl salicylate cleared sections. Electron microscopy showed that ultrastructure was well preserved, but pronounced abnormalities
were observed in the blood vessels of both the muscularis and submucosa. The walls of many of the vessels were disrupted and consisted of aggregations of collagen and large clusters of inflammatory cells. In other vessels the wall consisted of an amorphous cellular mass in which the lumen was sometimes seen to be filled with granular or fibrillary material.

The spectrum of non-infectious inflammatory bowel disease in hypogammaglobulinaemia

K Teahan, D Webster, A B Price, A J Levie, and I Bjarnason (Section of Gastroenterology, MRC Clinical Research Centre and Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ) Sixty per cent of patients with severe hypogammaglobulinaemia have severe diarrhoea of unknown aetiology. We studied nine such patients, seven had common variable and two had X-linked hypogammaglobulinaemia, receiving regular intravenous gammaglobulins. No pathogens were found except cytomegalovirus in one. Gastric biopsy specimens showed an erosive gastritis in one of six patients. Jejunal biopsy specimens were normal in four, had increased interepithelial lymphocytes in one, and subtotal villus atrophy in one which was gluten sensitive and confirmed on challenge. Colonoscopy was unremarkable (n=7), but three had pancolitis histologically with an increased eosinophil infiltrate. Studies with 1125iu leucocytes (scan and faecal collections) showed small intestinal inflammation in all nine with a faecal excretion of N<1% (ranging from 2.3-31%). Four were treated with elemental diet with loss of symptoms and reduced faecal excretion of 11C. In Postmortem studies (n=3) showed a form of inflammatory small bowel disease clearly distinguishable from Crohn’s disease.

This study shows a high prevalence of intestinal pathology in symptomatic patients with hypogammaglobulinaemia. The enteropathy was of a new disease entity and it responds to elemental diets and seems to be the main cause of diarrhoea in these patients.

The influence of fasting acinar, intraluminal content on motility patterns

D Smith, B Waldron, and F C Campbell (Department of Surgery, Ninewells Hospital and Medical School, Dundee, DD1 9SY) The influence of intraluminal gas and acinar secretion of resting gastrointestinal motility is unknown. This study has investigated the influence of fasting and an acinar liquid of variable viscosity on: (i) periodicity of the migrating motor complex (MMC), (ii) phase II contraction amplitude and frequency, and (iii) incidence of two contraction pattern abnormalities (non-propagated phasic activity and sustained uncoordinated phasic pressure activity).

In eight fasting volunteers, gastric, duodenal, and jejunal motility was recorded by a 280 cm multilumen perfused tube, passed to the caecum (i) in the baseline state, (ii) after total gas and fluid evacuation from the upper gastrointestinal tract and after intraluminal instillation of 350 ml of (iii) air, (iv) low (2-83 Centistokes) and (v) high viscosity (317/8 Centistokes) methylcellulose solution respectively. All studies showed fasting motility patterns. Total gastrointestinal gas and fluid evacuation reduced contraction amplitude of phase II (p<0.01). Contraction amplitude increased after instillation of gas and low and high viscosity liquid (p<0.02), while contraction frequency increased with high viscosity liquid only (p<0.05). Contraction pattern abnormality of intraluminal content. Periodicity of the MMC was unaffected by any alteration of intraluminal content.

Acinar intraluminal gas and liquid affects fasting motility; with manipulations of contraction amplitude, frequency, and patterns. Periodicity of the MMC is unaffected.

Gut-selective alpha 2 blockade can mimic the irritable bowel syndrome

D Evans, M J Benson, and D L Wingate (GI Research Science Unit, The London Hospital Medical College, 26 Ashfield Street, London E1 2AZ) Idoxafox is a new alpha 2 receptor antagonist which can modify gut motility and has been suggested as a treatment for irritable bowel syndrome (IBS). We have measured 24 hour ambulatory, duodenoejejunal fasting and fed gastrointestinal motility using a 3 channel strain-gauge catheter with subjects equipped with manipulations of intraluminal content. Periodicity of the MMC was unaffected by any alteration of intraluminal content.

Acinar intraluminal gas and liquid affects fasting motility; with manipulations of contraction amplitude, frequency, and patterns. Periodicity of the MMC is unaffected.

Is enteral feeding related diarrhoea initiated by an abnormal colonic response to intragastric diet infusion?

A H Raimundo, J Rogers, and D A B Silver (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS) Despite characterisation of small bowel motility and colonic inflows to intraduodenal diet infusion, the pathogenesis of diarrhoea occurring in up to 20% of patients receiving enteral nutrition is unclear. This study investigated the same responses to intragastric and intraduodenal feeding. Two groups of normal subjects were studied, using an 11-lumen orocaelcular tube and 3H-PEG was infused at 1 ml/min into a 20 cm segment of terminal ileum. After a steady state (5 h) colonic inflows were measured at 30 min intervals for 4 h before and after an intravenous infusion of a polymeric diet (1:38 ml/min, 6-3 g/ml: 1 kcal/ml) intragastrically (n=6) or intraduodenally (n=6). Small bowel motility was recorded at six sites (30 cm apart) spanning 150 cm. During fasting: phase II migrating motor complexes (MCCs) occurred predominantly in the proximal small bowel of both groups. Intraduodenal infusion resulted in conversion of the ‘fasting’ to a ‘fed’ pattern, with a complete absence of MCCs for 8 h. Intragastric infusion produced a similar pattern with the persistence of the ‘fasting’ pattern (fasting: 7-2 (1-8) MCCs, mean (SEM), diet infusion: 11-1 (2-4)). Fasting colonic inflow rates were similar before intraduodenal (19-1 (10-3) ml/30 min, mean (SEM)) and intragastric (9-8 (1-9) ml/30 min) diet infusion. Although intraduodenal infusion resulted in a significant (p<0.04) increase in colonic inflow (58-5 (21-8) ml/30 min) none of the subjects had diarrhoea. In contrast, despite the persistence of MCCs during intragastric infusion, colonic inflow did not increase above fasting values (12 (1-4) ml/30 min); however, four of the six subjects did have diarrhoea. These findings suggest that diarrhoea during enteral feeding results from an abnormal colonic response rather than from small intestinal dysfunction.

The role of a cholecystokinin (CCK) antagonist on the ileal brake mechanism in the rat

N J Brown, R E Rumsey, and N W Read (Sub-Department of Gastrointestinal Physiology and Nutrition, University of Sheffield, Western Bank, S10 2TN) It has recently been shown that the CCK antagonist L364718 reverses delayed gastric emptying produced by duodenal lipid infusion or ingestion of a fatty meal. We have shown that lipid infused into the ileum of both humans and rats delays intestinal transit of a meal – the ileal brake. The aim of this study was to investigate whether CCK receptors are involved in mediating the ileal brake. Eight rats were equipped with ileal cannulae 20 cm proximal to the ileocecal valve. Fasted animals were infused with saline or Intralipid into the ileum (0.3 ml/h) for 30 minutes before being gavaged with the meal. Rats were then placed in perspex chambers, the infusion continued for 160 minutes and the hydrogen concentrations monitored throughout the experiment. Two intraduodenal infusions of the time of the head of the meal (SCTT). The effect of L364718 (4 mg/kg, po) on SCTT of a meal, administered 30 minutes before ileal infusion was investigated.

Ileal infusion of Intralipid significantly delayed SCTT of the meal compared to the saline infusion (Intralipid vs saline, mean (SE) 192.5 (13.1) vs 117.5 (9.7) min; n=8; p<0.001). L364718 had no effect on SCTT of the meal during ileal saline, but significantly reduced Intralipid delayed SCTT of the meal (L364718/Intralipid vs saline/intralipid; 80 (12.1) vs 192.5 (13.1) min; n=8; p<0.01). These results suggest the CCK receptors may be involved in mediating the ileal brake mechanism in the rat.
Modulation of small intestinal motility in slow transit constipation by subtotal colectomy

M J BENSON, D KUMAR, D WALDRON, N S WILLIAMS, AND D L WINNATE (GI Science Research Unit, The London Hospital, London E1 1BB) We have previously reported proximal small bowel (PSB) motor abnormalities in 12 females with slow transit constipation (STC). Of these, six patients have subsequently undergone a subtotal colectomy for this condition: postoperative defaecation frequency increased in all patients (range x2–35/7 days; preop x1/14–14 days). Three months after surgery, a repeat 24 h ambulatory recording of 7, 8 motor activity was performed on six healthy volunteers served as controls (defaecation frequency x1/1–2 days).

Postoperative nocturnal migrating motor complex (MMC) duration, was increased from preop group, was increased from preop group, was near normal values postoperatively and 20, and 35 (6 7) minutes) (43 9) minutes (p<0.05).

Is the ileum normal in chronic idiopathic constipation?

B PANAGAMUWA, M OYA, J ORITZ, M R KEIGHLEY, AND D KUMAR (Department of Surgery, The Queen Elizabeth Hospital, Edgbaston, Birmingham) Chronic idiopathic constipation (CIC) is generally regarded as a colonic disorder. To evaluate terminal ileal motility in CIC we have studied seven patients (six women, one man) with CIC and six control subjects. Using a 2.5 mm long fine bore (OD 2.5 mm) catheter with microtransducers embedded 5, 20, and 35 mm from the tip, the catheter was positioned under fluoroscopic control such that the proximal transducer was near the ileocecal junction. The data were recorded on audiotape in a portable tape recorder. The subjects were completely ambulant during the study and ate normally. A total of 218 hours of recording was obtained (mean of 14 hours in 20 subjects, 20 hours in 20 controls). The mean cycle length was 141 (56) minutes (mean SD) in CIC and 118 (28) minutes in control subjects.

The effects of bolus doses of medium chain triglycerides on small intestinal structure

A P JENKINS AND R P H THOMPSON (Gastrointestinal Laboratory, Royne Institute, St Thomas’s Hospital, London SE1 7EH) Continuously infused medium chain triglycerides (MCT) are less trophic to the small intestine than long chain triglycerides (LCT). Bolus doses of LCT have a more potent trophic action than divided doses, but the effects of bolus doses of MCT are unknown. Two groups of eight female Wistar rats were isocalorically fed elemental diets giving 29% of calories as either LCT (Elanol) or as an MCT–rich mixture in twice daily bolus doses by gavage. A third group of eight rats was fed the same diet with glucose (GLUC) substituted for the remainder of the feed. After 21 days small intestinal weight, mucosal weight, protein, and DNA were measured.

The MCT diet caused diarrhoea, but both LCT and MCT similarly increased whole gut weight and mucosal weight compared with GLUC, whole gut weight: LCT 57.81 (1.65), MCT 60.34 (2.53), GLUC 49.41 (1.04) mg/cm, mean (SEM), p<0.001; AOVISA; mucosal weight: LCT 21.76 (0.70), MCT 22.37 (1.36), GLUC 17.83 (0.52) mg/cm, p<0.001. Mucosal protein and DNA reflected these changes.

Bolus doses of MCT exert a trophic effect on the small intestine that is comparable to that of bolus doses of LCT. Thus, the enterotropic action of MCT, like LCT, depends on the method of administration.

Longterm effects of elemental and enteral diets in Crohn’s disease

M H GIFFAER, P CANN, AND C D HOLDsworth (Gastroenterology Unit, Royal Hallamshire Hospital, Sheffield) Previous studies have concentrated on the therapeutic value of elemental and clusters in active Crohn’s disease, but their longterm benefit has not been established. Twenty seven patients with established Crohn’s disease who attained clinical remission after four weeks of elemental diet were maintained on elemental diet for up to 36 months. Twenty of these were willing to be tested for specific food intolerance through a predefined dietary elimination protocol; the others continued on normal diet. Crohn’s disease was relapsed in 89% of the relapses occurring within the first six months. Of the 15 patients with colonic involvement, 12 (80%) relapsed. In contrast, only three of 11 with isolated small bowel disease experienced early relapse. Of the 14 patients who completed the process of dietary testing, five could not identify any trigger foods. The remaining nine were maintained on elemental diets, three of whom relapsed early. Of the seven taking normal diet, five relapsed. Disease duration, previous intestinal resection, or previous steroid treatment did not affect the relapse rate. Eight patients (33%) obtained remission or improvement, averaging 23 months (12–36) without any medication. Long lasting remissions can be obtained in a third of patients with Crohn’s disease after treatment with defined elemental diets. Crohn’s involvement is associated with a high early relapse rate. Exclusion diets did seem to promote longer remissions in patients with small bowel disease only.

Lipid digestion, absorption, and metabolism in severely hypoxy subjects

C H E IMRAY, A R BRADWELL, A WRIGHT, I CHESSNER, AND J P NEOTPLEMOS (Academic Department of Surgery, Dudley Road Hospital, University of Birmingham and the Birmingham Medical Research and Expeditionary Society) The nutritional problems that occur in adult and neonatal respiratory failure are associated with increased morbidity and mortality. A similar severe weight loss occurs at extreme altitude and is associated with increased mortality and morbidity. At altitude anecodal and indirect measurements – for example, faecal fats – suggest the weight loss is in part due to malabsorption or malnutrition of fats. Fifteen climbers (14 men, one woman, aged 23–62) had anthropometry, blood gases, and isotopic fat studies performed at 100 m and 5500 m. There were significant falls in all anthropometric parameters measured (all p<0.001, paired t test). At 5500 m in all subjects were severely hypoxy: Pao2 33–71 (2.71) mmHg, Paco2 22–04 (1.67) mmHg, pH 7.466 (0.042), 10 μCi of the triglyceride ['H]oleic acid (OAA) and 10 μCi of the free fatty acid ['H]oleic acid (OA) were ingested with a standard breakfast containing 30 g of fat. Subjects were venceseted at 0, 2, 4, 6, and 8 hours and performed a [14C]CO2 breath test at hourly intervals from 0 to 8 and at 24 hours. Absorption as measured by the rate of appearance of ['C]GTO and ['H]OA in the serum, and digestion as measured by the ratio of [14C]/[14C] was both unchanged at altitude. However, at 5500 m, excretion of ['C]CO2 (from the β oxidation of ['C]GTO) was significantly raised (p<0.01) at 2, 3, 4, and 5 hours and depressed.
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"CO2 was unchanged over 24 hours. We have shown that the pancreas and the small bowel have enormous functional reserves for lipid digestion and absorption under severe duodenal infusions. Hypoxic nutritional problems seem to be primarily metabolic in origin. This could be an important reversible model for nutritional problems encountered in respiratory failure.

Bile, pancreatic juice, and small bowel secretions contain endogenous metal binding ligands

J J POWELL, K P R GARTLAND,* J K NICHOLSON,* C C AINLEY, and P H THOMPSON (Gastroenterological Laboratory, Rayne Institute, St Thomas's Hospital, London SE1 7EH and Biological NMR Unit,* Department of Chemistry, UCL, WC1H 0AJ) The gastrointestinal luminal speciation of trace metals is unknown. Dietary factors are important, but endogenous binding agents require consideration. 1H NMR spectroscopy (NMR) provides a rapid, semi-quantitative multicomponent analysis of low molecular weight compounds in biofluids. Samples of pancreatic juice (n=5) and bile (n=5) from patients with pancreatic and biliary drains, and small bowel contents from ileostomy patients (n=6) were centrifuged and supernatants analysed, both directly by NMR (50 MHz) and after dilution and dilution and subsequent analysis in H2O for NMR analysis. The following species were identified at 5–20 mMolar.

Spectra of pancreatic juice gave consistent sharp peaks (suggesting mobile unbound species for many amino acids, particularly branched chain, and succinate, glucose, acetate, and formate. Bile spectra showed lipids and bile acids probably in micelles, and mobile glycine and choline. Lactate and acetate were sometimes present at these concentrations. Small bowel contents yielded spectra similar to pancreatic juice and bile combined with high concentrations of succinate, acetate, lactate, and particularly formate, probably from bacterial action.

We have for the first time studied the low molecular weight components of human intestinal secretions by NMR. In particular, dietary copper and zinc may be influenced by the presence of such endogenous ligands at these concentrations and precipitation of aluminium and ferric iron may be slowed by species such as lactate, acetate, and formate.

Comparison of the stimulated pancreatic exocrine secretory response to intragastric and intraduodenal infusion of polymeric enteral diet

A H RAIMUNDO, J ROGERS, P FIELDEN, P G FROST, and D B A SILK (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS) Although the stimulated pancreatic exocrine secretory response to intragastric infusion of polymeric enteral diets in humans has been recently been characterised, less is known about the responses that occur during intraduodenal infusion. This study was undertaken to compare the stimulated pancreatic exocrine secretory response to intragastric and intraduodenal infusion of the same standard polymeric enteral diet (1:38 ml/min; 6-3 gNl; 1 kcal/ml). Two groups of normal subjects were intubated with an 11 lumen orocaelic tube. Intestinal contents were aspirated at 30 min intervals from the terminal ileum 4 h before and 4 h during continuous intragastric (n=6) and intraduodenal (n=6) diet infusion, and analysed for amylase, chymotrypsin, and lipase. During intraduodenal infusion ileal amylase activity increased significantly (p<0.05) greater than basal concentrations (349 558 (88 046) IU/l, mean (SEM) v 152 646 (51 790), as were chymotrypsin (575 5 (95 2) v 301 5 (55 9), p<0.05) and lipase concentrations (8952 (2683) v 3388 (1436), p<0.05). During intragastric diet infusion ileal amylase concentrations were also significantly (p<0.02) greater than basal concentrations (124 090 (2 89) v 29 8 (9 05), p<0.05) with no significant increase in chymotrypsin (152 3 (33 9) v 131 6 (53 8) or lipase (1528 3 (477 5) v 1070 4 (280 3)) concentrations during intragastric diet infusion. These findings suggest that under the present experimental conditions, which are similar to those often used clinically, the intragastric infusion of a polymeric diet fails to evoke a stimulated secretory response for lipase and chymotrypsin. If it proves difficult to evoke a pancreas response to exocrine secretory response during enteral feeding, then the more physiological pancreatic response is evoked during intraduodenal infusion.

The use of Doppler ultrasound in analysing the effects of atenolol on superior mesenteric artery blood flow

A F MULLER, K A STAINER, L FULLWOOD, M HAWKINS, and A J COWLEY (INTRODUCED BY DR C J HAWKEY) (Department of Medicine, University Hospital, Nottingham, NG7 2UH) Doppler ultrasound is increasingly being recognised as a useful, non-invasive tool for assessing the abdominal vasculature. Until now, however, it has not been used to assess the effects of drugs on blood flow. This study examined the effects of 100 mg atenolol on pre and postprandial superior mesenteric artery blood flow (SMABF, Doptek Ltd) and cardiac output (CO, by rebreathing carbon dioxide, VG Medi) in six patients aged (SEM) 60 (2) years on four occasions after an overnight fast and 30 minutes' supine rest. Parameters of SMABF recorded were: pulsatility index (PI) (between interval on ECG (to account for changes in heart rate), peak systolic (Vmax) and end diastolic (Vmin) velocities, and flow. On visits 3 and 4 patients received an 800 kcal meal, on the latter having taken atenolol 3 hours before the study. Peak postprandial changes over an hour were accepted. Results analysed by Wilcoxon.

Mean coefficients of variation for Vmax, Vmin, PI, r-t, flow, and CO were 9-1, 10-2, 10-5, 8-3, respectively. Feedingly significantly increased Vmax (88-1 (7-9) cm/s to 127 (9-3) cm/s, p<0.015), Vmin (14-1 (1) cm/s to 32-3 (2-8) cm/s, p<0.001) flow (391 (45) ml/min to 645 (57) ml/min, p<0.009), and CO (3-3 (0-2) l/min to 4-36 (0-21) l/min, p<0.001). Atenolol did not significantly alter fasting parameters. However, postprandially it reduced Vmax (127 (9-3) cm/s to 109 (8-8) cm/s, p<0.001), Vmin (74 (2-8) cm/s to 22-6 (1-6) cm/s, p=0.01), although the reduction in flow failed to reach significance (645 (57) ml/min to 541 (46) ml/min, p=0.08). PI was not altered by atenolol when corrected for heart rate. CO was reduced (3-2 (0-21) l/min to 4-36 (0-21) l/min, p=0.02). There was a correlation between the percentage reduction in both CO and SMABF with atenolol, r=0-79, p<0.05. The postprandial changes in parameters of SMABF are attenuated by atenolol. A relation exists between the reduction in CO and SMABF. This finding is of particular relevance to patients with chronic mesenteric ischaemia.

Effects of G1-21 on intestinal epithelial cell proliferation in parenterally fed rats

R A GOODLAD, M A GHATEI,* J DOMIN,* S R BLOOM,* and N A WRIGHT (Imperial Cancer Research Fund Histopathology Unit, 35-43 Lincoln's Inn Fields, London WC2A 3PN, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road, London W12 0NN) Enteroagglutinog has been implicated as having a trophic effect on the gastrointestinal tract, as has the related peptide glucagon-(1–21). Three groups (8/6) of rats were fed intravenously for three days, and then infused with 0, 20, or 80 μg/rat per day of G1-21 for a further three days. They were killed 24 h after injection with 1 mg/kg vincristine (to arrest cells entering metaphase). The rats were bled and killed at timed intervals after injection. The gastrointestinal tract was removed, weighed, and fixed. Samples of small intestine and colon were stained and microdissected and the mean number of metaphases per crypt determined and regressed against time to derive the crypt cell production rate (CCPR). No significant effect on the weight of the stomach, caecum, or colon was observed, but the weight and CCPR in the small intestine was significantly decreased by G1-21. Plasma enteroglucagon was also decreased by G1-21 treatment.

It is concluded that G1-21 is not trophic to the gastrointestinal tract and may even have an antiproliferative effect.

Effects of TGF-α on intestinal epithelial cell proliferation in parenterally fed rats

R A GOODLAD, C Y LEE, and N A WRIGHT (Imperial Cancer Research Fund Histopathology Unit, 35–43 Lincoln’s Inn Fields, London WC2A 3PN, and Royal Postgraduate Medical School, Ducane Road, London W12 0NN) Recombinant human epidermal growth factor (EGF) is a potent stimulator of intestinal epithelial cell proliferation. EGF shares the same receptor like transforming growth factor-α (TGF-α) which is found in high concentrations throughout the adult gut (and in greater quantities in the juvenile), leading to the suggestion that the true ligand for the EGF receptor may be TGF-α.

The effects of TGF-α were investigated in four groups of rats fed intravenously for three days (4 rats/group) and then infused with 0, 4, 20, or 100 μg/rat/day of TGF-α for a further three days. They were injected with 1 mg/kg vincristine, bled, and killed two hours later. The gastrointestinal tract was removed, weighed, and fixed. Samples of small intestine and colon were stained and microdissected and the mean number of metaphases per crypt determined. TGF-α significantly increased the weight of the small intestine and of the colon. TGF-α also significantly increased the two hour collection of mesenteric venous blood. A-1 (374), fundus, small intestine, and colon. It is concluded that TGF-α, like EGF, is also trophic to the entire gastrointestinal tract of the rat.
Human epidermal growth factor is digested by jejunal juice but preserved by food.

R J PLAYFORD, A C WOODMAN, D A VESEY, R MELETH, AND J CALAM (Department of Medicine, Royal Free Hospital, Dashwood Road, London W12 0NN) Epidermal growth factor (EGF) is secreted by the salivary and Brunner's glands. We investigated the effect of food on its stability in gastric and jejunal juice.

"EGF was digested by 100 µl of gastric or jejunal juice for 1 h at 37°C, and applied to a Sephadex G-75 column. EGF incubated in gastric juice eluted in the position of intact EGF at 53% (Vt=0.9, Vr=100%). However, incubation with jejunal juice caused displacement to 90% indicating digestion of EGF. Incubation with chymotrypsin-α (1 mg/ml) also displaced EGF to 90%, but trypsin, entero-

A limiting factor in the gastrointestinal absorption of aluminium

J FOWLER, C C AINLEY, AND R H THOMPSON (Gastrointestinal Laboratory, Rayne Institute, St Thomas's Hospital, London SE1 7EH) The intestine is constantly exposed to aluminium (Al) in the diet. Systemic absorption is tiny (<1%), but the reason is unknown. The small intestine of six anaesthetised male Wistar rats (300–350 g) was perfused with MOPS buffered (pH=7.0) isotonic saline and Al (93 µmolar) sulphate at 37°C, at 0–4 ml/min for 45 min. Residual luminal perfusate was removed by perfusing with alkali and the animals sacrificed. The small bowel was then divided into three equal lengths (proximal, middle; distal) the mucosa scraped off, weighed, and acid digested, and Al measured by inductively coupled plasma emission spectrometry.

The total Al perfused was 1.48 µmol/rat; 0.02 (0.09) (µmol/SD) (62%) was recovered in the effluent, and 0.53 (0.17) (36%) in the mucosa, of which 11.2% (4.8) was proximal, 17.5% (4.8) mid, and 71.3% (5.3) distal (p<0.001, distal vs others).

Under these conditions one third of the perfused aluminium was associated with the mucus or was intramucosal; this is in keeping with Al compounds as anticoagulant agents. The binding of metals to intestinal mucus has been previously documented and the distribution shown here suggests that aluminium may be bound to mucus, since mucosal mass is greater proximally.

These results may explain why the absorption of aluminium is promoted by low molecular weight ligands that could prevent binding to mucus.

Small intestinal low-affinity calcium-dependent ATPase in coeliac disease

D P K NG, J AMOAH, AND R G LONG (Medical Research Centre, City Hospital, Nottingham) Active calcium absorption takes place in the duodenum and upper jejunum. Coeliac disease is known to be complicated by calcium malabsorption and oesophageal histology of features of coeliac disease are seen in endo-

Diarrhoea in advanced human immuno-

deficiency virus (HIV) disease is associated with increased gut permeability in Caucasian and African patients

M S KAPEMBAWA, S C FLEMING, N SEWANKAMBO, D SERWADDA, R ROODGAME, S LUCAS, AND G E GRIFFIN (St George's Hospital Medical School; UCIM/Birmingham Medical School; Makerere University Teaching Hospital, Kampala) Diarrhoea and weight loss are common in Caucasian and African HIV disease and may be associated with jejunal villous atrophy (JVA). Intestinal permeability (IP) (passive absorption of sugar molecules) is known to be altered in other forms of JVA. We have therefore measured IP in London and Kampala patients at different clinical stages of HIV disease to test the hypothesis that IP increases in association with clinical progression. IP was determined by measuring 6 h urinary recovery of lactulose and mannitol (HPLC and pulsed amperometric detection) after an oral load of both sugars (10 g, 5 g respectively). London patients: acquired immunodeficiency syndrome (AIDS) 26, AIDS related complex 7, asymptomatic 7. Controls 19. Kampala patients: AIDS 14, ARC 6. Controls. Stool microscopy for entero-pathogens was performed in all patients.

Only patients with diarrhoea (>3 stools per day) had evidence of increased IP. Normal IP was detected in HIV in the absence of diarrhoea irrespective of clinical stage. Small intestinal permeability increased with progression of clinical HIV disease in both Caucasian and African HIV patients. Such change in IP occurred irrespective of presence of enteropathogens.

Segmental and histological localisation of brush border enzyme uptake during ontogeny in the guinea pig: relation to body iron stores

G CHOWRIEMOOTOO, E S DEBNAM, S K S RAI, AND O EPSTEIN (Departments of Physiology and Medicine, Royal Free Hospital School of Medicine, Rowland Hill Street, London NW3 2PF) In adult animals, intestinal absorption of iron is closely related to body iron stores.

Although neutones show an enhanced iron uptake, the mechanisms involved and the relation to body iron stores are unknown. Here we have adult and newborn guinea pigs to assess body iron status and to study the locus of brush border iron transport along the villus axis in duodenum and lower ileum. For uptake experiments, 1 cm sleeves of everted intestine were incubated for 5 min at 37°C in well stirred, soyabean trypsin inhibitor buffer (pH 7.4) containing 5 mM glucose and 100 µm "Fe" + 2000 µm ascorbate (100 mM/ml). Uptake was terminated by exposure to 4% glutaraldehyde and the tissue processed for autoradiography. Brush border iron uptake by adult duodenum was restricted to upper villus enterocytes, while in adult ileum and the neonatal duodenum and ileum, all cells lining the villus showed this ability. The high proportion of duodenal and ileal cells involved in brush border iron uptake is reduced despite substantial body iron (eg, liver iron, adult: 0.3±0.03 (18), neonate: 0.5±0.01 (15) µmol/g, p<0.05) but similar enterocyte iron levels to adults (adult: 0.09±0.01 (14), neonate: 0.01±0.01 mg/g (p>0.05)). These data may provide information on the mechanisms causing inappropriate iron absorption in idiopathic haemochromatosis in man.

Reduction of graft versus host (GVH) reactivity in experimental small bowel trans-

plantation (SBT).

C L INGHAM CLARK, G J SMITH,* B A PRICE, P W CRANE, J W FABRE,* A P LEAR, AND R F M WOOD (INTRODUCED BY R K S PHILLIPS) (Professors Surgical Unit, St Bartholomew's Hospital, London and Blond McIndoe Centre for Medical Research, East Grinstead) In SBT organised lymphoid tissue within the graft may cause GVH disease. This study was designed to test the effect of depletion of enteropanethelial tissue on GVH reactivity measured by graft cell migration into host spleen. Heterotopic vascularised SBT was carried out from PVG to DA rat strains in three brood of (PVG×DA) (n=6 each group). All animals received cyclosporin (CaS) 15 mg/kg per day after transplantation. Group 1, CaS alone. Group 2, CaS and mesenteric lymphadenectomy. Group 3, CaS and graft perfusion with a specific T lympho-
cyte immunotoxin of ricin A-chain coupled with ox-19, a T cell monoclonal antibody. Host spleen was harvested at seven days and immunochromatographic staining with ox-27 used to identify donor strain (PVG) cells. In group 1 (controls) 47% of cells in the spleen were of graft origin. In group 2 (mesenteric lymphadenectomy) this proportion was significantly reduced to 32% (p<0.01). In group 3 (mesenteric lymphadenectomy) a smaller still significant reduction to 39% was obtained (p<0.01). Mesenteric lymphadenectomy may disturb fat absorption. However, immunotoxin depletion of graft T cells may be a practical means of reducing GVH reactivity in SBT.
Suppression of Helicobacter pylori during the clinical use of omeprazole

M A DAW, P DEEGAN, S BEATTIE, E LEE, and C T KEANE, and C O'MORAIN (Department of Gastroenterology, Meath/Adelaide Hospital and Clinical Microbiology (TCD), St James's Hospital, Dublin, Ireland) Omeprazole heals duodenal ulcer due to inhibition of the gastric acid secretion. It may also clear Helicobacter pylori from the gastric antrum. This study aimed to (1) determine the efficacy of omeprazole in healing refractory duodenal ulcer (RDU), (2) evaluate its effect on H pylori and gastritis. Seventy patients with RDU were allocated to H2 antagonist associated with H pylori and chronic gastritis were studied. Endoscopy was performed and biopsy specimens taken from each patient before, at four weeks of omeprazole (20 mg/ day) treatment, and after a further four weeks off treatment. A rapid urease test (RUT), H pylori culture, histology, and transmission electron microscopy (TEM) studies were performed on these specimens to assess gastritis and H pylori at each stage of treatment. After four weeks on treatment, 10 (58-5%) patients had a negative RUT and H pylori culture, gastritis improved in nine (52-9%) patients, and in 14 (82-4%) the ulcer was healed. TEM showed the absence of H pylori in three biopsy specimens where the organisms were embedded in the tissue, although RUT and H pylori cultures were negative in all these patients. At eight weeks, nine patients who were H pylori negative reverted to positive and had severe gastritis. TEM showed H pylori in the same location as before treatment where H pylori was predominantly on the surface of the gastric mucosa and in the intracellular junction. In conclusion, omeprazole heals RDU, improves gastritis, and suppresses but does not eradicate H pylori.

Nodules in the duodenal bulb

S SRIDHR, J GRAHAM, and J D R ROSE (Department of Medicine, Ballochmyle Hospital, Mauchline, Ayrshire, and Pathology Department, Area Laboratory, Crosshouse Hospital, Crosshouse, Ayrshire) To determine the nature and incidence of nodules in the distal duodenal bulb we undertook a prospective study in which nodularity was recorded and biopsy specimens taken during routine upper endoscopic examinations. Twenty one patients with duodenal bulb nodules were found (1-6%). The histology of these nodules was reviewed by a single pathologist and showed heterotopic gastric mucosa in six patients, normal mucosa in five, sub-totally villous atrophy in three, duodenitis in three, giardiasis in one, and lymphoid nodules in one. One of these biopsies showed evidence of chronic gastritis. The biopsy specimen was technically unsatisfactory. Brunner's gland hyperplasia was not found. The diagnosis of coeliac disease was suspected but not confirmed in any cases. The high proportion of the cases not confirmed by distal duodenal biopsy. The patient with giardiasis had non-specific abdominal pain and diarrhoea. No evidence of immunoglobulin deficiency was detected in any patient.

Duodenal nodules were found in 1-2% of routine upper endoscopic examinations and were most commonly caused by gastric heterotopia. Routine biopsy of these lesions showed the treatable disorders of coeliac disease and giardiasis in 19%. The association of nodules in the duodenal bulb and coeliac disease is not well recognised.

Plasma aluminium concentration and 24 hour urinary aluminium excretion before, during, and after six weeks of treatment with sucralfate

P MISTRY, Z VARGHESE, and R E POUNDER (Academic Department of Medicine and Department of Nephrology and Transplantation, Free Hospital School of Medicine, London NW3) Ten dyspeptic patients (six women, four men), median age 51 years (range 32-74 years), were treated with sucralfate 1 g qds for six weeks. Thirty day aluminium concentration and 24 hour urinary aluminium excretion were measured before, during treatment (3 and 6 weeks), and after treatment (+3, +6, +9, +12 weeks). All the subjects had normal plasma urea and creatinine. There was no statistical significance of differences was tested by the Wilcoxon rank sum test for paired data.

Before treatment the median plasma aluminium concentration was 6 μg/l; it rose significantly during treatment at three and six weeks (13 and 12 μg/l, respectively; p<0.05 and p<0.005); three to 12 weeks after treatment there was a non-significant rise in the plasma aluminium concentration compared to before treatment (11, 12, and 12 μg/l). The 24 hour urinary aluminium excretion before dosing was 20 μg/24 hours; it rose significantly during treatment at three and six weeks (71 and 78 μg/l; p<0.005 and p<0.005) and also three weeks after stopping treatment (52 μg/l; p<0.05). Six to 12 weeks after stopping treatment there was no significant difference compared to before treatment (26, 10, and 18 μg/24 h, respectively).

Routine treatment with sucralfate causes significant aluminium absorption.

Optimal therapy for Helicobacter pylori associated peptic ulcer disease

S PATCHETT, S BEATTIE, E LEE, C KEANE, and C O'MORAIN (Department of Gastroenterology, Meath/Adelaide Hospitals, Dublin 8, Ireland) Successful healing of acute peptic ulcer disease (PUD) can be achieved in over 80% of cases with a range of medical treatments. However, recurrence of peptic ulcers remains a common therapeutic problem, with over 80% of patients relapsing in one year when treated with a course of H2 antagonists. Recent evidence suggests that eradication of Helicobacter pylori from the gastric antrum can result in complete healing of PUD. Helicobacter pylori in the gastric antrum can lead to prolonged remission equivalent to that obtained with maintenance H2 antagonist treatment. To date, attempts to eradicate H pylori are successful in only 70% of cases. Thirty consecutive patients with endoscopically proved PUD, histologically proved chronic antral gastritis, and who had H pylori infection on culture and histology were treated with a combination of tetracycline 500 mg tid and metronidazole 400 mg tid for four weeks, metronidazole 400 mg tid and tetracycline 500 mg tid for one week. All patients were endoscoped at entry, and four weeks after stopping treatment to check for ulcer healing and in the case of eradication. At each endoscopy two antral biopsy specimens were taken and assessed histologically and microbiologically for evidence of H pylori infection. Of 30 patients, 27 experienced complete healing of...
their peptic ulcers (90%). Gastritis improved significantly or was completely healed in 26 patients. Eradication of H pylori was achieved also in 27 patients (90%). Of the three patients that failed to heal, two were H pylori positive at eight weeks follow up and one was H pylori negative.

The eradication rate of 90% seen with this short term triple therapy regimen compares favourably with H2 antagonist treatment. No significant side effects were reported. This is of particular significance as only 10% of these patients would be expected to relapse in the following year.

Excess of DNA adducts in the forget of patients with familial adenomatous polyposis

A D SPIEGELMAN,1 D K SCATES,2 S VENTITI,2 AND R K S PHELPS1 (St Mark’s Hospital and Professorial Surgical Unit, St Bartholomew’s Hospital, London and Institute of Cancer Research, Royal Marsden Hospital, Surrey) Recent studies in Caenorhabditis elegans – for example, carcinogens – may damage DNA by forming adducts. In patients with familial adenomatous polyposis (FAP), DNA adducts might restrain tumour growth by causing loss, inactivation, or mutation of the FAP tumour suppressor gene. To test whether FAP mucosa contains an excess of DNA adducts we measured duodenal DNA adduct levels by 32P-postlabelling in 51 FAP patients and 30 controls. More FAP patients (49/51) than controls (24/30) had duodenal DNA adducts (p=0.027 Fisher’s exact test) and relative adduct labelling (RAL: adducts/10 nucleotides) was higher in FAP patients than controls (medians, ranges: 15, 0–162; 7.5, 0–40; p=0.0002, Mann-Whitney U test). Because duodenal tumours are more common than gastric tumours in FAP, we measured RAL levels in paired biopsy specimens from 31 FAP patients. Duodenal RAL was higher than gastric (medians, ranges: 15, 0–109; 8, 0–40; p=0.0003 (Mann-Whitney U test). Our findings are consistent with DNA adduct induced dysplasia/neoplasia; identification of the source and identity of critical adducts could help combat forget tumour development.

Omeprozole but not cimetidine markedly inhibits pepsin secretion in patients with refractory duodenal ulcer

M J ROGERS, J N PRIMROSE, N CARROLL, AND M J DALY (University Department of Surgery, The General Infirmary, Leeds and Astra Clinical Research Unit, Edinburgh, UK) One tenth of patients with duodenal ulcer (DU) suffer refractory ulceration (RDU) which remains unhealed despite three months’ treatment with H2 antagonists. We compared the clinical and pharmacological effects of the proton-pump blocker omeprozole 40 mg (OMEP) and cimetidine HCl (CIM) in patients with RDU and consistent acid hypersecretion.

Duodenal RAL was higher than gastric (medians, ranges: 15, 0–109; 8, 0–40; p=0.0003 (Mann-Whitney U test). Our findings are consistent with DNA adduct induced dysplasia/neoplasia; identification of the source and identity of critical adducts could help combat forget tumour development.

Mucosal iron uptake by duodenal biopsies from patients with primary haemochromatosis and chronic alcoholic patients with secondary iron overload

P D DUANE AND J T PETERS* (Department of Medicine, St James’s University Hospital, Leeds and Division of Clinical Cell Biology, MRC Clinical Research Centre, Harrow, Middlesex) Duodenal Fe uptake in control subjects (nine), patients with primary haemochromatosis (six) (PH), and chronic alcoholic patients with secondary iron overload (10) was measured by incubating biopsy samples in a physiological HEPEs buffer, pH 7.4, containing an Fe-acorbate chelate (Fe concentration range of 18–450 μM) and 51Fe. The amount of absorbed Fe was determined in a scintillation fluid marker. Kinetic parameters, Km and Vmax, were calculated from the uptake data.

Iron uptake showed saturation kinetics in control subjects and patients with PH. The Vmax in PH (9.1 (0.7) mean (SEM), pmol/min per mg) was similar to that in the controls (9.0 (0.8)), whereas the Km in PH (54.2 (9.3) μM) was significantly lower than that in controls (119 (19)), p<0.05. Iron uptake in the ALC group failed to show saturation kinetics. Cyanocobalamin uptake in ALC (0.129 (0.01) μL/mg tissue) was significantly higher than in controls (0.073 (0.010)), p<0.01.

Higher affinity by the duodenal mucosa for iron may be a factor in iron overload in primary haemochromatosis. In contrast, increased passive uptake of iron may explain iron overload in chronic alcoholism.

The effect of vagotomy on cytokinetics in duodenal ulcer

R H K GOMPertz, R A GOODLAD, J H BARON, R C N WILLIAMSON, AND A MICHALOWSKI* (Hammersmith Hospital and MRC Cyclotron Unit, London W12 ONN) Chronic duodenal ulcer can be induced in mice as an indirect effect of lower mediastinal irradiation, the resulting ulcers resembling those seen in humans (the abscopal ulcer model). Previous studies have shown significant changes in cell kinetics. Using a single nucleoside technique we have studied crypt cell production rate (CCPR) in 72 female CFLP mice weighing 25–40 g randomly allocated to one of six groups. Animals received a single dose of 18 Gy 250 Kv x rays to either the upper mediastinum (which causes ulceration; irradiation control) or to the lower mediastinum (which induces ulcers in 45% in seven days; ulcer group) followed, on the first postirradiation day, by anaesthesia, vagotomy, or sham vagotomy (a phantom procedure) and sham vagotomy, by a non-specific effect, inhibits ulceration. Studies were performed at day 4 after irradiation. Animals anaesthetised only showed a difference in CCPR between ulcer and control animals but there was marked variability in CCPR in the ulcer group, suggesting that the proliferative response was being focused to the area of future ulceration. Both operated groups showed significantly higher proliferation rates in the ulcer animals than the irradiation controls (14.5 ± 6.1 cells/crypt/10000, p<0.04 Anova). Vagotomy and sham vagotomy, which both inhibit ulcer formation in the short term, cause a prolonged proliferative response in the proximal duodenum of ulcer group animals. These results suggest that, in addition to reducing acid-pepsin attack, vagotomy may enhance duodenal mucosal defence.

Highly selective vagotomy for duodenal ulcer: cumulative ulcer related mortality during the first 20 years

I G MARTIN AND D JOHNSTON (University Department of Surgery, The General Infirmary, Leeds) Highly selective vagotomy (HSV) has the lowest operative mortality of any operation for duodenal ulcer (DU) and in the short term is very safe. However, there have recently been disturbing reports of recurrence of duodenal ulceration (RU) after HSV, raising the question of the long term safety of this procedure. Consequently we have reviewed both our own cumulative ulcer related mortality after HSV for DU and compared it to that reported in the literature.

Between 1969 and 1989, 730 patients underwent elective HSV for DU with one operative death (0.14%); 74 patients (10%) have developed RU but there was no subsequent ulcer related mortality: the cumulative ulcer related mortality was therefore 1 death per 3502 patient years of follow up. A review of the literature was undertaken and 17 papers found with sufficient detail to compare our cumulative ulcer related mortality; 3342 patients underwent HSV for DU with four operative deaths (0.12%); 409 (12%) patients developed recurrent ulceration with one ulcer related death (3%). Cumulative ulcer related mortality was 1 death per 3398 patient years of follow up.

HSV has shown itself to be safe in both the short and long term. We suggest that these figures for ulcer related mortality be a standard by which the safety of long term medical treatment can be judged.

Intraoperative testing for completeness of vagotomy: a role in the 1990s?

I G MARTIN, M J ROGERS, J N PRIMROSE, R L BLACKETT, AND D JOHNSTON (University Department of Surgery, The General Infirmary, Leeds)

With decreasing numbers of patients presenting for elective duodenal ulcer (DU) surgery, fewer surgeons in training are performing sufficient vagotomies to ensure proficiency. Intraoperative testing for completeness of vagotomy using the Grassi test (GT) may help in ascertaining both whether and where a vagotomy has been carried out.

We evaluated the GT in 67 patients who underwent elective highly selective vagotomy (HSV) for DU (49 M, 18 F, median age 42 years). Each underwent standard HSV followed by the GT. If positive (pH<3 in any area), rediagnosis was attempted. The cycle of rediagnosis and testing was repeated until the test was negative or the surgeon could find no further vagal fibres. A negative GT was not obtained in 34 patients (51%). Positive tests were associated with higher mean PAO2 before operation (45.2 ± 5.1 mmol/L, p=0.07). Only in finding fundal vagal fibres
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was the test regularly successful. There was a poor correlation between the GT and reductions in PAOp one week after operation (62% ± 69% NS) or the insulin test (PAO 0.23 ± 0.74 mmol/h NS). Ten of 67 patients (14.9%) developed recurrent urlection (RU) after a median of five years. With a positive GT six times of 34 (17.6%) developed RU and four of 33 (12.1%) with a negative GT (NS).

The GT was of limited use in the achieve ment of complete vagotomy; a negative test was obtained in just 49% of patients. Routine use of the GT to help surgeons in training cannot be recommended.

PANCREAS POSTERS

Tropical v ethanol induced chronic pancreatitis in South India–Madras

S CHARI, V MOHAN, Y JAYANTHI (INTRODUCED BY DR J F MAYBERRY), C SNEHALATHA, S MALATHI, M VISWANATHAN, AND N MADANAGOPALAN (Kilpauk Medical College and Hospital; Diabetes Research Centre and MV Hospital for Diabetes, Chennai) In a unique population based study 253 patients with tropical chronic pancreatitis (TCP) were compared with 52 patients with alcoholic chronic pancreatitis (ACP) seen over the previous six years at two centres. TCP patients were teetotalers, whose mean age at onset was 32.6 (11.9) years. Their mean duration of symptoms was 8 (1-73) years. ACP patients gave a history of prolonged heavy alcohol abuse (132 (67) g/day) over 16 (6-2) years; they were significantly older (mean age 42.9 (7-6) years, p<0.005) and had a shorter duration of symptoms (4 (1-3) years, p<0.005). Over 85% of patients in both groups had calcific pancreatitis. In TCP there was large (>10 mm) dense, discrete calculi, while in ACP calculi were small and speckled and had hazy margins. The frequency of pain, diabetes, and exocrine pancreatic insufficiency was similar in both groups. Most patients were lean (median body mass index 18.7 kg/m² and 18.1 kg/m²) but only 25% showed overt malnutrition. Thus TCP and ACP have distinct clinical profiles. With ACP the West, our patients developed TCP very quickly and within a short time of onset of symptoms. This could be due to environmental influences such as the indigenous forms of alcohol, arrack and toddy.

Inhibitory effect of the CCK antagonist CR-1409 on pancreatic growth after pancreateo-biliary diversion

P WATANAPA, E F EFA, R BEARDSHILL, J CALAM, M R ALISON, AND R C N WILLIAMSON (Departments of Surgery, Medicine and Histology, Hadassah Medical School, Royal Postgraduate Medical School, London W12 0NN) Pancreateo-biliary diversion (PBD) stimulates pancreatic growth, presumably by increasing cholecystokinin (CCK) secretion. We have therefore tested the CCK antagonist CR-1409 on the adaptive response to PBD. Male Wistar rats (n=108) weighing 200-225 g were randomised to receive either PBD (n=60) or triple small bowel transection and resuture (control, n=48). Half the rats in each group were further randomised to receive saline or CR-1409. Rats were killed 4, 7, or 14 days postoperatively, when blood was obtained for CCK assay and the pancreas was assessed for proliferative rate by three parameters: nucleic acid and protein content, bromodeoxyuridine (BrdU) labelling index, and metaphase arrest after vincristine (1 mg/kg ip) administration. PBD increased plasma CCK concentrations 91% at seven days and 137% at 14 days, irrespective of CR-1409 treatment. Total pancreatic RNA content was doubled at four days (2.15 ± 1.07 mg/100 g body weight: p<0.001) and at seven days (2.75 ± 1.07 mg/100 g: p<0.001), and trebled at 14 days (4.77 ± 1.32 mg/100 g: p<0.001); increments in DNA were not significant. PBD increased BrdU labelling index from 0.25 to 3.7% and mitotic index (after vincristine) from 0 to 0.6% at 14 days. CR-1409 completely abolished this proliferative response and also prevented the rise in DNA. This results confirm pancreatic hypertrophy and increased acinar cell mass following PBD. CR-1409 prevents this adaptive growth, probably by blocking CCK receptors.

Vitamin C deficiency: key risk factor for calcifying chronic pancreatitis in temperate and tropical zones?

P M KAY, D SCHOFIELD, D BILTON, C SNEHALATHA, *V MOHAN, *AND J M BRAGANZA (Department of Gastroenterology, Manchester Royal Infirmary, UK and MV Hospital for Diabetes, *Madras, India) The finding of oxidative stress in patients with calcifying chronic pancreatitis (CP) in temperate zones suggested that the much higher incidence of the disease, and propensity to calcify, in tropical zones may be due to dietary micronutrient deficiency, but previous studies did not support this theory with regard to selenium, β carotene, and vitamin E. The bioactive form of vitamin C, ascorbic acid (AA), is essential for refurbishing glutathione after its oxidation during xenobiotic metabolism. Therefore, plasma AA concentra tions were measured by high performance liquid chromatography. Causoid CP patients had significantly lower concentrations than controls (median and range 5-6, 0-6-12.7 and 13-5, 7-4-11.6 mg/100 g: p<0.001), and those with pancreatic calculi had negligible values. In Dravidian controls and patients (all with calculi), levels of AA were very low: 5-7, 0-11-8 and 2-8, <0-05. The data suggest that low bioavailability of vitamin C may be the key factor in promoting CP in tropical zones (when antioxidant demand increases upon chronic exposure to xenobiotics – for example, cyanogenic staples); and in facilitating pancreatic cell calcification irrespective of geography.

Is severe acute pancreatitis associated with excessive stimulation of neutrophils and macrophages?

D J ALEXANDER, R E BANKS, S W EVANS, J T WHICHER, AND M J MCMANON (University Departments of Surgery and Chemical Pathology, The General Infirmary, Leeds LS1 3EX, UK) It has been suggested that fatal acute pancreatitis (AP) results from excessive stimulus-secretion coupling in leucocytes. This hypothe sis was tested in 27 patients with AP measuring daily levels of tumour necrosis factor alpha (TNF-α) and elastase–α1-proteinase inhibitor (E-α1 PI) as markers of activity of macrophages and neutrophils respectively. TNF-α was measured using an immunoradiometric assay and E-α1 PI by a specifically developed ELISA assay. In 19 patients the AP was classified as mild and eight patients had a severe attack. Patients were studied for eight days. TNF-α levels were not raised in either the severe or mild group. E-α1 PI levels were greatly raised in both groups, and significantly more so in severe compared with mild attacks on three days (p<0.05).

These results suggest that neutrophils are activated during both severe and mild AP. This was no evidence that macrophages were activated in severe AP. Further work is needed to determine whether TNF-α and E-α1 PI are useful markers for assessing severity of AP.

Serum amylase estimation in the diagnosis of acute pancreatitis

M C WINSLET, C HALL, N LONDON, AND J P NEOPTOLEMOS (Academic Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH) The diagnosis of acute pancreatitis (AP) is usually based on a serum amylase level >1000 IU/L, although when alcohol is causative even hyperamylasemia may be an unnecessary provocation. The response of serum amylase to acute pancreatitis was assessed using the Phadebas method (n=300) and its relation to symptom duration, aetiology, and Ranson prognostic score was prospectively assessed in 422 patients with AP (biliary=295; alcohol=117; idiopathic=10) presenting within 24 hours of symptom onset.

Of patients with mild biliary pancreatitis (BP) (n=195), 99.4% had diagnostic amylase levels on presentation compared to 94% in the severe group (n=100). In alcoholic pancreatitis (AlCP) 83% of patients with mild criteria (n=107) had diagnostic amylase levels compared to 80% in the severe group (n=10). The incidence of diagnostic amylase levels was significantly increased in mild BP compared to AlCP (75.4% v 52.0%, p<0.05) and in all P mild compared to all P severe (52.0% v 85.7%, p<0.05) at 24 hours post presentation. Patients with idiopathic disease had diagnostic levels at presentation regardless of severity. Overall, at presentation 0.9% had normoamylasaemia and 5.5% had hyperamylasaemia with AP confirmed by urinary amylase, serum lipase, and computed tomography.

Non-diagnostic amylase levels are uncommon in patients with an alcoholic aetiology and a mild prognostic score. Nevertheless hyper- or normoamylasaemia is rare in patients with AP and should be interpreted in relation to symptom duration.

Cholecystokinin (CCK) bioassay: a simplified method of producing functioning isolated pancreatic acini

I S BAILEY AND C D JOHNSON (University Surgical Unit, F Level, Centre Block, Southampton General Hospital, Southampton) Radioimmuno assay for CCK has proved difficult. A sensitive bioassay using amylase release from isolated rat pancreatic acini has been described. However, this method is cumbersome and the long pre incubation time reduces acinar sensitivity. We have developed and tested a simplified. method of producing pancreatic acini. CCK and collagenase are injected into the pancreas of hooded litter rats (n=6) via the bile duct. The pancreas is removed and incubated for 45
minutes. Acini obtained by gentle disaggregation and filtration are washed and preincubated for a maximum of 10 minutes. Acini are incubated in 1 ml aliquots with test samples of CCK 8 and amylase release measured. Each pancreas produces sufficient acini for 40 samples. Median basal amylase release is 2.5% (1-6-3-3%) of total amylase content. A significant increase in amylase release (>basal +2 SD) is unlikely to be attributable to the number of acini. An incremental dose response occurs in all preparations with a mean 4-6-fold increase in amylase release between 2.5 pM and 40 pM CCK 8. Intra-assay coefficient of variation is 9-1 at 2.5 pM CCK 8, 10-7 (10 pM), 7-3 (40 pM).

These acini respond in a dose dependent manner in the range of plasma CCK concentration and may be used for bioassay of CCK in plasma.

Severity assessment of acute pancreatitis using the Hong Kong Model: is it applicable to patients within the UK?

D I HEATH AND C W IMrie (Royal Infirmary, Glasgow) In Hong Kong a blood glucose (BS) >11 mmol/l or urea (U) >7-4 mmol/l, or both, on admission predicts a severe attack of acute pancreatitis with a sensitivity of 75% and a specificity of 80-3%. We have prospectively evaluated these criteria in 122 patients with acute pancreatitis (94 mild and 28 severe attacks) treated in the United Kingdom. The median concentrations of U and BS on admission were 5-5 mmol/l (range 2-1 to 20-7 mmol/l) and 7-9 mmol/l (range 4-3 to 26-4 mmol/l) for the severe group and 4-7 mmol/l (range 1-9 to 15-9 mmol/l and 6-8 mmol/l (range 3-5 to 16-2 mmol/l) for the mild group. The Hong Kong criteria predicted severe attacks with a sensitivity of 33% and a specificity of 85%. Utilising a 'cut off' value of >4-9 mmol/l for U and >7-5 mmol/l for BS gave a sensitivity and specificity of 81% and 34% on admission and 65% and 77% for peak concentrations during the first 48 hours. They were equally valid for mild and severe pancreatitis and sufficiently sensitive to be of use as severity predictors in our study population, while peak values entailed a similar delay too, but had poorer sensitivity and specificity than the Glasgow scoring system (sensitivity of 78% and specificity of 86%).

The role of prophylactic gastroenterostomy (GE) in the surgical management of primary malignant low bile duct obstruction

A C SMITH, J F DOWSETT, A R W HATFIELD, AND R G C RUSSELL (Departments of Gastroenterology and Surgery, The Middlesex Hospital, Mortimer Street, London W1N 8AA) The surgical mortality rates (46 M, 57 F, median age 70 years (range 42-86)) with unselectable primary malignant low bile duct obstruction and no duodenal obstruction randomised to the palliative surgical arm of a multicentre prospective trial was examined to determine the role of prophylactic GE. Biliary bypass (27 using the gall bladder, 69 the common bile duct) was achieved in 96% (93%) and successful drainage in 95% (92%). Prophylactic GE was undertaken in 46, of whom 17 (37%) suffered major complications including gastric stasis (seven), gastrointestinal bleeding (six), pneumonia (six), renal failure (four), bile leak (three), sepsis (two), and wound leak (one), while in the 53 patients without gastric drainage serious complications were recorded in only 10 (18%, p<0.05). There was no significant difference in the 30 day mortality in the two groups (no GE=6/53 11%; GE=7/46 15%). Preadmission hospital stay (median 17 days) was identical in both groups. Subsequent duodenal obstruction developed in 10 of 53 (19%) patients who did not undergo initial GE, but only four (7%) required late drainage and the remaining six settled with conservative treatment. However, total hospital stay (THS) was similar (GE, median THS 26 days; no GE, median THS 25 5 days). There was a trend to longer survival in patients without prophylactic GE (no GE, median survival 26 weeks; GE, survival 18 weeks, p=0.08).

(1) Prophylactic GE is associated with a significant increase in major complications but not in 30 day or procedure-related mortality.

(2) Prophylactic GE is probably not indicated as only 7% require subsequent GE.

Meal-stimulated gut peptides after total pancreatectomy

R H K GOMPERTZ, G J POSTON, M CHATEL, S R BLOOR, AND R C N WILLIAMSON (Hammermill Hospital, Duke of York Road, London W12 ONN) The pancreatic response to food is an integral part of the digestive process. Total pancreatectomy inevitably leads to diabetes and loss of exocrine function. The pancreatic polypeptide profile (both basal and stimulated) is unknown. None patients with total pancreatectomy underwent three months to five years preoperatively were compared to seven healthy controls matched for age and sex. After an overnight fast, two basal blood samples were obtained, a standard breakfast was eaten, and further samples were taken at intervals for four hours. Plasma was frozen at -70°C for subsequent assay of vasoactive intestinal polypeptide (VIP), gastrin, pancreatic polypeptide (PP), glucagon-like peptide (GLP), cholecystokinin (CCK), pancreatic glucagon (PG), and somatostatin (S). The results were compared to THS. GE=6/53 (68 9) was significantly older (p<0.007) than the mean age of the 1969-64 patients. At all sites there was an increase in the proportion of well and moderately differentiated tumours in the latter series. For the antrum, the proportion of moderately and poorly differentiated tumours decreased, whereas they increased in the cardia. For the 1984-88 series, male sex and smoking, but not alcohol, were associated with tumours of the cardia, but reliable data are not available for the earlier series.

MRC Surgical Trial for Gastric Cancer: interim pathology results

I C TALBOT, P M FAYERS, J L CRAVEN, J W L FIELDING, P F M WRIGHT, A CUSCHIERI, AND MEMBERS OF THE COOPERATIVE GROUP OF THE MRc SURGICAL TRIAL FOR GASTRIC CANCER (Department of Pathology, St Mark's Hospital, London EC1V 2PS) This trial was established in 1984 to see if radical surgery for gastric cancer could lead to survival figures comparable to the excellent results of Japanese workers. In the five and a half years since the start of recruitment 246 patients have been randomised out of 473 with gastric cancer of whom 98% have undergone at least D2 resection and 90% have had surgery for local recurrence. The group of patients with cancer of the cardia and cardioesophageal junction has been excluded. Of the remaining 601 patients, 500 are currently undergoing treatment and 101 have died of gastric cancer.

The histology of 206 cases has been examined and shows invasion to the serosa or subserosa in 62%, compared with the opinion of the surgeon at operation that there was definite or suspected serosal involvement in 64%. Surprisingly, 21% of tumours are T1 (early gastric cancer). Sixty five per cent of tumours are Lauren intestinal type and 19% are diffuse. The data concerning node status and patient survival are incomplete at present. These preliminary findings confirm a close similarity to histological tumour types in other series but show a high proportion of early gastric cancers.

GI Cancer

Changing patterns of gastric cancer in Oxfordshire

E RIOS-CASTELLANOS, F SITAS, AND D P JEWELL (Gastroenterology Unit and ICRF, The Radcliffe Infirmary, Woodstock Road, Oxford, UK) The incidence of gastric cancer in Oxfordshire has been determined for two five-year periods. Tumours occurring between 1960-64 (n=215) and 1984-88 (n=200) were compared with respect to site, histological characteristics, and age and sex of the patient. The population at risk was obtained from the Oxford Record Linkage Study in order to calculate incidence rates. The incidence of gastric cancer in this normal population showed a steady increase from 100/100,000 in the 1960s to 150/100,000 in the 1980s. When analysed by site, there was a marked fall in the incidence of antral tumours (from 10 to 4-5/100,000), whereas the incidence of body and cardia tumours increased (from 3-3 to 6-5 and 2-8 to 5-0 respectively). These changes were particularly seen in men between 45 and 64 years of age. The mean age of the 1984-88 series (68-9) was significantly older (p<0.007) than the mean age of the 1960-64 patients. At all sites there was an increase in the proportion of well and moderately differentiated tumours in the later series. For the antrum, the proportion of moderately and poorly differentiated tumours decreased, whereas they increased in the cardia.

The 1984-88 series, male sex and smoking, but not alcohol, were associated with tumours of the cardia, but reliable data are not available for the earlier series.

Bile reflux and gastric adenomas in patients with familial adenomatous polyposis (FAP)

A D SPIEGELMAN, M GRANOWSKA, AND R K S PHILLIPS (St Mark's Hospital, London and Professional Surgical Unit, St Bartholomew's Hospital, London) Gastric adenomas occur in less than 10% of FAP patients, whereas duodenal adenomas occur in nearly all FAP patients. Furthermore, duodenal polyps cluster around the ampulla of Vater. To test
whether the presence of gastric adenomas was associated with reflux of duodenal contents, seven FAP patients with gastric adenomas and nine age and sex matched FAP patients without gastric adenomas underwent scintigraphic duodenogastric reflux scanning. Reflux was graded: 0 = no reflux, 1 = reflux into stomach only, 2 = into body, 3 = body and fundus; a = intermittent, b = prolonged). FAP patients with gastric adenomas had more severe reflux (median 3b, range 0–3b) than did controls (median 2a, range 0–2b; p = 0.035, Mann-Whitney U test).

These results are consistent with a role for bile in the differentiation of hyperplastic gastric polyps into adenomas, and suggest that gastro-enteroscopy might be affected by the development of measures to reduce duodenogastric reflux.

Nurse endoscopists (NE) can safely and accurately screen asymptomatic patients for colon cancer using flexible sigmoidoscopy (FS): results from 2200 examinations

W F MAULE (INTRODUCED BY DR C WILLIAMS) (Ochsner Clinic of Baton Rouge, Baton Rouge, Louisiana 70816) Two nurses learnt FS using a 60 Park Esophoscope. Instrument and lesion recognition was taught by didactic sessions, 35 mm slide review, and observation of a gastroenterologist (GE). Each nurse performed 67 examinations under the supervision of the GE. After completion of training 2007 screening examinations were independently performed by an NE. Patients were asymptomatic with negative faecal occult bloods. The examination was recorded on videotape and reviewed by the GE. All polyps <2 mm in diameter were biopsied.

Mean insertion depth achieved by NE (42 cm) was similar to that achieved by GE (46 cm) in a comparable group of 1200 patients. The frequency of examinations positive for at least one adenoma/carcinoma was also similar (NE 5.4% and 0.3%; GE 4.2% and 0–4%); 96% of neoplasms (177/185) were found within 40 cm of the anal verge. By 1 June 1990, 159 patients with at least one positive examination had undergone colonoscopy; 16% had additional proximal adenomas and 2% carcinomas. No complications occurred after sigmoidoscopy by NE and no ‘missed lesions’ were seen at video tape review.

Colon cancer screening by flexible sigmoidoscopy can be effectively and safely performed by nurses after appropriate training.

The significance of small colonic polyps found at flexible sigmoidoscopy

T ROKKAS, A KARAMERIS, AND G MIKOS (Departments of Gastroenterology and Histopathology, 401 Army General Hospital, Athens, Greece) During the past 18 months we performed flexible sigmoidoscopy on 900 patients. Sixty-three (7%) had one or more polyps in the rectosigmoid. Exclusion criteria were polyps of >1 cm in size, history of bleeding, inflammatory bowel disease, or past polypectomy. After excluding 18 patients, 459/900 (51%) with small polyps remained in the study. All these patients were submitted to total colonoscopy and biopsy of all polyps found. Histopathology showed that 27/45 (60%) patients had hyperplastic polyps and 18/45 (40%) had at least one adenomatous polyp. Among the 27 patients with hyperplastic polyps at flexible sigmoidoscopy, five (18.5%) had a more proximal hyperplastic polyp and nine (33.3%) had a more proximal adenomatous polyp. Three out of the 18 patients (16.6%) who had at least one adenomatous polyp in the rectosigmoid were found to have them more proximally. We conclude that a) size alone is not a good predictor of the histology of the polyp, b) because small polyps, either hyperplastic or adenomatous, in the rectosigmoid indicate a risk for adenomatous polyps proximally, all patients with small polyps found during flexible sigmoidoscopy should be submitted for total colonoscopy.

SMALL INTESTINE INFLAMMATION

Increased intestinal permeability in ankylosing spondylitis – drug effect or primary abnormality

A J MORRIS, C W HOWDEN, C ROBERTSON, A DUNCAN, H TOLLEY, R D STURROCK, AND R I RUSSELL (Gastroenterology Unit and Centre for Rheumatic Diseases, Royal Infirmary, Glasgow G31 2ER) We have shown that ankylosing spondylitis (AS) is associated with increased intestinal permeability (median 0.094, range 0.06–0.13) in patients with ankylosing spondylitis (AS; n = 12) and compared this with normal controls (C; n = 13). After an overnight fast, patients and controls were given a drink containing 100 μC (3.7 MBq) of 51Cr-EDTA. Urine was collected for 0–6 hours and 6–24 hours in separate containers. Patients had blood withdrawn for C-reactive protein, haemoglobin, erythrocyte sedimentation rate, and platelet count. Median (range) percentage of 51Cr-EDTA recovered in urine was 0.35 (0.09–0.54) over 0–6 hours and 1.23 (0.4–3.21) over 6–24 hours in C and 0.61 (0.15–1.29) over 0–6 hours and 1.31 (0.3–2.28) over 6–24 hours in AS. There was significantly increased intestinal permeability in the AS group compared with controls during the 0–6 hour period; p = 0.004 (Wilcoxon ranked sum test) but not during the 6–24 hour period; p = 0.54. Using correlation and linear regression the haematological and biochemical markers were compared with recovery of 51Cr-EDTA. There was no significant correlation with haemoglobin (r = –0.14, p = 0.73), ESR (r = 0.33, p = 0.07), platelets (r = 0.24, p = 0.442), or white blood count (r = 0.51, p = 0.08).

These results show increased small intestinal permeability in AS. This permeability is independent of disease activity as judged by the blood parameters. The increased permeability may be due to increased intestinal anti-inflammatory drugs, but an underlying intrinsic small bowel lesion cannot be excluded.

Small bowel ulceration in rheumatoid arthritis patients on non-steroidal anti-inflammatory drugs – an enteroscopic study

J MORRIS, R MADHOK, R D STURROCK, H A CAPPELL, AND J F MACKENZIE (Gastrointestinal Investigation Unit and Centre for Rheumatic Diseases, Royal Infirmary, Glasgow G4 0SF, Scotland) Recent case reports indicate that small bowel ulceration may complicate treatment with non-steroidal anti-inflammatory drugs (NSAIDs). Radioisotopic studies estimate that small bowel damage occurs in around 70% of patients on long-term NSAIDs.

We have examined the small bowel enteroscopically in 18 rheumatoid arthritis (RA) patients with unexplained iron deficiency anaemia. All had normal upper gastrointestinal endoscopy. Colonoscopic investigation was also normal in all 12 patients so examined. Small bowel enteroscopy was performed with Sonde instrument, 2.7 in long and 5 mm in diameter, allowing endoscopic examination of the small bowel mucosa to the distal ileum. Enteroscopy succeeded in 16 patients, the endoscope reaching a median 173 cm (range 100–250 cm) from the nares. Abnormalities were seen in 11 patients (64%), with erosions with red-spot lesions in three, and red-spot lesions alone in three. Enteroscopy was normal in five patients. The procedure failed in two patients.

This is the first report of endoscopically visualised haemorrhagic small bowel lesions in RA patients with iron deficiency anaemia. Small bowel enteroscopy is useful in detecting potential sources of blood loss from the small bowel.

NSAID enteropathy; the main site of chronic blood loss in patients on NSAID

J BARNASON, P SMETHURST, J HAYLLAR, AND A J LEVI (MRC Clinical Research Centre and Northwick Park Hospital, Watford, Middlesex HA1 3UJ) Seventy per cent of patients on long-term non-steroidal anti-inflammatory drugs (NSAIDs) develop small intestinal inflammation and it has been suggested that they bleed as a consequence. The role of the gastroduodenal mucosa in the gastrointestinal bleeding of patients on NSAIDs is uncertain. Thirty eight patients on NSAIDs (>6 months) underwent simultaneous study with indium-111 labelled red blood cells and chromium-51 labelled red cells to quantify intestinal inflammation and blood loss respectively. Endoscopy was performed and the gastroduodenal damage assessed macroscopically (LANZA grade) and microscopically (two biopsy specimens from duodenum, antrum, and body). Twenty four (62%) had NSAID enteropathy. The faecal excretion of indium-111 (range 0.1–1.6%; N = 15% correlated significantly (N = 56; p = 0.01) with the mean daily blood loss (range 0.05–10.1 ml/day). Inflammation and blood loss did not correlate significantly with LANZA grade or the microscopic findings.

The small intestine seems to be the main site of chronic blood loss in patients with NSAID enteropathy contributing to the iron deficiency which is so common in rheumatoid arthritis.

Direct in vitro infection of human small intestine and colon with HIV-1

S C FLEMING, M S KAPEMBWA, AND G E GRIFFIN (Division of Communicable Diseases, St George's Hospital Medical School, Cramer Terrace, London SW17 0RE) Direct infection of the intestine by human immunodeficiency virus (HIV-1) has been postulated but not shown. In an effort to directly infect human intestinal cells, we have exposed fetal intestinal explants...
to HIV-1 and monitored infection by immuno-
histochemistry (IHC), in situ hybridization (ISH), and biochemical assay. Human fetal (16-20 weeks) intestinal explants (2 mm) maintained in culture were exposed to DEAE-dextran 25 µg/ml for 60 min, washed and incubated with HIV-1 (strains RF or RUT) at 10° tissue culture infectious doses, for 2 hr. After thorough washing, explants were maintained in culture. Tissue culture fluid (TCF) and explants were snap frozen on days 4, 7, 10, and 14 (P36, and 21) and co-cultured with Jurkat T-cells to detect infectious virus particles. Reverse transcriptase (RT) activity and p24Ag levels were assayed in TCF. IHC staining for HIV proteins (p24 and gp41) and ISH for viral RNA were performed on 8 µm frozen sections. RT and p24Ag levels in TCF rose between days 7 and 14. Jurkat cells cultured confirmed the presence of infectious virus. Lamin prepa (LP) cells resembling macrophages or lymphocytes of non-specific nature and the colon stained positively (IHC) for p24 and gp41. Similar LP cells positively stained for viral RNA using ISH. Epithelial cells showed no evidence of HIV-1 infection at any time.

Cells of the small intestine and colon can be directly infected by and support the replication of HIV-1, and this may be important in the pathogenesis of HIV related enteropathy.

Reversal of intestinal secretion by polymeric oral rehydration solutions (ORS) in a model of human cholera

A V THELLIANAYAGAM, F H MOUARD, J A DIAS, S CARNABY, M L CLARK, AND M J G FARTHING (Department of Gastroenterology, St Thomas' Hospital, London EC1A 7BE) We have shown in an animal model that ORS containing polymeric glucose as substrate (P-ORS) promote greater water absorption than equivalent monomer-ORS, resembling human ORS, and that the major determinant to study this in humans, eight healthy subjects underwent triple-lumen jejunal perfusion (with and without pretreatment with 15 µg cholera toxin) comparing two P-ORS (P36 and P34 (mOsm/mml); mean length G5) with a monomer ORS (G90 mmol/l) of identical electrolyte composition (Na 60, K 20, Cl 60, citrate 10 mmol/l). In normal intestine, water absorption was greater from G90 than either of the P-ORS (p<0.05), while in secreting jejunum, P36 (186 mOsm/kg) promoted greater water absorption than G90 (240 mOsm/kg) (4.9 median, 3-9-6.5 ml/cm per hr, p<0.03). Glucose absorption was greater from P36 (1.0, 2-7-1.5 mmol/cm per hr) than from G90 (0.8, 0.2-0.9, p=0.03). P36-ORS reversed the secretory state to 89% of that in normal jejunum compared to 76% by G90 (p<0.03). These results show that P-ORS unlike G-ORS can return water absorption in secreting intestine almost to normal, presumably due to a combination of hypo-osmotic and increased glucose absorption. This probably explains the dramatic clinical benefit of complex carbohydrate-containing ORS in reducing stool volume in acute diarrhoea.

The effect of SHT3 receptor antagonist on the ileal brake mechanism in the rat

N J BROWN, R D RUMSEY, AND N W READ (Sub-Department of Gastrointestinal Physiology and Nutrition, University of Sheffield, Western Bank, S10 2TN) It has recently been shown that delayed gastric emptying produced by lipid can be reversed by SHT3 antagonists. We have shown that ileal infusion of lipid delays small intestinal transit in both humans and rats – the ileal brake. The aim of the study was to investigate whether SHT3 receptors are involved in mediating the ileal brake in the rat. Seven rats were equipped with ileal cannulas 20 cm proximal to the ileocecal valve. Fasted animals were infused with saline or Intralipid into the ileum (0-3 ml/hr) for 30 min before gavageing with the meal. Rats were then placed in peripex chambers, the infusion continued for 160 minutes and the hydrogen concentration monitored throughout the experiment to obtain stomach to cecum transit time of the ileal break (SCCT). The effect on SCCT of the meal of the SHT3 antagonist Granisetron (40 µg/kg sc) injected 30 minutes before the ileal infusion, was investigated. Ileal SCCT significantly delayed SCCT of the meal compared to ileal saline (Intralipid v saline; mean (SE) 181.7 (3.1) 115.3 (3); n7; p<0.001). Granisetron significantly delayed SCCT of the meal (Granisetron/saline v saline/saline; mean (SE) 160.10 (115.3) 7; p<0.05), but reversed the Intralipid delayed SCCT of the meal (Granisetron/Intralipid v saline/ Intralipid; 80.2 (6) 181.7 (3.1); n7; p<0.001). These results show that SHT3 receptors stimulate gastrointestinal motility, and they may be involved in mediating the ileal brake.

Primary bile acid diarrhoea (PBAD) – an ileal carrier defect?

A J VAN TILBURG, F W M DE BOOIJ, J W O VAN DEN BERG, AND M VAN BLANKENSTEIN (Department of Internal Medicine, University Hospital Dijkzigt, Rotterdam, The Netherlands) In 1973 Hess Thaysen first described chronic bile acid losing diarrhoea without ileal abnormalities, PBAD, proposing defective active ileal bile acid transport as its cause. We describe the results of in vitro quantification of active bile acid transport using brush border membrane vesicles prepared from terminal ileal biopsy in 10 patients with PBAD. Transport was quantified as in vitro Na+-dependent bile acid transport (INBAT, expressed as pmol taurocholate per mg brush border membrane protein per 15 sec) and in vitro Na+-independent capacity (INBATC expressed as pmol taurocholate per gram ileal biopsies tissue per 15 sec). The lowest INBAT and INBATC values found in the 10 patients with PBAD corresponded with the 19th resp. 27nd percentile values of a control group of 132 patients.

Both INBAT (mean 88, range 30-136) and INBATC (mean 158, range 85-268) were significantly higher in the 10 patients than in the control group (INBAT: mean 63, range 1-244; INBATC: mean 98, range 1-408), confirming earlier findings of high INBAT values in various types of bile acid malabsorption. Our findings in 10 patients suggest that in adults PBAD is rarely caused by (genetic) ileal bile acid carrier defects.

F CARDIN, G GORI, P A MCMORRICK, G WAINNAMETHE, N M McCINTYRE, AND A K BURRINGTON (Transplantation Unit, Department of Public Health and Primary Care, Royal Free Hospital & School of Medicine, London) Early rebleeding from peptic ulcers in the initial hospital admission can be predicted by clinical and statistical models. However, no such models exist for bleeding varices, although early rebleeding is very frequent. We prospectively studied predictive factors associated with early rebleeding from varices within a five year follow-up in 384 patient admissions. All were initially treated with vasoactive drugs, and surgery and surgery used for continued bleeding, which occurred in 42% (n=163). A Cox model using 20 variables describing severity of bleeding, stage, type of liver disease, and mode of admission, identified the following independently predictive variables: active bleeding on endoscopy irrespective of the injection (p<0.001), encephalopathy (p<0.01), number of units transfused (p<0.01), and age (p<0.01). The relative risk for a patient related to 30 day mortality which showed that early rebleeding itself was predictive of early death. A model derived in 180 subsequent patient admissions treated with emergency surgery alone at diagnosis showed a 67% (n=60) in the group treated within five days (p=0.001).

Transplantation for primary biliary cirrhosis – the Birmingham experience

D J MUTIMER, K G GUNSON, J M NEUBERGER, J A BRANESKELLS, P H ELLISON, AND J ALLEN (Liver Unit, Queen Elizabeth Hospital, Birmingham) One hundred and fifty two patients with late primary biliary cirrhosis (PBC) were referred for consideration of liver transplantation (LT) in the period February 1989 to February 1994. There were 100 (91 women, mean age 51 years) underwent LT in this period. There are 72 survivors (median follow up 505 days, range 111-2808 days) and 28 deaths (median interval from LT to death 18 days, range 1-54 months) from postoperative complications. Early mortality (within 3 months) was 8%. The 5 and 10 year actuarial survival is 72% with most deaths occurring in the early (<3 months) postoperative period. Median bilirubin at time of LT was 279 µmol/l (range 27-870). Univariate analysis identified prior admission for hepatic encephalopathy, creatinine, INR, lower albumin, and LT number (reflecting unit experience) as being associated with post LT outcome. Advancing age and previous upper abdominal surgery were not associated with death after LT. Cox multivariate analysis confirmed the independent importance of LT number and age (components of the best Cox model). Twelve-month actuarial survival of the four secondary and tertiary centres were 55%, 67%, and 94% (p<0.002). Preoperative prognostic index (Christensen, predicting survival without LT) correlated poorly with postoperative outcome. Most patients died with multi-organ system failure and sepsis (often opportunistic).

Despite no improvement in pretransplant condition, results of LT for PBC are improving. Extrahepatic (biliary) syndrome reflects very late disease and is associated with poorer outcome after LT.

AUDIT

A predictive model for very early rebleeding from varices

The effect of SHT3 receptor antagonist on the ileal brake mechanism in the rat

N J BROWN, R D RUMSEY, AND N W READ (Sub-Department of Gastrointestinal Physiology and Nutrition, University of Sheffield, Western Bank, S10 2TN) It has recently been shown that
Management guidelines for dyspepsia: do they work?

R H JONES, S LYEARD, AND J L DUNLEVY (Primary Medical Care, University of Southampton) The Southampton Dyspepsia Study has tested the feasibility and efficacy of introducing clinical guidelines for the management of dyspepsia. All 245 general practitioners in the Southampton Health District were divided into study and control practices. Investigation and referral data were collected for six months from November 1988 before the study group were invited to a series of consensus meetings with hospital specialists; less than 20% of eligible GPs attended these meetings. Management guidelines were produced and distributed to study practices in October 1989 and data collection repeated for six months starting November 1989.

There was a 5% rise in referrals to general medical and surgical outpatients but a 25% fall in referrals for dyspepsia. This was accompanied by a 13% increase in requests for endoscopy (p<0.05) and a corresponding fall of 14% in requests for barium meals (p<0.05), although the study and control groups differed only in requests for endoscopy, which increased by 20% in the study group compared with 6% in the controls (p=0.01).

There were changes in the referral behaviour of study and control practices are unexplained, but cast doubt on the value of management guidelines developed in this way.

A simple questionnaire as a method of reducing workload from open access endoscopy

J M MARREDO, R P JAZRAWI, P M GOGGIN, P J FINCH, AND T C NORTHFIELD (Division of Biochemical Medicine, St George's Hospital Medical School, Crammer Terrace, Tooting, London SW17 0RE) The introduction of an open access endoscopy service resulted in an increased workload and in many unnecessary examinations. Since gastric cancer is unlikely in patients less than 45 years old the aim of this study was to test prospectively the efficacy of a simple questionnaire in reducing endoscopic workload in these patients. A total of 94 patients referred for endoscopy with dyspeptic symptoms completed a questionnaire of 14 items. The score was higher in patients with serious pathology (duodenal or gastric ulcer, cancer) than in those without (9.9±6.9, p<0.001), hence a cut off point of 7 was chosen. Not performing endoscopies in patients under 45 years of age with a score of 7 or less would have resulted in 18 (21%) fewer endoscopies while missing only 3% of cases of serious pathology (one duodenal ulcer). For patients under 45 the sensitivity of a score of 8 or more in detecting serious pathology was 98%.

A stepwise discriminant analysis gave five questions which best predicted the presence of pathology. In order of importance these were pain relieved by food, pain waking patient at night, alcohol excess and a familiar history of ulcer. These results suggest that the introduction of a simple scoring system should prove an effective and safe method of reducing endoscopic workload in those aged less than 45.

What do patients want to know about inflammatory bowel disease?

A MARTIN, I CASTAGLIUOLO, L LEONE, G C STURMINOLO, G MASTROPAPAOLI, F D MARIO, AND R NACCARATO (Università di Padova, Divisione di Gastroenterologia, Istituto di Medicina Interna, Via Giustiniani, 2 – 35100 Padova, Italy) Information is not only a patient’s right but also improves compliance and management. Apart from verbal consultation, in most instances, informative material is provided without prior analysis of what patients think is important to know. Our aim was to assess patients needs of information in order to plan educational programmes more correctly. We used a self administered 44 item questionnaire dealing with three main subjects: general knowledge of the disease, on what aspects is information is required, what methods are preferred, and the perception of information on anxiety. One hundred consecutive outpatients, 50 with ulcerative colitis (UC) and 50 with Crohn’s disease (CD), were studied.

Sixty two per cent of patients with UC and 78% with CD thought that they had inadequate information on their disease. Highest priority was given by CD patients to: aetiology, diet, symptoms, history, new treatments, risk of treatment, cancer, and consequences for work. UC patients established priorities in diet, psychosocial and, diet, symptoms, new treatments, and risk of cancer. For 73% a specifically designed book was the best method, followed by leaflets (25%) or video cassettes to be viewed at home (20%). Overall, 35% of patients thought that inadequately presented information would increase their anxiety.

(1) Seventy per cent of patients consider themselves to be poorly informed about their disease. (2) The topics for an educational programme have been identified and are different for UC and CD. (3) Badly designed information would increase anxiety in over one third of patients.

Current British medical therapy in ulcerative colitis

A COLE, G M PEARSON, M WHITEHALL, AND C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) Changing and novel treatments for inflammatory bowel disease may influence established guidelines. We therefore surveyed current therapeutic practice in a proportion of BSG consultant members and present data from 50 responding medical gastroenterologists. Salicylates are still the mainstay of maintenance treatment but 60% would select mesalamine (Asacol) in 40% selecting sulfasalazine. Factors considered important influencing choice were efficacy (86%), side effects (74%) and prior experience (74%). However, only 34% correctly identified dosage equivalents of the two drugs. Fibre manipulation was the only major dietary advice (high fibre 16%, low fibre 4%).

For patients with active total colitis requiring hospitalisation all used steroids (60% iv); 56% would add oral salicylates (38% mesalazine and 28% would use metronidazole (none would use vancomycin); 8% would give anti-diarrhoeal drugs. While 42% would offer surgery for severely disabled disease after five to seven days, a larger number (48%) would wait for 10 or more days (up to 56 days). Improvements in maintenance treatments (median rank (1), acute treatment (2), and drugs with fewer side effects (3) were perceived as most important future drug needs, with non-absorbable steroids (median rank 1), cytokine modifiers (2), identified as most promising.

Clinical opinion is changing; mesalamine has supplanted sulfasalazine for maintenance treatment and delayed surgery during relapse would often be considered.

Workload implications of the relentless increase in incidence of Crohn’s disease

D SEDWICK, J DRUMMUND, J CLARKE, AND A FERGUSON (Gastro-Intestinal Unit, Western General Hospital, Croyde Road, Edinburgh and Commonwealth Services Agency, Trinty Park House, Edinburgh) We are continuing to use the Scottish Hospital In-Patients database to examine the incidence of Crohn’s disease (CD) in young people aged <16 years and to analyse the patient workload of CD for Scotland (population 5·1×106 in 1988). We previously reported a threefold rise in the incidence of juvenile onset CD between 1968 and 1983. Further analysis of the incidence in the 5 years since then showed a continuing rise to 29 per million aged <16, and no change in the incidence of ulcerative colitis.

Total discharges and bed-days for CD in NHS hospitals in Scotland have been studied. In 1971 there were 646 discharges, 11 606 bed-days with a mean stay of 18 days; by 1988 there were 1981 discharges, 25 083 bed-days with a mean stay of 12·7 days. Estimation of workload by the end of the century, by linear regression, showed 5500 bed-days (95% confidence intervals 32 692 to 37 907). These changes in inpatient, and associated outpatient, workload must be taken into account when planning gastrointestinal services. A significant subset in the age range 11–15 years has been identified in the 1980s and the special needs of these adolescents with inflammatory bowel disease should also be considered.

High dose ranitidine prophylaxis of gastric haemorrhagic lesions

A T COLE, S BRUNDELL, N HUDSON, A B HAWTHORNE, AND C J HAWKEY (Department of Therapeutics, University Hospital, Nottingham) Conventional doses of ranitidine protect the gastric mucosa against aspirin induced injury, but incompletely. Ranitidine 150 mg bd suppresses aspirin induced gastric microbleeding. We therefore assessed the effects of higher doses. Twenty healthy volunteers took aspirin 600 mg bd for 14 days with ranitidine 150 mg bd, 300 mg qds, 600 mg bd, or placebo. Mucosal injury was quantified by numbers of haemorrhagic and non-haemorrhagic lesions and microbleeding in washings.

Aspirin increased gastric haemorrhagic erosions from 0 to 6 (median) (2.75 to 10.5 interquartile range, p<0.001) and antral non-haemorrhagic erosions to 3 (1–450, p<0.001). Total gastric haemorrhagic erosions were reduced by ranitidine 300 mg qds to 3 (0–5, p=0.022) and by ranitidine 600 mg bd to 3 (0–5, p=0.049) but not by ranitidine 150 mg bd (5 (2–8)). There were no statistically significant effects on non-haemorrhagic erosions. Microbleeding was induced by aspirin from mean 1·14 (95% confidence limits 1·03 to 1·91) μl/min to 12·3 (8·5 to 16·7) μl/min, p<0.001. This was significantly reduced by ranitidine 300 mg qds to 2·93 (2·38 to 4·88) μl/min, p<0.001 and to 4·55 (2·35 to 6·55) μl/min, p<0.001, by ranitidine 600 mg bd.

High doses of ranitidine offer effective prophylaxis of the human gastric mucosa against aspirin. The principal action is to prevent aspirin induced haematema and melena.
Incidence and significance of stigmata of recent haemorrhage in ulcer patients without clinical evidence of recent bleeding

A KALABAKAS, R KOURGIAS, D KARAMANOLIS, AND P SWAIN (The London Hospital, Whitechapel, London and Tameson General Hospital, Pires, Athens) We examined prospectively the incidence and significance of stigmata of recent haemorrhage (SRH) in patients without clinical evidence of recent bleeding. Seventy-nine consecutive patients found to have peptic ulcer at routine endoscopy (duodenal ulcer 51, gastric ulcer 25, DU+GU 3) were carefully examined for presence of SRH; 27/79 (34%) had SRH (adherent clot 9, red spots 9, black spots 7, two had spidaneous bleeding). No visible vessels were seen. No patient in this series had further bleeding. Mean haemoglobin in no SRH group 11-5, mean Hb in SRH group 11 8 (NS). Comparing patients with and without SRH analysis of sex, age, race, smoking habit, diet, ulcer history duration, drug history, other diseases, family history, ulcer type, number, size, blood count indices, iron TIBC, and ferritin showed no significant differences. These results indicate that SRH are commonly observed in ulcers in patients without clinical evidence of recent bleeding. Presence of SRH in patients without clinical evidence of bleeding were not associated with risk of further bleeding or anaemia.

Prolongation of intragastric bleeding by acid

S G MANN, S DIDCOTE, P HYMAN TAYLOR, AND C J HAWKEY (Department of Therapeutics, University Hospital, Queen's Medical Centre, Nottingham) Blood coagulation is extremely sensitive to a lowering of pH in vitro, and acid gastric contents may prolong bleeding from peptic ulcers. We investigated the effects of intragastric pH on biopsy-induced bleeding in 13 fasted volunteers. At endoscopy, two hours after famotidine 40 mg or placebo, greater curve biopsy specimens were taken and the bleeding site washed every five minutes for 25 minutes, with water or HCl, pH 1 5. Bleeding in aspirated washings was measured as orthotolidine reaction. Each subject was studied under each of the four possible treatment conditions, one week apart, in a pre-determined random order. The volumes of blood lost vary significantly between treatments. However, after placebo pretreatment, bleeding persisted for longer into acid than water washings, with 18-9 (11 1 to 32 2) μL/5 minutes (geometric means with 95% confidence intervals; 7 7 to 12 8) μL/5 minutes (p=0 016) at 20 minutes and 18 2 (9 4 to 35 4) μL/5 minutes μL/5 to 11 4) μL/5 minutes at 25 minutes (p=0 021). Famotidine had no obvious effects on timing of bleed despite producing a higher median pH of aspirate during water washes (pH 6 9 ± 2-4). We conclude that the pH of aspirated gastric contents may influence overall volume of intragastric bleeding, however, repeated contact of lesions with low pH washings seem to prolong bleeding duration.

Omeprazole v placebo for acute upper gastrointestinal bleeding: a randomised double blind controlled trial in 1154 patients

T K DANESHMEND, C J HAWKEY, M J S LANGMAN, R F A LOGAN, R G LONG, AND R P WALT (Department of Therapeutics, University Hospital and City Hospital, Nottingham) Meta-analysis suggests that H2 receptor antagonists may improve mortality and morbidity from upper gastrointestinal bleeding (UGIB). Thus inhibition of gastric acid may be therapeutic. We tested this hypothesis by examining the effect of omeprazole on UGIB in the largest clinical trial yet. Over 40 months, 1154 consecutive medical admissions (age ≥18 years) with acute UGIB were randomised to placebo or omeprazole (bolus injections: 80 mg stat, then 40 mg tds for 24 h, then 40 mg orally bd for 3 days or until operation death or discharge). Endoscopy was performed within 24 h. Omeprazole reduced stigmata of bleeding (44% to 32% p=0 001), and of active bleeding seen at endoscopy (14 4% to 10% p=0 001). Of 44 patients receiving omeprazole and 30 given placebo died (20 6 respectively after operation). However, more of these omeprazole recipients were operated upon for lower gastrointestinal lesions and gastric cancer (omeprazole six and four respectively; placebo 9 and one). Omeprazole reduced the frequency of endoscopic stigmata and of active bleeding: a com-

Adrenaline injection or laser photoacogulation for bleeding peptic ulcers - a randomised study

R CARTER AND J R ANDERSON (University Depart- ment of Surgery, Royal Infirmary, Glasgow) Forty-nine consecutive patients, bleeding from peptic ulcers that would conventionally have required surgical intervention, entered a study to receive either endoscopic adrenaline injection (1:10 000) or laser photoacogulation. Twenty two were women and 27 men, with a mean age of 63 3 (range 19-89). Patients were included only if they had a visible vessel at endoscopy; 23 were actively bleeding. Five patients were excluded and proceeded to surgery: prophylactic endoscopic coagulation or haemorrhage (n=2), torreal haemorrhage (n=2), or because ov- erlying adherent clot prevented intervention in a critically ill patient (n=1). The remaining 44 patients were randomised (laser group n=21; injection group n=23). There were no statisti- cal differences between the two groups with regard to age, ulcer site or size, shock or haemoglobin on admission, and the number of patients who had rebled.

Haemostasis was achieved initially in all patients. There was one rebled in the laser group and four in the injection group (p>0 05). Transfusion requirements did not differ between groups (p>0 05). Mortality was 1/21 (laser) compared to 0/23 (injection) (p>0 05). Healing rates at endoscopy (after 8 weeks) were similar in both groups (p>0 05). Our results suggest that injection of adrenaline can achieve similar results to laser photoacogulation at a fraction of the cost.

Optimising patient care in upper gastrointestinal haemorrhage: specialised units are the answer

J D SANDERSON, N FOLEY, AND F R VICARY (Department of Gastroenterology, Whittington Hospital, Highgate Hill, London N19) In 1988 we reported a low mortality for upper gastro-

intestinal haemorrhage managed on a special- ised unit using agreed protocols. After this we sought to confirm that this low mortality was due solely to the use of the unit by prospecti- vely recording all data related to each bleed. In 1989 our mortality was again low (11 out of 220 patients admitted with upper gastrointestinal haemorrhage died (5%)); 45% of patients were over 65 years, 21 had emergency surgery (10%). Transfusion criteria were hypovolaemia or a haemoglobin of less than 10 g/dl, or both. There were 57 duodenal ulcers (36%), 28 gastric ulcers (17%), and 19 cases of oesophageal varices (9%) of whom 6 died (32%). Of the peptic ulcers, 50 showed stigmata of recent haemorrhage and the mortality for this group was 0 7.

Our population data and transfusion policy are similar to those in other reported series. The operative rate is below average. However, we believe this comprehensive audit shows the danger of making assumptions about the importance of the use of a special unit in producing a low mortality in upper gastrointestinal haemorrhage.

PANCREATIC INFLAMMATION

The correlation betweenzymogen activation and tissue damage in acute pancreatitis

D I HEATH, A CRUICKSHANK, M GUDGEON, A SHENKIN, AND C W IMRIE (Royal Infirmary, Glasgow) It is widely assumed, although unproved, that the pivotal event in the produc- tion of an attack of acute pancreatitis is the inappropriate intraglandular activation of zymogens. Thus, measured concentrations of trypsinogen activation pep- tide (TAP) differ significantly between mild and severe attacks are in agreement with this hypothesis. In this study we have examined the relation between zymogen activation (through measurement of urinary TAP and phospho- lipase A2 (PLAP) concentrations and markers of tissue injury (through measurement of serum interleukin-6 (IL-6) and C reactive protein (CRP) concentrations).

Twenty four patients with acute pancreatitis were studied (10 severe and 14 mild). Serum and urinary samples were taken six hourly for a further three days. Specimens were centrifuged, aliquotted, and stored at −20°C until analysis. Comparison of the areas under the curve has shown a good correlation between IL-6 3 CRP concentra- tions (r=0 70 Spearman rank correlation). However, the correlations of IL-6 with TAP and PLAP were only 0 57 and 0 65 respectively. The results suggest a complex relation between the markers of the inflammatory response (IL-6 and CRP) and the markers of zymogen activation.

Synthetic antiproteases prevent ARDS in acute experimental pancreatitis

M DOBOSZ, Z ZLEDZINSKI, A BARBICKI, P KUSIECKI, B ZWADA, AND L ZWADA (POLISH SOCIETY OF GASTROENTEROLOGY) (The Second Department of General Surgery, Department of Pathology, Medical Academy of Gdansk, Kierunka 1 Street, 80-742 Gdansk, Poland) Acute pancreatitis is often associated with respiratory complications. This study examined the influence of two synthetic anti-
proteases – gabebrate mesilate (FOY) and nafamostat mesilate (FUT-175) on pulmonary dysfunctions in canine necrotising pancreatitis. Seven animals received no treatment during a 10 hour observation period. The other two groups of six animals each were treated – one with intravenous continuous infusion of FOY and the other with FUT-175, both in doses of 1 mg/kg per hour. In the untreated animals we observed the decrease of mean arterial pressure from 100-80 mmHg to 60-70 mmHg and cardiac output from 3-2-1.7 l/min, and arterial PO2 from 105-75 mmHg. Pulmonary vascular resistance increased from 101–316 dynes × sec × cm⁻². Histological evaluation of the lungs showed interstitial oedema, thickened alveolar septa and focal atelectasis, and occasionally intravascular thrombosis. FOY and FUT-175 prevented the animals from haemodynamic disturbances, hypoxaemia, and histological alterations in the lungs. Synthetic antiproteases seem to be of value in the treatment of the acute respiratory distress syndrome complicating acute pancreatitis.

The effect of SMS 201-995 on experimental pancreatic carcinogenesis in the Syrian golden hamster

G HADDICK, D J HARRISON, AND D C CARTER
(University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW)
Cholecystokinin and secretin can influence the development of chemically induced pancreatic cancer in the hamster-nitrosamine (BOP) model. Somatostatin and some of its analogues, which suppress the effects of most gastrointestinal hormones, have been proposed as hormonal treatment for pancreatic cancer. We have investigated the effects of the long-acting somatostatin analogue, SMS 201-995 (Sandoz) on pancreatic carcinogenesis in the hamster-nitrosamine model

Step-wise increasing doses of intravenous SMS 201-995 suppressed pancreatic juice output from a median basal value of 212 mg/kg bodyweight per h (Q1;Q3=121:324) to a median value of 5 µg/kg per h (Q1;Q3=46:102) at 10 mg/kg SMS bd for three days a week for one or six weeks did not affect pancreatic wet weight or DNA content whereas saline did to controls.

More SMS-treated animals (5 µg/kg) developed invasive pancreatic carcinoma after 15 weeks of carcinogen (4/10 animals) v 0/10, p<0.05) and tumour was more extensive (17/75 histological sections affected v 0/71, p<0.001). When carcinoma in situ and microcarcinoma are analysed with invasive lesions, SMS-treated animals were still significantly more affected than controls (33/75 sections n=971, p<0.001). The effect of SMS 201-995 on pancreatic carcinogenesis is complex. Further work is required before its use in human pancreatic cancer is justified.

Flow cytometry analysis of BOP treated hamster pancreas

G HADDICK, E P MILLER, D J HARRISON, AND D C CARTER
(University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW)
The nitrosamine BOP produces pancreatic ductal adenocarcinoma. There is evidence that ductal cells may be less capable than acinar cells of repairing BOP-related DNA injury. This study investigated the DNA content of hamster pancreas during carcinogenesis to determine whether neoplastic changes are associated with changes in DNA content (EPICS CD flow cytometer). Cytostat sections showed typical morphological changes. Flow cytometry showed a growth fraction of 8.4 (2.1%) in control pancreas. This increased to 17.5 (5%) (p<0.05) by week 15 and 20 weeks (19-4 (6.5%) and 21-1 (6.2%). In only seven of 210 samples analysed we foundanequipiment peaks. These had DNA indices <1-3 and represented only a small proportion of nuclei; there was no relation to histological appearances and their significance is uncertain.

Cell cycle activity after BOP treatment is intense and seems to result from DNA repair/ regeneration rather than carcinogenic progression. Further investigations are being undertaken into the defence mechanisms of specific pancreatic cells against carcinogen-induced injury.

Experimental pancreatic carcinogenesis: contrasting effects of dietary fatty acids

D E KHO, B FLAKS, H OZTA, C B WOOD, R C N WILLIAMSON, AND N A HABIR
(University Department of Surgery, Royal Postgraduate Medical School, London and Department of Pathology, University of Bristol Medical School) Since fatty acid supplements can influence tumour development, the effects of oleic and stearic acid were compared in the azaserine model of pancreatic carcinogenesis in rats. Weaning male rats (Leeds strain, n=40) were randomised to one of four groups: normal diet with or without carcinogen (azaserine 30 mg/kg IP) + 20% oleic acid diet or 20% stearic acid diet. At 15 weeks, all but a few of the histological sections of pancreas were examined for acido- philic atypical acinar cell foci (AACF) and volumetric indices were derived. Pancreatic weight was unchanged between groups. With azaserine alone, 2-16 (53%) (mean; SEM) of pancreas was occupied by AACF (0% in controls). Oleic acid trebled this percentage (to 7-71 (10%); p<0.001), whereas stearic acid reduced it by 82% (to 0.39 (14%); p<0.05). The mean volume of foci was similarly increased by oleic acid (4-0 (0.62) mm³: p=0.02) but reduced by stearic acid (0.48 (0.15) mm³: p<0.01) compared with azaserine alone (2-50 (0.53) mm³). Changes in the fatty acid profiles of the pancreatic total lipid extracts reflected the diets administered. As in mammary and colorectal carcinogenesis, dietary stearic acid inhibits the development of pancreatic cancer whereas oleic acid has a promoting effect.

Cytotoxicity of ursodeoxycholic acid (UDCA) to human biliary epithelial cells (BECs)

B GUDJONSSON (The Medical Clinic, Álafémin, Reykjavik, Iceland) Review of reports of surgical treatment for pancreatic cancer shows considerable discrepancy between pathological material, statistical methods, and results. Pathological material may consist of more than adenocarcinoma of the pancreas such as carcinoma of the ampulla, cystadenocarcinoma, and islet cell carcinoma. Survivors may then be inadequately separated in the results. Survival percentage can be calculated from up to six different denominators of patients, which can lead to high percentage figures in spite of few actual survivors. Use of lifetime methods may further increase the figures. Investigators tend to ignore that up to 10% of published five year survivors have not been resected. Favourable results tend to be published more than once which further blurs the overall assessment.

Review of close to 250 papers published in the last five and a half decades shows approximately 200 survivors out of 55 000 reported patients, for less than 0-4% overall survival. Benefits of resections have not been proved. Survival percentage is only valid if based on total number of patients diagnosed with cancer of the pancreas at a particular institution.

LIVER POSTERS

Endothelial cell damage in primary biliary cirrhosis (PBC)

A D BLANN AND C M MCCOLLUM (INTRODUCED BY R D MARTIN) (Department of Surgery, University Hospital of South Manchester, Nell Lane, Didsbury, Manchester M20 8LR UK) The aetiology of PBC remains unknown, but immunological mechanisms such as immune complexes are implicated in the initiation of injury. Both transformations in endothelial cell lining of the hepatic sinusoids and destruction of bile ducts have been reported. Hepatic endothelial cell damage was evaluated in 12 patients with PBC using a number of indices of inflammation and cytotoxicity.

Von Willebrand Factor Antigen (vWFAg), measured by ELISA, hyaluronic acid (HA) (estimated by radiometric assay), and endothelial cell (EC) cytoplasmic (assessed by isotope release assay) were all raised (p<0.001, p<0.001, and p<0.05 respectively). There were increased levels of immune complexes (p<0.05), reduced levels of CH50 (p<0.05), but C reactive protein levels were normal. There were good correlations between vWFAg and EC cytotoxicity (p<0.001), HA and EC cytotoxicity (p<0.002), and vWFAg and HA (p<0.01). No other correlations involving any combination of EC or inflammation indices were significant.

The evidence of damage to the endothelium in this study suggests that immunological mechanisms alone are not responsible. Despite strong in vivo and in vitro data showing EC damage, these indices failed to correlate with inflammation markers. This suggests that there may be other mechanism(s) contributing to damage to endothelium.

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early improvements were seen in serum liver enzyme levels and the longer term results are disappoint- ing. We have established in an in vitro chromium-51 release cytotoxicity assay to assess bile salt cytotoxicity to BECs from the livers of patients undergoing orthotopic liver transplantation for end stage PBC. Chromium-51 release corre- lated well with that of lactate dehydrogenase (r=0.95, p<0.05). When assayed at 750 μmol/l, the toxicity of LCA was 21% (per cent chromium-51 release minus control), whereas that of UCDA was significantly greater (35%). Chenodeoxycholic acid (CDA) was also significantly more toxic (75%). There was a general trend towards detoxification after con- junctive, especially with taurine. Caution must be exercised in extrapolating any clinical infer- ence from this limited in vitro study but our results highlight the relative toxicity of dihydroxy bile salts to BECs and suggest that they may be implicated in the progressive biliary obstruction seen in PBC, rather than monoxyhydro bile salts. UCDA had pro- nounced cytotoxicity (35%), which is of interest in view of the poor longterm results of UDCA treatment in PBC.

Elevated plasma interleukin-6 in alcoholic hepatitis: correlation with mortality and disease severity

N SHERNON, G BIRD, J G M ALEXANDER, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital, Denmark Hill, London SE5 9RS). Production of the cytokine interleukin-6 (IL-6) in response to endotoxin and tumour necrosis factor (TNF) is a major factor in mediating the acute phase response, and these cytokines have been shown to determine the clinical features associated with multiorgan failure in sepsis. There are clinical similarities between sepsis and severe alcoholic hepatitis (AH) and in both diseases levels of endotoxin and TNF are raised. Plasma concentrations of IL-6 were assayed by ELISA in 86 samples from 48 AH patients and in 69 subjects in five control groups (21 normal, 10 alcoholic cirrhosis, 10 alcoholics, 18 chronic liver disease, 10 chronic renal failure). AH patients were studied in the first week of admission and clinical details (95% confidence interval: CI) were: INR (1-5 to 1-7), bilirubin (154 to 245 mmol/l), serum creatinine (127 to 183 μmol/l), mortality (32%). Concentrations of IL-6 in AH were raised (CI 18-6 to 36 ng/l) when compared with all the control groups (upper CI’s 11-2 to 16-1, p<0.001). Plasma IL-6 was higher in patients who died (CI 24 to 73 ng/l) compared with survivors (13 to 26 ng/l) but these correlations were found between increased plasma IL-6 and decreased survival, increased neutrophil count, INR, creatinine, and bilirubin. The associations with neutrophil count (p<0.01) and INR (p<0.05) were found to be independent after multiple regression analysis. There was no association between plasma IL-6 and infection, plasma endotoxemia or plasma TNF concentrations. These data suggest that some of the clinical features of severe alcoholic hepatitis may be mediated by high plasma concentrations of IL-6 and confirm that the pattern of cytokine release in severe alcoholic hepatitis is similar to that seen in the multiple organ failure of sepsis.

Ethanol induces lipotrope wastage in the rat

K C TRIMBLE, A M MOLLOY, J M SCOTT, AND D G WEBR (Departments of Clinical Medicine and Biochemistry, Trinity College, Dublin). Hepatic steatosis in humans and the rat is associated with excess ethanol intake and with dietary choline deficiency. Supplementation of an ethanol diet with choline prevents the develop- ment of steatosis. This suggests that ethanol disordered phospholipid metabolism contrib- utes to ethanol induced steatosis and it has been proposed that this is a result of increased oxidative degradation of choline. We have used a radioreceptor technique which quantita- tively oxidative metabolism of 1-carbon units of the lipotropes choline and methionine and their oxidative intermediates betaine and sarcosine to test this hypothesis in chronically ethanol fed and also control rats. Groups of animals were injected intraperitoneally with the above C14 methyl labelled metabolites and transferred to respiration chambers so that 1-carbon oxidation could be assessed over a four hour period by assaying expired air for C14 CO2. After seven and 21 days on ethanol oxidation of administered choline was increased with respect to controls by factors of 1-9 and 3-6 respectively (p<0.0001). Betaine oxidation was increased in both similar factors 2-27 and 4-34 respectively (p<0.00001). Oxidation of methionine was little changed at seven days but increased threefold at 21 days (p<0.0001). Sarcosine methyl group oxida- tion was also found to be elevated. These results show a wastage of methyl groups from choline via the choline oxidase system and also suggest an increased loss of 1-carbon units from methionine, previously undescribed.

Expression of intrahepatic hepatitis D virus (HDV) antigen in chronic HDV infection: relation to the pathogenesis of chronic liver disease

J Y N LAU, L J HANSEN, Y G BAIN, K CHAGGAR, D VERNAG, P B PORTMANN, J G M ALEXANDER, AND ROGER WILLIAMS (Liver Unit and Department of Immunology, King’s College Hospital and School of Medicine & Dentistry, London SE5 9RS) Intrahepatic HDV-Ag is an excellent marker of active viral replication in the liver. However, it is uncertain whether HDV is cytopathic of whether liver damage is immune mediated. To elucidate the biological significance of hepatitis HDV-Ag, its expression in immunohistochemically and radiolabelled serum liver biochemistry and histological inflammatory activity (lobular inflammation, piecemeal necrosis, portal inflammation) in 97 biopsy specimens from 67 patients seropositive for total antibody to HDV. Seventy four biopsy specimens (76%, 51 patients) were positive for intrahepatic DHV-Ag (distribution: nuclear 100%; nuclear with cytoplasmic in one specimen only). Compared with the HDV-Ag negative group the HDV-Ag positive patients had significantly higher serum transaminase (54 (28) vs 122 (82) I/U/ml; p<0.001) and total histological inflammatory activity (p<0.025). Among the HDV-Ag positive group, there was a positive correlation between the proportion of hepatocytes containing HDV-Ag and either the serum transaminase or histological inflamma- tory indices. Pronounced fibrosis, unrelated to HDV-Ag expression, was present in 67% of the specimens. In 22 HDV-Ag positive patients with follow up biopsies at two years (range: 1-5), the proportion with cirrhosis increased from 36% to 73% (p<0.025). Serum trans- amine remained constant during this period but the proportion of HDV-Ag positive cells dropped with histological deterioration. This absence of an association between HDV-Ag expression and histological liver damage does not support the view that HDV is directly cytopathic to hepatocytes. The absence of cytoplasmic HDV-Ag expression also suggests that HDV-Ag is unlikely to be the viral target antigen in HDV-related chronic liver disease.

Clinical significance of myeloproliferative disorders in patients with ‘idiopathic’ extra- hepatic venous obstruction

F CARDIN, M GRAFFEO, P A MCCORMICK, S SHERLOCK, N MCINTYRE, AND A K BURROWS (King’s College Hospital Royal Free Hospital & School of Medicine, London) The aetiology of extrahepatic venous obstruction (EHVO) is unknown in 50% of cases. Recently in a study of 33 adult patients, seven had obvious myeloproliferative disorder, seven had a latent disorder, and two developed it within five years. We have evaluated the long term outcome of adults with ‘idiopathic’ EHVO to establish if any latent myeloproliferative disorder can be predicted from the clinical course. In a group of 118 EHVO patients followed up for a median of 120 months (2-468), 63 (53%) had a precise aetiology but only six (5%) with myeloprolifera- tive disorder. Recently we reported a median of 70 months (19-384). Only two of 17 (12%) developed overt myeloproliferative disorder during follow up at one and six years. These did not have a different course with respect to bleeding varices compared to the remainder of the patients. The mean bleeding index (before surgery) was 0-08 episodes/month in both groups and was 0-03 and 0-02 episodes/month after surgery in the ‘idiopathic’ group and remainder respectively. The incidence of overt myeloproliferative disorders less than 10% in patients with EHVO. Failure to diagnose a latent disorder does not seem to influence the course of variceal bleeding, and thus is of little clinical and prognostic significance.

RFLP analysis of HLA class II associations in primary biliary cirrhosis (PBC)

J UNDERHILL, P DONALDSON, D DOHERTY, G BRAY, M LOMBARD, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital and School of Medicine & Dentistry, London SE5 9RS) There is no association between PBC and HLA class I but early studies reported associations with DR2 and DR3 and a more recent study showed an increased frequency of DRw8 and a decrease in DR5. Using standard serological tissue typing methods DRw8 is difficult to distinguish from DR5 and DRw6. However, assignment of these and other types by restric- tion fragment length polymorphism analysis (RFLP) is unequivocal. The aim of the present study was to establish if RFLP analysis in a large series of patients with PBC to confirm or refute the reported HLA class II associations in PBC. Genomic DNA was prepared from 111 patients with PBC, 43 of whom subsequently underwent liver trans- plant for end stage disease. The DNA was digested with Taq1 restriction enzyme and probed with full length cDNA probe for the DR gene. After autoradiography DR gene types were assigned according to a standard international protocol. Antigen frequencies
were compared with those of 96 adult controls. The frequency of DR1 was raised in the patient group (34% of 20% controls, χ²=4.6, p<0.05). This was not significant after correction for multiple testing, DRB8 was raised (34% of 20% controls, χ²=6.0, p<0.05). There were no significant differences in antigen frequencies between patients who underwent liver transplantation and those who did not. In conclusion, while there seems to be an association between HBC and HLA DRB8, it is weak. This suggests that other class II genes close to DR may be involved in susceptibility to PBC.

We are currently using molecular techniques to investigate the HLA class II genes at the DP and DQ loci in PBC.

Predicting variceal bleeding in cirrhosis using endoscopy, haemodynamic evaluation by Doppler ultrasound (DUS) and clinical variables

S SIRINO, G DI FEBO, L BOLONDI, S GAJANI, M VACICRA, M MIGLIOLI AND L BARBARA (Istituto di Clinica Medica e Gastroenterologia, Università di Bologna, Italy) To evaluate the role of endoscopic, clinical, and DUS data in the assessment of risk of varical bleeding, we have prospectively studied 88 cirrhotics (65% men, mean age 56-5 years). Varices were classified according to the JRSHP rules and the severity of liver disease according to the Child-Campbell criteria. The DUS parameters evaluated were: portal vein calibre (P), portal flow velocity (PFV), portal flow volume (VPF), and congestion index (CI). F2-F3 varices were present in 56 (64%) patients, 41 (47%) had red sign discrimination, the mean Campbell’s score was 7.7, 15 (17%) patients had already bled, and 12 (14%) had had sclerosis. During a mean follow up period of 14 months 20 (23%) patients bled. Clinical and endoscopic variables were used in a stepwise discriminant analysis on bleeding: varical size, red signs on varices, nutritional state, previous bleeding, and previous sclerotherapy (all p<0.0001) had the best discrimination function (cases classified correctly: overall 85%; non-bleeders 90%; bleeders 70%). Adding to the analysis the DUS parameters, P, PFV, and VPF (all p<0.0001) showed a significant discrimination but did not improve the classification (cases classified correctly: overall 83%; non-bleeders 82%; bleeders 83%).

DUS does not increase the ability of endoscopic and clinical variables to predict the overall risk of varical bleeding. However, more studies are needed to verify the role of DUS since it seems capable of reducing the false negative rate.

Liver transplantation (LT) for non-cholestatic cirrhosis (NCC)

D J MUTYUM, B K GUNSON, J M NEUBERGER, J A C BUCKELS, P MCMASTERT, AND E ELIAS (Liver Unit, Queen Elizabeth Hospital, Birmingham) Results of LT for patients with NCC are inferior to LT for patients with primary biliary cirrhosis (PBC). The mortality of patients with NCC was 12% (12-month actuarial survival NCC 58%, PBC 72%). Factors predicting PBC survival with and without LT have been more clearly defined. We have examined 54 adults with NCC (median age 42, range 16-64 years; cryptogenic cirrhosis 17, autoimmune chronic active hepatitis (AIH) 13, chronic hepatitis B 8, α1 antitrypsin 8, others 8) to identify preoperative variables associated with death after LT. There were 32 survivors (median follow up 506, range 41-2331 days) and 22 deaths (median interval from LT to death 29, range 0-129 days). In univariate analysis the preoperative albumin (p<0.01), thromboplastin time (p<0.01) and white blood cell count (p<0.01) were significantly associated with death after LT. The positive predictive value of an unsupported serum albumin ≥28 g/l for survival after LT is 86%. Outcome was not related to patient age, previous PBC, or Child-Campbell’s grade. In a logistic regression model, the presence of cirrhosis, or preoperative bilirubin or urea in this analysis. Survival for AIH (6/13) was worse than that of other NCC (26/41), (NS), which may be explained by a lower serum albumin (mean 26.8 vs 26.0 in AIH v 26 in other NCC, p<0.05). AIHCA survival after LT seems to be independent of age and unrelated to duration of previous immunosuppression. Most deaths in NCC were associated with multiveseve system failure and sepsis (often opportunistic).

Early referral may improve survival after LT in patients with NCC. We recommend that patients be referred for consideration of transplantation when serum albumin falls to 28 g/l.

Wilson’s disease in Scotland

R R PARK, M MCCABE, G FELL, AND R J RUSSELL (Gastroenterology Unit, Royal Infirmary, Glasgow G31 2ER) We have investigated the prevalence and clinical features of Wilson’s disease (WD) in Scotland. Patients with WD were identified by searching hospital records or by contacting patients’ relatives (65% men). In May 1989, 83 patients were referred. The patients’ median age was 17 (range 2-60 years). The mean follow up period, the 33 patients alive in 1989, the point prevalence was 4 per million. Data was available for 28 patients (16 women). Ten patients (mean SEM) age 18 (1.9) years) presented with neurological problems, 12 (14 (1.7) years) had hepatic problems, and 6 (12 (0.9) years) were asymomatic. At presentation liver biopsies were normal (4), slightly abnormal (3), cirrhosis (7), not performed (10), and at postmortem, cirrhosis (4). All patients started on penicillamine which was stopped in nine patients due to abnormal peripheral blood count (6), rash (2), and patient’s own choice (1). Seven patients have been evaluated on trientine. Of the 12 patients examined at the end of the study period, 12 were well, one had poor hepatic functions, four neurological function, and two poor hepatic and neurological function. Four of these patients were not attending a hospital clinic. Twelve of the 33 patients died: from complications of chronic liver failure (2), acute liver failure (4), pneumonia associated with immobility (4), other causes (2). Of the patients who died, one had no further treatment and had stopped penicillamine by her own choice and one patient had been told inappropriately to stop treatment by a general physician.

In conclusion, there is a low prevalence of Wilson’s disease in Scotland. The high mortality may partly be the result of inadequate clinical supervision and inappropriate management.

Poor effect of UDCA in cryptogenic chronic liver disease: an implication of HCV

A FLOREANI, M CHIAMONTE, P FABRIS, T NGATCHE, AND R NACCARATO (Department of Gastroenterology ‘R Forlini’, Institute of Internal Medicine, University of Padova, Italy) Ursodeoxycholic acid (UDCA), effective in improving liver enzyme activities in cholestatic liver disease (CLD), has also been proposed in the treatment of chronic liver disease. In November 1988, we started a prospective randomised trial of UDCA a placebo in cryptogenic CLD. All patients underwent liver biopsy. The two subgroups were balanced on the basis of the presence of cirrhosis. Forty patients were included (17 men, age 47 years, range 25-68). Treated patients received UDCA 450 mg/day for six months. At the interim analysis 32/40 (80%) were found to be anti-HCV positive (Ortho HCV antibody ELISA test system). Results were analysed at three and six months by clinical examination and standard liver function tests. Of the 32 anti-HCV positive patients (16 treated, 16 on placebo), no patient had a complete normalisation of liver enzymes. In the UDCA group no significant change in serum aspartate and alanine transaminases was observed at three and six months, while γ glutamyltranspeptidase showed a significant decrease at a six month interval (from 65±17 to 47±17 U/L, p<0.05). In the placebo group a significant decrease at a six month interval in AST as well in ALT (p<0.01 and p<0.025 respectively) was observed. Of the eight anti-HCV positive patients with cirrhosis, the presence of anti-HCV positive subjects must be taken into account in the interpretation of the results of UDCA trials.

Bleeding varices in PBC and its prognostic significance

M R BAGIANI, M GUARDACISONE, P MCCORMICK, C RASINO, N M McINTYRE, AND A K BURROUGHS (Academic Department of Medicine, Royal Free Hospital and School of Medicine, Department of Epidemiology & Population Science, School of Hygiene and Tropical Medicine, London, UK) Bleeding varices is often considered as a poor prognostic sign and in some centres an indication for liver transplantation. However, in patients normalised serum enzymes while no effect was noticed in the four patients receiving placebo. These preliminary results suggest that UDCA is not effective in patients with anti-HCV positive chronic hepatitis C; the presence of anti-HCV positive subjects must be taken into account in the interpretation of the results of UDCA trials.
Evidence of frequent false-positive results using Ortho ‘anti-HCV’ Elisa test in hepatocellular carcinoma sera

P J JOHNSON, S N ZAMAN, H SMITH, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital and King’s College School of Medicine & Dentistry, London SE5 9RS) Using the Ortho Elisa test, 48% of 173 patients with hepatocellular carcinoma and cirrhosis had a positive test for antibodies to the hepatitis C virus (HCV). HCV RNA was detected in one of 44 of those with cirrhosis alone. Among the cirrhotic HCC patients, alcoholic, cryptogenic, and HBV-related cirrhosis were frequently and HBV seropositivity (23%, 64%, and 48% respectively), as were the sera groups among patients without HCC (23%, 46%, and 70% respectively). Overall, and within individual groups, there was a strong correlation between serum IgG concentration and the optical density value in the test system which could account for the variation in positivity. Thus anti-HCV positive patients had a mean IgG value of 19-75 g/l (80% had raised levels) compared to 13-9 g/l in HCV negative patients (22% had raised levels).

Using a new (Abbott) anti-HCV Elisa test, only 43 of 91 sera positive in the Ortho test gave positive results and 41 of these were confirmed as anti-HCV ‘positivation’ by a second test. Among these Ortho positive sera, only 10 of 39 (25-6%) HBSAg positive sera were positive in the Abbott assay, whereas 14 of 15 (93-3%) with HBSAg negative (presumed non-A, non-B) sera were positive. Until the specificity of currently available assay systems is confirmed, suggestions implicating a major role for HCV in the pathogenesis of HCC are premature.

Detection of novel antibodies to hepatitis C virus in patients with chronic active hepatitis (CAH)

C J TIBBS, J GLAZE BROOKS, B RODGERS, D PHIPPARD, H SMITH, G J ALEXANDER, A L W F EDLESTON, AND R WILLIAMS (Liver Unit, King’s College Hospital, London and Wellcome Diagnostics, Beckenham, Kent) Antibody to the C-100-3 region of the hepatitis C virus core antigen is detected in 90-95% of patients with post-transfusion hepatitis in the USA, as shown by the currently available Ortho test and in 44-50% of those with sporadic non-A non-B chronic active hepatitis (CAH). In the present study Elisa techniques have been developed to detect antibody to two further components of HCV designated BHC-7 and BHC-9. One assay detects reactivity to both antigens, the other to BHC-7 alone. Sera from 36 patients with histologically documented, autoantibody negative CAH of presumed non-A non-B viral aetiology were tested in the Ortho HCV assay and the new assays. Sera from 12 (33%) of these patients were reactive in the first tests, 12/39 (33%) reacted in none. Of the remaining 12 sera, seven were reactive to C-100-3 and BHC-9 and five were unreactive to C-100-3 but reactive in the BHC-7 assay.

Assays detecting antibody to multiple antigens may increase the sensitivity of the serological identification of HCV.

Prevalence of antibodies against different hepatotropic viruses in cirrhosis of the liver

J STRANSKY, L ZIKMUNDova, J KÖNIG, AND E HONZAKOVA (INTRODUCED BY R J LEICESTER (Hepatological and Viriological Department, National Institute of Health, Prague 8, National Reference Laboratory Prague, Czechoslovakia) In 62 patients with confirmed cirrhosis in paired sera antibodies against the hepatitis A, B, C viruses, Epstein-Barr virus, and cytomegalovirus (HAV, HBV, HCV, EBV, CMV) were measured. Thirty three patients with cirrhosis caused by HBV infection (including 16 HBSAg positive ones) were compared with 29 patients where all HBV markers were negative. Mean age 58.3 years (33-80). In patients with HBV in the case history anti-HAV IgG were detected in 70% and anti-HCV in 18%; in cirrhosis without HBV markers in 62% and 34% respectively. Five patients had antibodies against HAV, HBV, and HCV. In both groups a medium to strongly activated EBV infection was recorded: in cirrhosis after HBV infection in 67% and in cirrhosis without HBV markers in 59%. CMV infection was only in exceptional cases slightly activated. The difference between both groups was not significant. The results suggest that the majority of patients with cirrhosis had suffered once to three times from viral infections in the past. In 26% HCV infection was proved and more than half of the patients with cirrhosis have concurrently a strongly activated EBV infection.

Detective study on the prognostic value of antibodies to HCV (aHCV) in cirrhotic patients – interim report

M2 antibodies and rough (R) mutants in urine of ‘normal’ women with recurrent bacteriuria, and in women with PBC

F VALLE, P BUTLER, H BAUM, J HAMILTON-MILLER, W BRUMMITT, N MCINTYRE, AND K BURROUGHS (Departments of Academic Medicine for Microbiology, Royal Free Hospital School of Medicine, and Department of Biochemistry, Kings College, London) M2 antibodies cross react with urinary organisms and recurrent bacteriuria is frequent and associated with worse survival in PBC. Laboratory R mutants induce M2 antibodies, and PBC stools have a high prevalence of R mutants. Thus a bacterial trigger may initiate/worsen PBC. We investigated if significant bacteriuria is associated with R mutants and M2 antibodies by outpatient urine screening of women with PBC (n=104), recurrent bacteriuria but no liver disease (n=58), chronic non-PBC liver disease (n=183), and normal women (n=239). R mutants in urine were found in 39% of 23 PBC, 41% of 22 recurrent bacteriuric group, and only 5% of 19 non-PBC liver disease (p<0.05).

M2 antibodies were found in 69% of 58 recurrent bacteriuric group and 67% of 22 PBC patients with R mutants, with immunoblotting showing cross reactivity between bacteria and mitochondria), in six (18%) of 33 women with non-PBC liver disease (three had recurrent bacteriuria and one the R mutants), and in no controls (p<0.05). These results suggest that M2 antibodies are induced in women with recurrent bacteriuria but no liver disease, who have a similarly high prevalence of urinary R mutant bacteria to that found in PBC. M2 antibodies in PBC may be linked to recurrent urinary infection.
An immunopathological study of the bile duct lesions in primary biliary cirrhosis

S Dourakis, D Fish, and R Goldin (Department of Histopathology, St Mary's Hospital Medical School, London W2 1PG) It has been shown that increased numbers of dendritic cells are associated with the bile duct lesions in primary biliary cirrhosis (PBC). We have examined 10 paired biopsy specimens from patients with PBC and 12 from liver biopsies taken at the time of routine cholecystectomy. The biopsy specimens were stained for beta-2 microglobulin, HLA-DR, T cells (UCHL-1), and B cells (MB2) using an avidin-biotin immunoperoxidase technique. The control livers were lined by epithelial cells expressing beta-2 microglobulin but not class II HLA antigens. There were only very occasional dendritic, T, and B cells within the bile duct epithelium. In the biopsy specimens from patients with PBC the epithelial cells regularly expressed class II HLA antigens. Significantly increased numbers of dendritic cells were detected in PBC. Furthermore, the increase was greater in the first biopsy specimen than in the second. Increased numbers of T cells were present and were spatially associated with the dendritic cells. Although the numbers of T cells were fewer in the second biopsy specimen the number of B cells was greater. These findings are consistent with the hypothesis that activation of T cells by dendritic cells is an early event in the pathogenesis of PBC.

Effects of benzodiazepine receptor antagonist Flumazenil in hepatic encephalopathy

X Lesage, D Lescut, A Cortot, J D Guiet, and J Paris (Clinique des Maladies de l'Appareil Digestif, Service d'Explorations Fonctionnelles Digestives, Hopital Hursel et Hopital B, CHU Lille, France) In view of the possible involvement of gamma amino butyric acid (GABA)/benzodiazepine (BZP) receptor in the pathogenesis of hepatic encephalopathy (HE), we tested the efficacy of BZP antagonist Flumazenil in HE complicating alcoholic cirrhosis. Twelve patients (3 women, 9 men, mean age 54 years) with HE (R Classification, 11 Child C) received 1 mg Flumazenil IV. Brain sialyl 30 mins after injection (i) clinical staging of HE was done according to Conn classification, Como Glasgow Score (CGS), and number connexion test (NCT); (ii) an automated electroencephalographic analysis (AEA) was performed. Eight of 12 patients (67%) had a transient improvement in their mental state confirmed by CGS or NCT. (p<0.001). Among those eight, the cause of HE was a severe infection in seven cases. Although the AEA was not statistically modified in the 12 patients, an acceleration >50% of cerebral activity was recorded in 4/12.

Flumazenil could be an effective treatment of HE. Stratification of patients according to the aetiology of HE might be useful in further assessment of the efficacy of Flumazenil in HE.

Longterm anticonvulsant therapy worsens outcome in paracetamol induced fulminant hepatic failure

G P Bray, R T Keys, P M Harrison, J G O'Grady, G J M Alexander, and Roger Williams (Liver Unit, King's College Hospital, Denmark Hill, London SE5 9RS) Potentiation of paracetamol hepatotoxicity by long-term anticonvulsant treatment may be one factor that adversely influences outcome after overdose and although supported by animal studies, there have only been a few clinical reports to date. In the present study, the clinical course of 18 patients on longterm anticonvulsant treatment was compared with two published series of paracetamol induced fulminant hepatic failure (FHF) from this unit. 297 patients seen between 1973 and 1985 and 99 between October 1986 and April 1988. Mortality in the epileptic patients who did not receive N-acetylcysteine (NAC) was higher than in either of these series (93-3% vs 64-6% and 57-9%, p<0.025). There were also trends towards deeper coma (grade 3 or 4, 93-3% vs 75-4%, 1968-86), acidosis (pH<7.30, 40% vs 22-6%, 1973-85), and severe coagulopathy (PT >100%, 53-3% vs 31-7%, 1973-85). Two patients died without intending suicide. If the patients had been given NAC, mortality in epileptics was similar to the control group (1968-86; 1/3 vs 15/42). The one patient who died had been given NAC early after the overdose.

(1) Longterm anticonvulsant treatment enhances paracetamol hepatotoxicity but this effect is reduced by NAC. (2) This may be due to induction of liver CYP450 or inhibition of glucuronidation. (3) NAC should be given to all epileptics up to 24 hours after overdose and later if hepatic necrosis develops.

n-Butyrate reduces sialyltranserase mRNA levels and activity in cultured human hepatoma cells

P Lance, S Shah, J T Smith, J T Y Lau, and H Baumann (INTRODUCED BY J R BENNETT) (Department of Medicine, VA Medical Center, State University of New York and Roswell Park Cancer Institute, Buffalo, New York USA) The addition of stalic acids to cell surface macromolecules by sialyltranseras (STs) modifies many intercellular recognition processes, and increased sialylation distinguishes hepatic metastases from primary colorectal cancers. n-Butyrate, a short chain fatty acid, is a normal constituent of faeces and portal blood, and causes differentiation of several cultured human cancer cell lines. We have isolated a partial CDNA for a human hepatoma Sialyltransferase, the first of its kind, and used it to investigate mRNA levels in human hepatoma cells of the Hep G2 line treated with n-butyrate. Exposure to 5 mM n-butyrate for 24 h reduced ST mRNA levels and enzyme activity by 70-80%. In nuclear run-off assays, n-butyrate increased transcription of liver hepatocytopen and decreased that of a1 acid glycoprotein but did not alter transcription of ST. In absence of a direct transcriptional effect implies that n-butyrate must either alter the stability of ST mRNA or interfere with the nuclear processing and export of ST transcripts, or a combination of both. Further studies presently elucidate the pathogenesis of primary and metastatic hepatic cancers.

Chromosome 5 allele loss in hepatitis B virus negative hepatocellular carcinoma

S Ding,1 N Harib,1 C Wood,1 L Bowles,1 J Delhanty,1 and J Dooley1 (Liver Unit, Royal Free Hospital School of Medicine,1 Department of Surgery, Hammersmith Hospital,1 Department of Genetics and Biometry, University College, London) The molecular mechanisms involved in the development of hepatocellular carcinoma (HCC) are not clear, in particular tumour suppressor gene loss. The aim of this study was to identify consistent changes in DNA (allele loss) in HCC without the presence of HBV hepatitis. We have prepared DNA from tumour and non-tumour tissue from 11 patients with HCC (hepatitis B virus (HBV) positive, 4; HBV negative, 4; fibrolamellar, 3). Southern analysis was performed with a panel of hypervariable minisatelites probes assigned to chromosones 5, 7, 11, 17, and 18, and the pattern of banding in tumour DNA compared with that in non-tumour DNA. Non-tumour DNA from three of the patients with HBV negative HCC had an informative (heterozygous) pattern with probe m8s (terminal region of long arm of chromosome 5), and in all three there was loss of an allele (band) in tumour DNA. No loss was found with this probe in either HBV positive or fibrolamellar HCC. As yet probes for other regions of chromosome 5, as well as for chromosome 7, 11, 17 and 18 showed no loss. These findings indicate allele loss using p144D6 (on chromosome 17p, close to the locus of p53 gene) in HBV negative (2 of 4) and HBV positive (1 of 4) HCC. In summary, these data show allele loss in the terminal region of the long arm of chromosome 5 in HBV negative HCC which may represent the site of a tumour suppressor gene.

Activation of liver-derived fibroblasts and development of tumour metastasis

M Loizidou, R Carpenter, R Lawrence, H Lawrie, A Cooper, P Alexander, and T Taylor (University Surgical Unit, P Level, Centre Block, Southampon General Hospital, Southampon) Experimental metastases grow preferentially at sites of healing after tissue injury. Recent studies implicate proliferating, cultured fibroblasts as mediators of tumour growth. We studied primary and effect on metastasis of fibroblasts derived from healthy tissues and trauma sites. Traumatised and non-traumatised liver, colon, and omental were disaggregated enzymatically and cultured for seven days. Fibroblast proliferation was assessed by cell counting; cell type was confirmed immunocytochemically. Fibroblasts from injured and non-injured tissues were inoculated with human colorectal cancer cells and tumour take assessed in immunodeficient mice. Traumatised tissues gave accelerated primary fibroblast growth compared to healthy tissues: fibroblast cell counts (×105) were 38 mean (5-6-76 range) for mechanically traumatised liver; 15 (10-20) for anastomosed colon; 85 (33-96) for pristane-irritated omentum. Respective control readings were 0 (0-2-3-0), <0.1 (0-5), and <0.1 (0-26). p<0.01. Co-cultivation in vivo of activated liver-derived fibroblasts with cancer cells resulted in an increased tumour take in 21/28 animals (75%) compared with 11/26 (42%) when non-stimulating fibroblasts were used (p<0.02).

Fibroblast activation and proliferation is a common response at sites which facilitate tumour growth. Fibroblasts in primary culture derived from such sites facilitate experimental tumour metastases.

Selective radionuclide localisation in primary liver tumours

Gut, first published as 10.1136/gut.31.10.A1162 on 1 October 1980. Downloaded from http://gut.bmj.com/ on September 21, 2003 by guest. Protected by copyright.
Hepatic protective effects of propylene glycol against paracetamol-induced liver damage in mice

R D HUGHES, C D GOVE, AND ROGER WILLIAMS (Introduction by A R W HATFIELD) (Department of Medicine, Westmead Hospital, Sydney, Australia) Sex related differences in rat drug metabolism occur because of sex specific hepatic cytochrome P450 (P450) isozymes. In order to investigate the action of EGF on hepatectomy results, 11 male rats, r-rat IFNy (r-rat IFNγ) treatment decreases the activity of specific P450 isoforms. Thus, r-rat IFNγ produced a specific 40% and 17% reduction in androstenedione 7α- and 16α-hydroxylation respectively. Androstenedione 7α-hydroxylation was unaltered by r-rat IFNγ. Similar changes in the androstenedione hydroxylation pathways occurred after administration of naturally derived rat IFNβ.

Immunoprecipitation studies showed that the specific constitutive steroid 16α-hydroxylase, were decreased by r-rat IFNγ to 42% of control (p<0.05). Furthermore, slot blot hybridisation with a specific cDNA probe and RT-PCR analysis established that hepatic P45011A2 mRNA levels were decreased after r-rat IFNγ to 35% of control (p<0.0005).

In male rats, r-rat IFNγ treatment decreases the activity of specific P450 isoforms (P45011A2 and P45011B1) and the expression of the 81% of 16p3-hydroxylase).

Effect of an antibody to rat-EGF on hepatic regeneration after partial hepatectomy

D A VESEY, A C SLEDEN, AND H J F HODGSON (Department of Medicine, Royal Free Hospital, London, UK) Recent evidence implicates TGF-α, produced within the liver, as the natural ligand of the hepatocyte epidermal growth factor (EGF) receptor, attributing EGF-receptor down-regulation after partial hepatectomy (Hpx) to enhanced TGF-α expression. This implies that inhibiting the action of EGF should not inhibit regeneration, yet this has been reported (Hepatology 1989; 9: 992). We therefore injected groups of rats (n=5) to sham, Hpx, or Hpx with or without intravenous infusion of 3 mg of rabbit IgG, either anti-rat EGF or non-immune IgG. DNA synthesis after 24 h assessed by BrdU as newly incorporated DNA was reduced ‘H-thymidine incorporation, but there was no significant difference between the two groups. Serum from animals receiving anti-EGF IgG retained immunoreactive EGF, but serum from non-immune IgG, anti-EGF IgG blocked completely the action of EGF on DNA synthesis in primary hepatocyte cultures. Administration of an EGF antibody thus does not block the replicative response of the liver to Hpx, supporting evidence for an alternative ligand.

The British Society of Gastroenterology

J R NOVELL, N I MARKEHAM, A HILSON, AND R E F HODGSON (Department of Surgery and Department of Nuclear Medicine, The Royal Free Hospital, London) Fifteen patients with primary inoperable malignancies (8 hepatocellular carcinoma and 7 cholangiocarcinoma) were treated with Lipiodol (CIS UK) administered via the hepatic artery. The mean age was 60 years (range 42–75 years). All patients had ‘T’ colloid liver scanning before treatment. The median total administered activity was 600 MBq in cholangiocarcinoma (range 300–1160 MBq) and 760 MBq in hepatocellular carcinoma (range 525–2064 MBq). Tumour activity was assessed by scintigraphy at 2 and 7 days. As expected, no hepatocellular tumours showed selective localisation of the isotope. Five patients are surviving between two and 12 months after treatment, a one year survival of 57%. All have shown reduction in the size of their tumours. Two patients have died from disease progression and one from hepatorenal failure. One patient has undergone resection of two tumour nodules which proved to be totally necrotic. Only one patient with cholangiocarcinoma showed radiation activity in the region of the tumour, and is surviving 12 months from treatment. One other patient has survived 17 months from treatment. Five patients have died from tumour progression.

‘131I-Lipiodol’ treatment also seems to offer advantages over current non-surgical treatments for hepatocellular carcinoma in terms of cytotoxic potential and low toxicity. It does not prolong survival in cholangiocarcinoma.

Male-specific cytochrome P45011A2 is decreased in rat liver by interferon

P I CRAIG,* I MEHTA,* M MURRAY,* D MCDONALD,* AND G C FARELL† (Department of Medicine, Westminster Hospital, Sydney, Australia and Department of Biochemistry, University of Stockholm, Sweden) The aim of this study was to clarify the mechanism by which cytochrome P450 (P450) is decreased after interferon (IFN). In male rats, administration of recombinant rat IFNγ (r-rat IFNγ) 24 hours before sacrifice significantly decreased P450 levels to 78% of control. Regioselective microsomal androstenedione hydroxylation was then assessed to determine whether r-rat IFNγ selectively decreases the activities of individual P450 isoforms. Thus r-rat IFNγ produced a significant 40% and 17% reduction in androstenedione 7α- and 16α-hydroxylation respectively. Androstenedione 7α-hydroxylation was unaltered by r-rat IFNγ. Similar changes in the androstenedione hydroxylation pathways occurred after administration of naturally derived rat IFNβ.

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probably TGF-α, for EGF receptors in the liver.

Regenerating non-parenchymal cells inhibit hepatocyte proliferation in vitro

A C WOODMAN AND H J F HODGSON (Department of Medicine, RPHS, Hammersmith Hospital, Du Cane Road, W12 ONN) Background Evidence suggests that hepatic regeneration after partial hepatectomy is terminated by TGF-β expression in non-parenchymal cells. We have used co-cultures to study the control of parenchymal cells. Normal rat liver at 1 h after partial hepatectomy were co-cultured with non-parenchymal cells (NPC), isolated by collagenase perfusion and isopinic centrifugation, from either normal or regenerating livers of August rats. The mitogenic response of hepatocytes to epidermal growth factor (10 ng/ml) was assessed by [3H]-Tdr incorporation. Regenerating NPCs, but not normal NPCs, significantly inhibited (P<0.005; paired t-test) the proliferative response of the hepatocyte. In 153172 (19.016) 100/20000 hepatocytes with regenerating NPC compared to 244768 (16.504) with normal NPC (mean ±SEM, n = 5). When norepinephrine (NE) (10 -6 M), which reduces the expression of TGF-β1, was added to NPC cultures, NE was increased when hepatocytes are cultured alone, was added to hepatocytes co-cultured with regenerating NPC no significant difference (P>0.005; paired t-test) was seen in the degree of inhibition. In 153172 (19.016) 100/20000 NE was compared to 153173±19016 dpm–NE. This suggests that regenerating non-parenchymal cells may control hepatocyte proliferation in vitro by mechanisms independent of TGF-β.

Impaired extraction of atrial natriuretic peptide by perfused livers from rats with experimental cirrhosis

D C Gove, M Z Panos, and Roger Williams (Liver Unit, King's College Hospital and School of Medicine, O'Dentery, London SE5 9RS) In cirrhosis plasma concentrations of atrial natriuretic peptide (ANP) are often increased in the presence of sodium retention. Isolated perfused kidneys from rats with cirrhosis show respones to atrial natriuretic factor (J Hepatol 1989; 1: 70). The resistance may develop as a consequence of chronically raised circulating concentrations of ANP. We have used the isolated perfused liver of rats to examine the possibility that reduced hepatic clearnace contributes to the increased plasma ANP concentrations in cirrhosis. Cirrhosis was induced by weekly intragastric administration of carbon tetrachloride. Nine livers (5 cirrhotic and 4 control) were perfused via the portal vein using a single pass system with Krebs-Ringer bicarbonate buffer containing 10 mmol/l glucose and gassed with O2:CO2 (95:5% v/v). After a 10 min stabilisation period, controls were perfused with 10 pmol 125I-ANP (0.01–0.05 μCi/pmol). Samples of effluent perfusate were collected at 2 min intervals for 10 min. The livers were then perfused with ANP free medium for 5 min followed by perfusion with 50 pmol 125I-ANP and the sampling sequence was repeated. Hepatic clearance of ANP at 10 pmol/l was reduced in cirrhotic livers (4.96 ± 0.75 SEM) fmol min g l−1 compared to controls (7.98 ± 0.43) fmol min g l−1, p<0.02, Student’s t test. At 50 pmol/l ANP extraction was 32.7 ± (3.1) fmol min g l−1 in cirrhotic livers and 68.7 ± (9.0) fmol min g l−1, p<0.01, in controls. Liver weight 17-0 (1-7) g cirrhotic, 18-6 (2-1) g control and perfuse flow rate 35.3 (5-6) ml/min cirrhotic, 47.3 (3-2) ml/min control were not significantly different. Reduced extraction of ANP by the cirrhotic livers may contribute to the raised plasma ANP levels in cirrhosis. In turn, renal resistance to ANP may be a consequence of chronically raised circulating levels of ANP.

Hepatic perfusion index: are the flow changes due to portal venous obstruction

D M Hemingway, D Nott, S Grime, S A Jenkins, and T G Cooke (Department of Surgery, Royal Infirmary, Glasgow, and Royal Liverpool Hospital) The hepatic perfusion index (HP1) is raised in patients and experimental animals with occult and overt liver metastases due to a decrease in portal venous inflow (PVI). The aim of this study was to determine whether the decrease in PVI in animals with liver tumour resulted from portal venous stenosis, liver tumor pressure and flow, portosystemic shunting, and portal and splanchnic vascular resistance were measured at 2, 6, 10, and 20 days after the intraperitoneal inoculation of HSN sarcoma cells. Hepatic microcircuit was measured at 10 and over liver tumour at 20 days after inoculation. Portal flow fell significantly at 10 days (8.2 ± 0.61) (ml/min) p<0.05 and at 20 days (7.7 ± 0.7) (ml/min) was significant, compared to control animals (14 9 ± 0.5) (ml/min). Portal pressure did not rise significantly; portosystemic shunting was not seen. Portal vascular resistance was significantly raised in tumour-bearing rats (1-62 ± 0.43) mmHg/ml.min per g of liver compared to controls (0.55 ± 0.07) mmHg/ml per min. Splanchnic vascular resistance was also increased at 20 days (12.8 ± 2.4) mmHg/ml per min control value 7.0 (0.9) mmHg/ml per min p<0.05 (Kruskal-Wallis analysis of variance). The reduction in portal flow during the growth and development of liver tumour is unlikely to be due to portal venous obstruction since portal pressure does not rise, and portosystemic shunting is not seen. The rise in PVR and SVR suggest the presence of a circulating tumour-associated splanchnic vasocostructor.

Hepatic copper distribution in Wilson's disease and hepatic copper overload

D C Bingle, S K S Sral, and O Epstein (Departments of Protein and Molecular Biology and Medicine, Royal Free Hospital School of Medicine, London) The raised liver copper (Cu) levels found in Wilson's disease (WD) are thought to be responsible for hepatotoxicity, but Cu overload secondary to other liver disease is not toxic. It has been suggested that differences in hepatic distribution of the metal are responsible. We have used differential centrifugation and gel filtration to investigate the subcellular distribution of Cu in WD, hepatic Cu retention secondary to cholestasis, and normal liver. In all livers most of the postnuclear Cu was found in the supernatant and there were no gross differences in the distribution of Cu in the other fractions. In none of the livers were lysosomes a major site of Cu storage. Gel filtration of supernatants resolved three peaks in all livers. In livers with normal Cuy levels CuZn superoxide dismutase was the major Cu binder, while WD and livers with raised Cu >75% of the Cu was associated with metallothionein. In contrast to previous results, which suggest that Cu in WD is predominantly lysosomal, we have shown that most of the freely soluble copper is present in the supernatant, where it is associated with metallothionein and furthermore there are no clear differences between Cu distribution in WD and other diseases with raised Cu levels. It seems that gross differences in Cu distribution are not responsible for the toxicity of Cu retention in WD.

Evidence of peripheral autonomic denervation: a new disease in cirrhosis and association with cardiovascular autonomic dysfunction

M T Hendrickse, M J Nicholls,* and D R Trager (Departments of Medicine and Pharmacology, University of Sheffield) Autonomic dysfunction has been described in chronic liver disease using standard cardiovascular tests. Using a sensitive test of peripheral (postganglionic sympathetic) autonomic function, the occult cholelithiasis secretory test (SWTT) and sweat test we investigated peripheral autonomic function and its relation to cardiovascular tests in chronic liver disease (CLD). In the SWTT we intradermal injection of pilocarpine (14-9 pmol) in patients with cirrhosis and 6 healthy control subjects, one foot was heated to 40ºC and the other kept at room temperature. In 20 patients with chronic liver disease we measured the sudomotor response with a sensitive test of pilocarpine (14-9 pmol) injection. Pilocarpine injections produced a significantly greater response in the non-heated arm in patients with cirrhosis compared to controls (P<0.001). This increased pilocarpine response in the non-heated arm of patients with cirrhosis is consistent with peripheral autonomic denervation in cirrhosis. In 20 patients with chronic liver disease we evaluated peripheral autonomic function and its association with cardiovascular autonomic dysfunction and demonstrated that the existence of peripheral autonomic denervation is related to the presence of cardiovascular autonomic dysfunction in chronic liver disease. We have also demonstrated that the existence of cardiovascular autonomic dysfunction in chronic liver disease is related to the presence of peripheral autonomic denervation in chronic liver disease. These findings have important implications for the assessment of peripheral autonomic denervation in chronic liver disease. We have also demonstrated that the existence of peripheral autonomic denervation in chronic liver disease is related to the presence of cardiovascular autonomic dysfunction in chronic liver disease. These findings have important implications for the assessment of peripheral autonomic denervation in chronic liver disease.
Postoperative platelet and leucocyte counts were significantly higher than preoperative values (p<0.02). At six months postoperatively, respective platelet and leucocyte counts were 150 (16) and 6-8 (0-6) (×10^9/l; mean values (SEM)). Splenomegaly was reduced significantly, as shown by a 20 (3%) decrease in spleen size on ultrasonography (p<0.02).

Intractable ascites, present in all patients before transplantation, was no longer detectable at six months in all cases. Of the seven patients who had observed early leakage and varices preoperatively, only two still had grade III varices at six months, which further diminished to grade I at one year. The mean portal-caval pressure gradient, measured directly at four years, was 150 (16) with 14 (6) mm Hg, decreased with 54 (77%) after recirculation of the graft (p<0.05). In conclusion, a functioning auxiliary heterotopic liver graft effectively decompresses portal hypertension and reverses associated hypersplenemia.

Oesophageal staple transection (OST) as a salvage procedure following failure of acute injection sclerotherapy

P A MccORMICK, L GREENSLADE, F CARDIN, R E HOBBS, N McIntyre, and A K BURRIGIDES (Haemostasis and Liver Transplantation Unit, Royal Free Hospital School of Medicine, London NW3) We have shown that acute sclerotherapy and oesophageal staple transection (OST) are equivalent treatments in cirrhosis with acute variceal bleeding. The optimal treatment for patients who fail injection sclerotherapy has not been established. Over a 66 month period our policy has been to use OST in patients who fail acute sclerotherapy (a maximum of three injection sessions in five days): 18 cirrhotics received this treatment. The mean age was 57 years (range 38-80); 14 M/4 F; nine alcoholic, four cryptogenic, two primary biliary cirrhosis, and three others. Mean Pugh’s score on admission was 9-2 (±2-1) (3 grade A, 7 grade B, and 8 grade C). Ten patients died during the initial hospital admission from continued bleeding or liver failure, or both. Three patients were discharged but suffered early rebleeding and required shunt surgery at one, four, and eight months, after which two died. Six patients survived long term and have been followed up for a mean of 27 months (range 12-60). Mean Pugh’s score at discharge was 9-2 (±2-7). The high mortality in this series is less than the 73% reported in the literature. Nevertheless, it suggests that because of the underlying severity of liver disease in this subgroup failure of emergency sclerotherapy could be considered as an indication for urgent liver transplantation instead of surgery to treat bleeding.

Human bile analysis and gall bladder acid secretion in cholesterol and pigmented stones

J N PLEVRIK, P C HAYES, and I A D BOUCHER (Department of Medicine, Royal Infirmary, Edinburgh) Bile from eight gall bladders with pigmented (PGS) and 13 with cholesterol (XOLS) stones was analysed for pH, Ca²⁺, total calcium (TCa), dry total weight (DTW), lithogenic index (LI), cholesterol, and bile salts (BS). Fresh epithelia from 11 of these gall bladders (5 PGS, 6 XOLS) were mounted in the Ussing Chamber, perfused with Ringer-KGB and studied for 70 min. pH, PCO₂, and HCO₃ were measured at 0 and 70 min in the mucosal compartment.

Bile pH correlated with TCa (p<0.04, n=21), Ca²⁺/TCA (p<0.009, n=21), and DTW (p<0.03, n=21). DTW correlated with cholesterol (p<0.02, n=21) and inversely correlated with Ca²⁺/TCA (p<0.014, n=21). Bile from gall bladders with PGS had lower pH (6-90 (±0-1) vs 7-23 (±0-1) (XOLS) p<0.05), increased Ca²⁺ (1-92 (±0-3) vs 1-04 (±0-1) (XOLS) nmol/l), and increased bile acids by 65% of those treated with TCA (521-9 (±8-8) vs 26-04 (±3-9%), p<0.02). The acidification ability of the gall bladders with PGS was higher compared with XOLS (DpH -0-1 (±0-3); v -0-03 (±0-02), p<0.05).

Alkaline bile was found from low Ca²⁺ and high solids, mainly cholesterol and Ca. Gall bladders with PGS compared with those with XOLS secrete more acid and have more acidic bile with more Ca²⁺ available to form insoluble salts other than CaCO₃.

The natural history of undissolved gall bladder residues in patients with incomplete gall stone (GS) dissolution

J P M ELLUL, J R F WALTERS, D GLEASON, and R H DOWLING (Gastroenterology Unit, Guy’s Campus, UMDS of Guy’s and St Thomas’ Hospitals, London SE1 9RT) We and others find that 24–40% of GS patients treated with oral bile acid (SBA) and sensitive to bile acid contact solvents (MTBE) are left with residual debris which is said to cause no symptoms, but there are no published data to support this claim. We therefore studied the outcome in 54 patients, all of whom had had symptoms before treatment but who had become asymptomatic during treatment with oral UDCA (n=47) or UDCA+CDCA (n=7) despite being left with GS remnants (<5 mm max size in 56%), when the bile acid was removed.

When seen at follow up, 1–97 (median 30) months after stopping bile acids, 17 patients (32%) had undergone cholecystectomy (8 in the absence of symptoms, 7 for biliary colic, and 1 for pancreatitis). Four of these cholecystectomies had been performed within six months, but none more than 34 months, after stopping treatment. Of the remaining 37 patients, only two had developed recurrence of biliary colic, neither of whom had undergone cholecystectomy. By actuarial analysis, the annual incidence (6%) of biliary colic was linear, reaching 30% at five years. Thus by 36 months, 68 (SEM) (7%) of the patients did not undergo surgery while at 60 months 70 (9%) remained symptom free.

(i) The majority of patients with incompletely dissolved GS residues remains asymptomatic after stopping bile acid treatment. Therefore, (ii) a policy of observation only is justified in these patients.

Cholecdocholithiasis in postcholecystectomy pain evaluated by endoscopic retrograde cholangiopancreatography (ERCP)

G L CARLSON, M RHODES, S E STOCK, J LAVELLE, R LENDRUM AND C W VENABLES (Departments of Surgery, Radiology and Medicine, University of Newcastle upon Tyne) ERCP plays an important part in the management of patients with persistent symptoms after cholecystectomy. Individual predictive factors for the presence of common duct stones in such patients have not been investigated, and in particular, the predictive value of a previous common duct exploration is unknown. Between 1976 and 1989, 46 consecutive ERCPs were undertaken for persistent postcholecystectomy symptoms, from three months to 15 years after the operation in patients ranging from 23 to 85 years of age.

Patients were grouped according to whether the common bile duct had been explored at operation and as to the presence of any additional abnormality. Patients were divided into those with no abnormality (n=15), acute duct stenosis, and abnormalities. Successful cannulation of biliary and pancreatic ducts was performed in 384 patients (82%). Abnormal findings were recorded and a comparison of proportions made to the evaluation of the predictive value of previous common duct exploration and abnormalities in addition to abdominal pain. The presence of any abnormality (p<0.001) or a history of common bile duct exploration (p<0.001) was of highly significant predictive value for the presence of common duct stones at ERCP. Furthermore, a history of duct exploration was of predictive value even in those patients with an abnormality in addition to acute duct stenosis (p<0.05), while the reverse was true in the case (p=0.02). A history of common duct exploration is therefore highly significant in patients with postcholecystectomy symptoms and should direct attention to early ERCP.

Postendoscopic serum bile acid (SBA) test in healthy subjects and in primary biliary cirrhosis (PBC) patients

A FLORENI, M PLEBANI,* D FAGGIAN,* S GAZZONI, T BERNARD, and M CHIARAMONTE (Department of Gastroenterology, Institute of Internal Medicine and Department of Clinical Biochemistry, *University of Padova, Italy) The aim of this study was to evaluate a modified postendoscopic SBA test with and without a chelating agent in normal subjects and in PBC patients. The kinetics of total SBA with a standard meal was carried out on two successive days after overnight fasting in 19 PBC patients (6 stage I, 9 stage II, and 4 stage IV) with six healthy controls. Day 1: serum samples were obtained at 0, 90, and 240 minutes after a standard meal (Bik Gulden, Italy); day 2: same protocol but with a bile acid chelating agent (DEAE-Dextran, 1500 mg po) 20 minutes before the standard meal. Total SBA were measured by RIA (Becton Dickinson, Orangeburg, USA).

In normal subjects we found a decrease of the SBA levels at minimum time (1 hour) after DEAE-Dextran ranging from 16-5 to 82-5% (mean 56%). In PBC we observed two types of kinetics: (i) 13 patients had SBA curves with a postendoscopic peak similar to that observed in the controls. All these showed a decrease in the bile acid peak after DEAE-Dextran (mean 58%, range 22-5–95-5%); (ii) six patients (all stage IV) do not show the postendoscopic peak and none showed any response to DEAE-Dextran.

Postendoscopic SBA test used with and without DEAE-Dextran indicates the presence of two subpopulations in PBC: one with postendoscopic increase of SBA and sensitive to bile acid chelating agent and the other, without this response to the standard meal, that does not respond to bile-sequestering agent.
Exfoliative cytology of biliary strictures is valuable

M Rhodes, R M Coon,* T W J Lennard, and A Allen* (Departments of Surgery and Physiological Sciences,† Medical School, Newcastle upon Tyne) Cholesterol nulceation is an important factor in the formation of gall stones. Hypersecretion of gall bladder mucus is associated with cholesterol nulceation and subsequent gall stone formation in animal models. Aspirin, which inhibits mucus secretion elsewhere in the gastrointestinal tract, prevents gall stone formation in animals and reduces gall stone recurrence in humans. This study examines the effect of aspirin on mucus synthesis in human gall bladder explants.

Six explant cultures were treated with H-glucosamine (74 kBq/mg) for 24 hours at 37°C, with or without acetylsalicylic acid. Mucin and other glycoproteins were isolated by papain digestion (72 hours) and exhaustive dialysis to remove non-incorporated radioactivity and digested protein.

H-glucosamine was readily incorporated into glycoprotein; 19993 to 34423 (n=8) counts per gram wet tissue weight. Gall bladder wet weight had a lower DNA content (r=0.996) and total tissue glycoprotein (r=0.98). Fractionation of glycoprotein on Sephrose 4B showed radioactivity was incorporated into two glycoprotein peaks, one eluting with standard gall bladder mucin (59% of total radioactivity), the other of low molecular weight and probably membrane glycoprotein. Acetylsalicylic acid (230–666 μg/ml) significantly reduced total H-glucosamine incorporation (43–89%), p<0.01 (unpaired t test).

This study provides a method for measuring human gall bladder mucus synthesis and shows its inhibition by acetylsalicylic acid at concentrations not incompatible with a therapeutic dose.

Mechanism of acid secretion in the bovine gall bladder: evidence of Na/H exchange

J N Plevris, P C Hayes, and J D Boucher (Department of Medicine, Royal Infirmary, Edinburgh EH3 9YW) There is increasing evidence that the gall bladder epithelium is capable of secreting acid. The aim of this study was to investigate in vitro the mechanism of acid secretion in normal gall bladder epithelium. Eight fresh bovine gall bladders were studied. The isolated gall bladder was cannulated and perfused with physiological solutions, placed in a beaker with Ringer solution, and suspended from a hook; 95% O2, 5% CO2 was bubbled into the beaker. The pH was continuously monitored in the luminal fluid for 60 minutes. When normal saline (NS) 0.9% was used in the luminal side of the gall bladder, a significant decrease in the pH was observed between 0 and 60 minutes (6.81±0.15 v 6.53±0.12, p<0.01, n=4). The addition of amiloride (100 μM), which is a specific Na+/H+ inhibitor, in the luminal fluid appeared to inhibit acidification. Reinroduction of NS 0.9% solution in the luminal side resulted in further decrease of the pH. The use of sodium free luminal solutions inhibited acidification.

The bovine gall bladder mucosa is capable of secreting acid. The most likely mechanism seems to be an apical Na+/H+ exchange in the epithelial cell.

The role of accessory sphincteroplasty in the management of pain associated with pancreas divisum

R C G Russell and B A Theis (Department of Gastroenterology, The Middlesex Hospital, London) Of 59 consecutive patients referred between 1976 and 1990 with pancreatic pain and pancreas divisum, 24 patients underwent accessory sphincteroplasty (AS). The indication for AS in all cases was severe pain causing major disruption of lifestyle, in the absence of focal disease. There were 18 women and six men (median age 34 years), of whom 11 had unremitting chronic pain of variable intensity (CP), the remainder describing recurrent attacks, being pain free in between (RP). The median length of history was 5.5 years (range 1–20).

Preoperatively, 12 patients had undergone 18 laparotomies and five patients underwent non-operative procedures for their pain. Two patients were diabetic, 12 had steatorrhoea, and 23 had lost weight: a median of 9 kg in weight (range 3–20 kg). There was no gross mortality, and during a median postoperative stay of 12 days (range 7–46) seven patients had a total of 10 minor complications. Eight patients (7 CP, 1 RP) required further surgery at a median of 14 months postoperatively (range 3–40). Of the remaining 16 patients, Visick I or II status at 6 months and 1, 3, and 5 years was: 9/10, 9/10, 9/7, 7/5 in patients with RP, and 2/4, 2/4, 2/3, 2/3 in those with CP. One patient developed diabetes and another steatorrhoea during a median follow up of 36 months (range 3–90).

Sphincteroplasty is of value in the management of patients with recurrent but not chronic pain associated with pancreas divisum and a successful drainage procedure seems to preserve exocrine and endocrine function.

Inhibition of mucus synthesis by aspirin in the human gall bladder

Preoperatively, 12 patients had undergone 18 laparotomies and five patients underwent non-operative procedures for their pain. Two patients were diabetic, 12 had steatorrhoea, and 23 had lost weight: a median of 9 kg in weight (range 3–20 kg). There was no gross mortality, and during a median postoperative stay of 12 days (range 7–46) seven patients had a total of 10 minor complications. Eight patients (7 CP, 1 RP) required further surgery at a median of 14 months postoperatively (range 3–40). Of the remaining 16 patients, Visick I or II status at 6 months and 1, 3, and 5 years was: 9/10, 9/10, 9/7, 7/5 in patients with RP, and 2/4, 2/4, 2/3, 2/3 in those with CP. One patient developed diabetes and another steatorrhoea during a median follow up of 36 months (range 3–90).

Sphincteroplasty is of value in the management of patients with recurrent but not chronic pain associated with pancreas divisum and a successful drainage procedure seems to preserve exocrine and endocrine function.

Acidosis and lyssolecithin production by bacteria disrupt the vesicle and may be the precipitating event in gall stone formation.
Endoscopic therapy in the management of benign biliary strictures

P I CRAIG, S J WILLIAMS, A R W HATFIELD, D AVANITIDES, M NG, A C SMITH, and R C G RUSSELL (Departments of Gastroenterology and Surgery, The Middlesex Hospital, Mortimer Street, London) The endoscopic management of benign biliary duct strictures was reviewed in 36 patients (17 M, 17 F; median age 60 years (range 29–81)) seen between 1983 and 1989. Twenty-eight patients had had previous biliary surgery (cholecystectomy (27) with common bile duct (CBD) exploration (12), cholecodochoduodenostomy (3)) two days to 29 years previously. The clinical presentation was jaundice (21), pain (19), and sepsis (7). Strictures were located in the low CBD (9), mid-CBD (16), or hilum (11). Endoscopic treatment was attempted in 32 patients, being technically successful in 27. Balloon dilatation as initial treatment was successful in five of eight patients; the three failures were subsequently stented. Endoscopic stents were primarily inserted in a further 19 patients with an initial good result in 18. Stent changes (median 3; range 1–15) were necessary in 13 of the 22 stented patients. Stents were removed from 11 patients; eight of whom remained well median 8 months (range 2–24) later; symptom recurrence necessitated stent reinserition in the three others. Three of 32 endoscopically-treated patients died two days–40 months after presentation (biliary cirrhosis 2; cholangitis 1).

Endoscopic treatment is the treatment of choice in patients with benign biliary strictures if surgery is undesirable.

Gall stone index: a predictor of outcome for common bile duct stones treated by endoscopic sphincterotomy?

A LAURI, R C HORTON, A K BURROUGHS, and J S DOOLEY (Hepatobiliary Unit, Royal Free Hospital and School of Medicine, London NW3) Common bile duct stones (CBDS) can be successfully removed by endoscopic sphincterotomy (ES) in 95% of patients. However, no analysis of factors contributing to failure has been made. We have studied the outcome of 100 consecutive patients with CBDS (M:F 55:45, mean age 69±5 years). Seventy five patients underwent ES, without any mortality or complications requiring emergency surgery. Clearance of CBDS was successful in 45 of the 75 patients (60%). Success depended upon stone size and number. A total of 174 stones were detected with mean diameter 14 mm (corrected for x ray film magnification, range 3–35 mm). Successful clearance as a function of size and number was:

\[ \text{<9 mm, 93–3%; 10–19 mm, 44–3%; } \geq 19 \text{ mm, 20%; 1 stone, 83%; } \geq 2 \text{ stones, 56%.} \]

Since size alone was not a powerful discriminator of success, we have calculated a stone index (multiplying stone diameter (mm) by number of stones present. There was a highly significant difference in index between the group with successful v failed clearance (19·6 (2·1) vs 50·0 (6·9); p<0·001). The positive predictive value for clearance of the index was 81%.

Successful common bile duct clearance depends upon gall stone size and number. Success may be predicted by calculating a simple index incorporating both variables. Such an analysis may provide a method of identifying patients in whom failure is likely, thereby allowing an earlier decision to use other methods such as stent insertion.

Should endoscopic biliary stenting be the initial manoeuvre in acalculous biliary obstruction?

J J EARNSHAW, C TEASMALE, and D E BECKLY (Freedom Fields Hospital, Plymouth) Forty two patients with acalculous biliary obstruction had a diagnostic ERCP with subsequent insertion of a straight 10F biliary endoprosthesis across the stricture. There were 21 men and 21 women, median age 70 years (40–86 years). The majority (64%) had pancreatic carcinoma, but 21% had malignant obstruction at the porta hepatitis. Jaundice was relieved in all but three of the 42 patients, each having obstruction at the porta hepatitis. Five patients (12%) died within a few days of stent insertion. ERCP may have contributed to two deaths, one from biliary peritonitis and one from alcoholic pancreatitis causing biliary obstruction. Three patients with advanced malignancy deteriorated rapidly and died from bronchopneumonia. Four patients (10%) had complications; three had pyrexia due to possible ductal perforation. All settled with conservative treatment. One patient had a haematemesis requiring transfusion. After stent insertion, nine patients were submitted for potentially curative surgery including four Whipple’s operations. Median hospital stay in the endoprosthesis only group was six days (2–32 days). Late complications including cholangitis (25%) and recurrent jaundice (40%) required antibiotic treatment or stent replacement, or both. In two patients stent reintervention was impossible and surgical bypass was necessary. One patient developed gastric outlet obstruction and needed a gastroenterostomy. Median survival in the endoprosthesis group was 11 weeks (2–34 weeks). Survival after surgery was 40 weeks (4–80 weeks) with two longterm survivors.

ERCP and insertion of endoprosthesis is a useful initial manoeuvre in acalculous obstructive jaundice, being both diagnostic and therapeutic. Subsequent evaluation for curative surgery is not precluded and in selected cases worthwhile palliation may be achieved by stenting alone.