The British Society of Gastroenterology

The 1985 Spring Meeting of the British Society of Gastroenterology was held under the Presidency of Professor Eric Blair at the University of Sussex from 20–22 March 1985. Abstracts of the 157 oral or poster presentations included in the scientific sessions are printed below.

ENDOSCOPY

T1
An audit of surgical and bag dilatation treatment of achalasia

J F Mayberry, H I Smart, and M Atkinson (University Hospital of Nottingham, Nottingham) Between 1959 and 1983 56 people from the Nottingham area presented with achalasia and 49 received treatment. In 26 the initial treatment was with a pneumatic bag; in one case a hydrostatic bag was used. Twenty two patients underwent a surgical myotomy. Patients treated endoscopically (mean age 52 years) were 10 years older than those treated surgically (mean age 42 years). Six of the seven patients who received no treatment and all who died were diagnosed before the introduction of pneumatic dilatation in the area in 1977. Surgery resulted in a significantly longer stay in hospital (mean 24 days; range 7–162 days) than endoscopic dilatation (mean five days; range 2–12 days; t=2.7; p<0.005). Twenty seven surgical myotomies were performed on 22 patients. Ten of the procedures were complicated by such problems as chest infections, empyema, and oesophageal strictures. Fifty four endoscopic dilatations were performed on 27 patients and only two minor complications were recorded – a mucosal tear and a chest infection.

Endoscopic pneumatic or hydrostatic dilatation is a safe procedure that can be performed on patients of any age with minimal complications. It can be safely repeated and requires only a brief stay in hospital. It should be offered as the first line of treatment for achalasia. Surgical myotomy should only be considered after a minimum of three bag dilatations have failed to achieve symptomatic relief.

T2
Endoscopic treatment of pyloric stenosis

S L Grainger, D G Maxton, and R P H Thompson (Gastrointestinal Laboratory, The Rayne Institute, St Thomas’ Hospital, London) Therapeutic procedures have extended the value of upper gastrointestinal endoscopy, but some conditions remain in the surgeon’s domain. We have recently seen two elderly patients with benign symptomatic pyloric stenosis who were unfit for gastric surgery. Using a balloon catheter we dilated the pylorus and relieved pyloric obstruction.

A wide channel endoscope (Fujinon, UGICT) was positioned in the gastric antrum after atropine and diazepam premedication. A deflated 6 mm maximum diameter balloon dilatation catheter (Meditech) was passed through the biopsy channel of the endoscope and under direct vision sited with the midpoint of the balloon in the pylorus. The balloon was fully inflated, left in position for one minute and pulled back while still inflated. The procedure was repeated with an 8 mm balloon catheter. Pyloric dilatation was carried out twice at an interval of six months in one patient, who then has been free of symptoms for a year. In the second patient, who also has a tight benign oesophageal stricture, the pylorus has been dilated every two to three months.

Wider dilatation of the pylorus could be achieved with custom-made larger balloons that could be passed through the endoscopic channel, but with 8 mm dilatation both patients are free of vomiting and have gained weight. Endoscopic balloon dilatation of the pylorus should be considered in patients with pyloric stenosis who are unfit for surgery.

T3
Prospective randomised study of ERCP

Prospective randomised study of ERCP

A541

and endoscopic sphincterotomy (ES) in acute pancreatitis

N D Slater, N London, J P Neoptolemos, D L Carr-Locke, and D F Fossard (Departments of Surgery and Gastroenterology, Leicester Royal Infirmary, Leicester) It has been suggested that early surgical decompression of the biliary tree in acute gall stone pancreatitis may accelerate resolution of the disease. Emergency surgery carries a high mortality and ES is an alternative method. In a prospective study 40 patients have so far been randomised and graded on admission to ERCP (20) or conventional treatment (20). If common bile duct stones were found at ERCP, ES and stone extraction was attempted. ERCP was performed within five days in all patients and within three days in 17. Six had CBD stones, ES and stone extraction was successful in four, partially successful in one, and a failure in one. Gall stone pancreatitis was confirmed in 13 of the ERCP group and 16 of the conventional group. Of four severe cases in the conventional group one died whereas there were no deaths in three severe cases in the ERCP group. Six who underwent ERCP and three who were treated conventionally developed complications of their pancreatitis. There were no complications of either ERCP or ES.

Endoscopic sphincterotomy may be safely and successfully undertaken during attacks of acute pancreatitis and offers potential advantages in the management of patients with CBD stones. Only analysis of the larger trial will show significant benefit over conventional treatment.

T4

10 French gauge straight biliary prostheses perform significantly better than 8 French gauge pigtail prostheses
Inflammatory bowel disease
T5-13

Pathology of iatrogenic ileal strictures caused by non-steroidal anti-inflammatory drugs

J LANG, J BJARNASON, A J LEVI, AND A B PRICE (Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex) Long term treatment with non-steroidal anti-inflammatory drugs (NSAID) is associated with migratory abnormalities of

11Indium labelled leucocytes to the distal ileum. This might represent a terminal ileitis but to date histopathological confirmation is lacking. From 555 small bowel resections received in the department in the past 10 years we have confidently identified three patients with 'idiopathic' ileal strictures who in retrospect are best explained as complications of NSAID administration. One patient was on long term phenylbutazone for back pain and the two others, both with rheumatoid arthritis of at least 15 years duration, had received various NSAID preparations. The initial presentation of two was with obstruction that was believed to be Crohn's disease of the terminal ileum on radiological examination. A third patient had multiple distal ileal strictures found incidentally at autopsy. The microscopy of the three cases suggested an evolutionary pattern from initial mucosal ulcerative lesions, through a phase of transmural inflammation and finally a stricture dominated by submucosal fibrosis. Granulomas, fissuring ulceration and evidence of an arthritis were all absent.

This study supports the implications of the work with 11Indium labelled leucocytes that NSAID do indeed cause ileal inflammation and ultimately strictures. The appreciation of this pathology is important for failure to recognise such cases easily leads to a mistaken diagnosis of Crohn's disease. Furthermore a review of the literature suggests that many patients with alleged inflammatory bowel disease may also have received non-steroidal anti-inflammatory drugs.

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ADS capsules 1g bd (15) or placebo (15) for six weeks. All other therapy was ceased. Patients were reviewed weekly, and plasma, urine and faecal concentrations of ADS and its metabolites determined by HPLC. Sigmodoscopy and biopsy was repeated at six weeks. The groups were similar in age, duration of disease and duration of current attack.

Four patients receiving placebo and two receiving ADS were withdrawn because of diarrhoea. Five patients known to be allergic to SAZ tolerated ADS well. Good clinical response was found in six patients receiving ADS and two receiving placebo (p=0.09). Plasma concentrations of ADS were higher (p<0.05) in those patients who improved. Faecal ADS, 5-ASA and acetyl 5-ASA varied widely and showed no correlation with response.

We conclude that ADS showed an advantage over placebo which needs to be confirmed by larger studies. Plasma ADS concentrations were higher in responders. ADS was safe in SAZ sensitive patients but appeared to cause watery diarrhoea in two patients.

Increased formation of leukotriene B4 and sulphinpropionate-leukotrienes by rectal mucosa of patients with Crohn's disease and ulcerative colitis

B M PESKAR, K W DREYLING, B MAY, M THIEVES, K MORGENROTH, H GOEBELL, AND B A PESKAR (Department of Medicine, University of Essen, Essen, and Departments of Medicine 'Bergmannsheil', Pathology and Pharmacology, Ruhr-University of Bochum, Bochum, FRG). Leukotrienes (LT) have pronounced biological activities. While LTB4 is a potent chemoattractant, the sulphinpropionate (SP)-LT C4, D4, and E4 contract GI smooth muscle, induce vasconstriction and plasma exudation and enhance mucus production. We have investigated formation of LTB4 and SP-LT by normal rectal mucosa and mucosa of patients with Crohn's disease (CD) and ulcerative colitis (UC).

Azidosalicylate (ADS) in the treatment of ulcerative colitis (UC): a controlled clinical trial and assessment of drug disposition

D J HETZEL, F BOCHNER, D M IMHOFF, G E GIBSON, R J FITCH, R HECKER, J LABROOY, AND D J C SHEARMAN (Royal Hospital Adelaide, Adelaide, South Australia) Sulphasalazine (SAZ) is an effective treatment for ulcerative colitis but side effects are common. Azidosalicylate is a sulphonamide free analogue of SAZ which is split by colonic bacteria at the diazo bond into two molecules of 5-aminosalicylate (5-ASA). The present study assessed the efficacy, safety and disposition of ADS in patients with ulcerative colitis, in a double blind trial.

Thirty patients with mild to moderate left sided UC were randomly allocated to ADS capsules 1g bd (15) or placebo (15) for six weeks. All other therapy was ceased. Patients were reviewed weekly, and plasma, urine and faecal concentrations of ADS and its metabolites determined by HPLC. Sigmodoscopy and biopsy was repeated at six weeks. The groups were similar in age, duration of disease and duration of current attack.

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T6

Azidosalicylate (ADS) in the treatment of ulcerative colitis (UC): a controlled clinical trial and assessment of drug disposition

D J HETZEL, F BOCHNER, D M IMHOFF, G E GIBSON, R J FITCH, R HECKER, J LABROOY, AND D J C SHEARMAN (Royal Hospital Adelaide, Adelaide, South Australia) Sulphasalazine (SAZ) is an effective treatment for ulcerative colitis but side effects are common. Azidosalicylate is a sulphonamide free analogue of SAZ which is split by colonic bacteria at the diazo bond into two molecules of 5-aminosalicylate (5-ASA). The present study assessed the efficacy, safety and disposition of ADS in patients with ulcerative colitis, in a double blind trial.

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pressed as immunoreactive LTC₄.

In the absence of ionophore normal rectal mucosa synthesised (ng/g ww 20 min, mean±SEM) 1.8±0.3 LTC₄ (n=28) and 0.9±0.1 LTC₄ (n=33). Muscosa of patients with CD released 5.2±3.1 LTC₄ (p<0.025, n=4) and 3.1±1.0 LTC₄ (p<0.001, n=11). Muscosa of patients with UC formed 3.6±0.1 LTC₄ (n=2) and 9.7±3.7 LTC₄ (p<0.001, n=10). In the presence of ionophore normal rectal mucosa synthesised 5.1±0.9 LTC₄ (n=28) and 5.4±1.2 LTC₄ (n=33). Muscosa of patients with CD formed 13.2±4.0 LTC₄ (p<0.01, n=4) and 23.6±6.1 LTC₄ (p<0.001, n=11). Muscosa of patients with UC released 17.0±3.0 LTC₄ (n=2) and 33.2±7.0 LTC₄ (p<0.01, n=10). Nordihydroguaiaretic acid (3-3 µg/ml) but not indomethacin (1 µg/ml) significantly reduced mucosal release of LTC₄ and LTc₄, 5-arachidonic acid (2-5 mM) inhibited formation of LTC₄ by 63% (p<0.025, n=6) and of LTC₄ by 38% (p<0.05, n=7).

The results show increased basal release of LTB₄ and SP-LT by rectal mucosa of patients with active CD and UC indicating the presence of endogenous stimuli of LT formation. In addition, mucosa of CD and UC shows increased responsiveness to an exogenous stimulus, ionophore A23187. Muscular LT formation is decreased by inhibitors of lipoxigenase, but not by indomethacin. In view of these results, clinical trials with potent lipoxigenase inhibitors should clarify the role of increased LT formation in the pathogenesis of CD and UC.

T9 

Faecal leukocytosis in acute gastroenteritis

T KORDOSSIS AND G E GRIFFIN (Department of Communicable Diseases, St George’s Hospital Medical School, London) Faecal leukocytosis (FL) is an indicator of intestinal inflammation and is thought to occur in bacterial but not viral acute gastroenteritis (AG). Acute gastroenteritis is defined as acute self-limiting diarrhoeal disease (<10 days). The aim of this study was to correlate FL with the presence of enteropathogens isolated from the stools of AG patients.

Diarrhoeal AG stool specimens (n=969) were submitted to routine microbiological examination. A methylene blue stained wet mount preparation of each stool was examined for polymorphonuclear leukocytes (PMN). Faecal leukocytosis was defined as >10 PMN in 10 high power microscope fields. Stool from patients with ulcerative colitis (n=10) and patients with no GI disease were positive and negative controls.

Enteropathogens (EP) were detected in 55% of stools; Bacteri a 242 (25%), Viruses 52 (5-3%) and parasites 47 (4-8%). Faecal leukocytosis was detected in 60% of stools with bacterial EP. 5% stools with viral EP and 17% stools with parasite EP. Faecal leukocytosis was detected in 32% of stools with no demonstrable EP. These results show that FL is a response to bacterial but not viral AG. The correlation is, however, not absolute and stool microscopy for FL only serves as a crude screening test. The presence of FL in 32% of stools in which no EP was detected suggests the presence of as yet unknown bacterial enteropathogens.

T10

Changes in ileal absorption after total colectomy

D G NASMYTH, K BROOKS, I BURKINSHAW, N S WILLIAMS, AND D JOHNSTON (The University Departments of Surgery and Medical Physics, The General Infirmary, Leeds) The frequency of defaecation after total colectomy and ileoanal anastomosis is reduced by an ileal reservoir, but compared with an ileostomy, ileal absorption may be impaired by bacterial proliferation and the development of partial villous atrophy. Ileal absorption was therefore investigated in 10 controls with no known gastrointestinal disease and 23 patients who had undergone colectomy for ulcerative colitis or adenomatous polyposis; 11 with an ileostomy and 12 with an ileal reservoir. The whole body retention (WBR) of a γ labelled synthetic bile acid; 75Se taurocholic acid (SeHCAT), was measured on a whole body counter at 0, 2 and 168 hours after oral administration (40 Kbq) in all subjects and at intermediate times in 16 to determine excretion rates. SeHCAT is similar to endogenous bile acids in respect of absorption, enterohepatic circulation and excretion. Its retention which correlates with faecal excretion is a sensitive index of ileal function.

Whole body retention in the reservoirs (9-5%, 3-18% median and range) was not significantly different from that in ileostomies without ileal resection (n=9) (15%, 3-36%), but both were significantly less than the controls (33%, 13-15%) p<0.01, p<0.05, Mann-Whitney. Two ileostomies had an ileal resection (>30 cm) and had WBR of 0% and 1%. The results suggest that ileal absorptive capacity is reduced in the reservoirs, but is no worse than in ileostomies, and better than that after modest ileal resection.
T11
Is the pattern of idiopathic inflammatory bowel disease different in the elderly?
SANJEEV GUPTA, S H SAVERYMUTTU, A KESHAVARZIAN, AND H J F HODGSON (Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Ducan Road, London) Surveys of inflammatory bowel disease in elderly patients have suggested a female preponderance, a more severe clinical course than in younger people, with a higher incidence of toxic dilatation, perforation, haemorrhage, and severe rectal disease, and frequent recourse to surgery. We studied the 31 patients with ulcerative colitis and Crohn's disease presenting to us in their seventh, eighth or ninth decades over a five year period, 12.4% of the total cases of idiopathic IBD seen in that time. The sex incidence was similar (14 men, 17 women), with 55% of patients fulfilling criteria for UC and 45% for CD. The disease distribution was similar to that seen in other patients (UC proctitis seven, left-sided six, pancolitis four, CD rectal one, left-sided three, pancolitis four, ileocolonic three, small intestinal three). No patients with UC had toxic dilatation or perforation, and all responded to medical therapy, with one death due to drug-induced agranulocytosis. Among patients with CD, the severe complications were two cases of fulminant colitis (one successfully treated by colectomy, one patient dying suddenly during medical treatment), one liver abscess requiring surgery, and one case of multiple fistulae requiring surgery. In CD 3/14 patients required surgery, and 3/14 patients died (fulminant colitis one, multiple fistulae and mesenteric vascular occlusion one, unrelated medical condition one). Whilst elderly patients may tolerate repeated surgery poorly, and are at risk from unassociated medical conditions, the clinical presentation and course of inflammatory bowel disease did not seem different to or more severe than that seen in younger individuals.

T12
Autoimmune variant of protracted diarrhoea of infancy: how is tolerance to self enterocytes lost?
R MIRAKIAN, C A RICHARDSON, P MILLA, J WALKER-SMITH, AND G F BOTTAZZO (The Middlesex Hospital, Department of Immunology, Hospital for Sick Children, Gt Ormond Street, and Queen Elizabeth Hos-pital for Children, London) Protracted diarrhoea of infancy (PDI) is an heterogeneous syndrome with a high mortality rate. Its pathogenesis is still unclear despite intensive investigation. Circulating autoantibodies to enterocytes (EC-Ab) have been detected by indirect IFL in a group of children (16/27) affected by this syndrome. A strong association with polyendocrine diseases (7/16) and with organ and/or non-organ specific antibodies (15/16) has been found in these patients. In vivo immune complex deposition along the basement membrane of the mucosal epithelium and/or the apical border of the enterocytes have been seen in 6/8 jejunal biopsies by direct IFL. The data confirm an autoimmune variant of PDI in spite of the unusual finding of autoimmune diseases in childhood. The expression of HLA class II molecules on the enterocytes of eight pathological jejunal biopsies was studied and compared with naturally occurring HLA-DR staining on two control specimens in order to understand how immunological tolerance might be lost. Monoclonal antibodies to the non-polymorphic region of HLA-DR molecules and to specific HLA-DR, DP, DQ loci were applied and revealed by IFL technique. Increased expression of HLA-DR molecules (non-polymorphic region) in the villi and a de novo expression in the crypts was present in 4/8 jejunal biopsies. In the same biopsies also, specific HLA-DP molecules were de novo expressed both in the epithelium and in the crypts. a phenomenon never observed in the normal tissues. We postulate that the loss of tolerance to self-enterocytes could be due to an aberrant expression of HLA-DR molecules on the enterocytes which would present self antigens to 'non-educated' T lymphocytes.

T13
Defective suppression in the autologous mixed lymphocyte reaction in patients with Crohn's disease
D KELLEHER, A MURPHY, C FEIGHERY, C A WHELAN, P W N KEELING, AND D G WEIR (Departments of Clinical Medicine and Immunology, Trinity College, and St James' Hospital, Dublin, Eire) Crohn's disease (CD) patients have been reported to have a defect in suppressor T cell function. As no specific antigen is recognised in CD, we studied the general of help and suppression using the autologous mixed lymphocyte reaction (AMLR).

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In the AMLR purified T cells are exposed to DR+ cells (B cells or monocytes) from the same donor in a one week culture. These T cells are designated autoreactive T cells (Ta) and function primarily as suppressor cells. Their ability to help is assessed by a further incubation with purified B cells with assessment of Pokeweed mitogen (PWM) driven immunoglobulin synthesis. Suppressor function is assayed by culturing with B cells and fresh T cells from which suppressor cells have been removed by irradiation. The reduction in PWM driven immunoglobulin production on addition of Ta allows calculation of percentage suppression.

Nine patients with CD not receiving corticosteroids were studied. Four patients had active disease and five were asymptomatic. Ten healthy age matched controls were also studied. T lymphocytes from CD patients had markedly defective suppression of IgG synthesis when exposed to both B cells (~6±4% vs 88±3%, p<0.01) and monocytes (~2±45% vs 87±3%, p<0.001) and of IgM synthesis B cells (71±6% vs 36±6%, p<0.001) and monocytes (70±9±5% vs 41±11%, p<0.02). Help was enhanced for IgM synthesis and B cell activated T lymphocytes (75±6±5% vs 50±10%, p<0.05) but not for monocyte activated T lymphocytes. The difference for IgG synthesis was not significant. Defective suppression was more marked in patients with inactive disease.

In conclusion we have found a consistent defect in the generation of suppression by the AMLR in patients with CD. This may be of pathogenic significance in the development of cell mediated tissue damage. This phenomenon is unlikely to be because of the inflammatory response as it is seen in inactive patients. Increased DR display with disease activity may increase generation of suppression.

GASTRODUODENAL

T14-30

T14
Antibody response to gastric Campylo-bacter-like organisms
B J RATHBONE, S SHIRES, J I WYATT, B WORSLEY, L K TREJDOSEWICZ, R V HEATLEY, AND M S LOSOWSKY (Department of Medicine, St James's University Hospital, Leeds, Department of Pathology, Depart-
The association between chronic gastritis and Campylobacter-like organisms (CLO) is now well documented. It is unknown, however, whether these organisms are merely commensal or do have a pathogenic role. Little is known about the immune defences to gastric CLOs, and elucidation of this may help determine their significance.

Serum antibodies were studied in 30 dyspeptic patients. All patients were endoscoped and detailed antral and body histology, including Warthin-Starry staining was carried out (19 patients were CLO positive by silver stain histology). Initial investigation by immunofluorescence on formalised whole bacteria smears demonstrated low but significant antibody titres (up to 1/1000) in all patients. Using a quantitative ELISA (enzyme-linked immunoassay) with whole glyoxal-immobilised CLOs obtained from microaerophilic broth culture, IgG, IgA and IgM antibody titres were measured.

All patients had demonstrable serum antibodies to CLOs. The bacteria positive patients had significantly higher IgG titres than the bacteria negative patients (p<0.01). The IgM and IgA were also higher in many of the bacteria positive patients.

These studies show antibodies to CLOs in all patients tested, both in those with and without gastritis and in bacteria positive and negative patients. The significantly raised serum IgG concentration in bacteria positive patients suggest that viable gastric CLOs are capable of evoking a systemic humoral immune response. Immune defences at the gastric mucosal surface may hold the key to the presence or absence of this ubiquitous organism.

T15
Clinical and experimental significance of the newly discovered activity of baclofen (PCP-GABA) as a stimulant of gastric acid secretion

S PUGH, M R LEWIN, S WILLIAMS, T BARTON, AND G CLARK (Department of Surgery, Rayne Institute, University College, London) Baclofen (PCP-GABA) is widely used as an antispasmodic agent under the trade name Lioresal (Ciba-Geigy) but it also has another unexplored action, in that it stimulates gastric acid secretion via the vagus nerve in animals. The dose which causes acid stimulation is within its therapeutic range (15-60 mg/day) and is safe, but hitherto unassessed, in man. We present our results of its use in man compared with pentagastrin and also modified sham feeding (MSF). Standard methods were used to assess acid secretion stimulated by MSF, pentagastrin (6 μg/kg IM) and baclofen (0-6 mg/kg iv – mean dose 38-2 mg) in 10 normal volunteers (Ethics Committee approved). Results were (mean ± SD) pentagastrin stimulated peak acid output 34.7±11.3 mmol/h, baclofen 11.1±4.0 mmol/h and MSF 16.5±9.7 mmol/h. There was no statistical difference between baclofen and MSF stimulated outputs. Both were significantly (p<0.01) less than pentagastrin stimulated output. We suggest that this action of baclofen has the following implications in man: (1) GABA has a role in the central regulation of acid secretion. (2) It may be useful as a test for the completeness of vagotomy (perhaps intra-operatively). (3) Patients already on baclofen (including many elderly or infirm patients) may be at risk from baclofen induced hyperacidity. Further work is required in all three areas.

T16
Twenty four hour intragastric acidity before and during treatment with Enprostil

CANTANA, B SHARMA, R ORCHARD, A GRUNDON, AND R E POUNDER (Academic Department of Medicine, Royal Free Hospital School of Medicine, London) Enprostil is a synthetic dehydro-prostaglandin E2 currently undergoing clinical trial in the treatment of duodenal and gastric ulceration.

We have studied the effects of Enprostil 35 μg bd and 70 μg po on the intragastric pH profile, and nocturnal acid and pepsin output of nine volunteers with duodenal ulcer disease.

For the 24 hour period mean hourly hydrogen ion activity was: placebo 23.6 mmol/l ±3.4 sem. 35 μg bd 14.5±2.78 (a 39% reduction) and 70 μg mcg 18.2±2.4 (a 33% reduction). The suppression for each of the doses given at 11pm over the night-time period was 69% for the 35 μg dose and 67% for 70 μg. Thus the higher dose produced no significant advantage by further reducing nocturnal intragastric hydrogen ion activity. No reduction in intragastric acidity was seen during the morning following 70 μg nocte, but 35μg nocte given at 0730 still produced a 27% reduction in intragastric hydrogen ion activity between 1300 and 1800.

Nocturnal pepsin output was reduced from 5-15 IU/h ±1.9 on placebo to 1.9±0.91 on 35μg bd and 1.67 IU/h ±0.6 on 70μg nocte. This was caused by lowering of pepsin concentration rather than volume in contrast to the effect we have seen with H2 antagonists.

Enprostil produces a significant reduction in gastric secretion; since it is a prostaglandin known to have cytoprotective effects, the results of current ulcer healing studies should be of great interest.
T18
Don’t freeze pepsin!

M Deakin, J K Ramage, A Paul, S Gray, J Billings, and J G Williams (Department of Gastroenterology, Royal Naval Hospital Haslar, Hants) Measuring pepsin kinetically by the digestion of an albumin-bromophenol blue substrate on a centrifugal analyser we have achieved a coefficient of variation of ≤3% intra-batch. The main limitation is the method of storing specimens.

Specimens were collected from four volunteers by continuous aspiration in 15 minute aliquots, during basal periods and after stimulation with sham-feeding, imipramine and pentagastrin. The peptic activity in 34 of the resulting specimens and pentagastrin. The peptic activity in 34 of the resulting specimens were measured immediately, and aliquots frozen to −20°C and −50°C were analysed after one week.

The mean peptic activity before freezing was 80±1 IU/L. After freezing for one week at −20°C it was 44±5 and at −50°C, 14±3 IU/L. The loss of peptic activity was pH dependent with a greater loss of activity in those specimens below a pH of 1-3. Duplicate samples were diluted with 50% glycine buffer at pH 2. This protected the pepsin in some specimens but still resulted in a loss of 36% of mean peptic activity in specimens stored at −50°C.

A further 86 specimens were measured immediately and then stored at 4°C. After 24 hours 97% of activity remained; after four days 87%; and after seven days 83%.

The method of storage in our laboratory is now at 4°C with analysis within 24 hours.

T19
Does smoking affect the response to cimetidine in duodenal ulcer disease?

M Deakin, J K Ramage, D G Colin-Jones, S Gray, J Billings, and J G Williams (Royal Naval Hospital, Haslar, Hants) Boyd and Wormsley have suggested that smoking may impair the pharmacological response to therapy in duodenal ulcer disease. This hypothesis is supported by two recent trials, which have shown lower healing rates in smokers with a suggestion that this may be overcome by a large single nocturnal dose of an H2 antagonist.

We have studied the evening and overnight intragastric pH profiles, and nocturnal acid and pepsin output of eight volunteers with duodenal ulcer disease while smoking (20–50 cigarettes/day) and after abstention from tobacco for 36 hours. The subjects were studied five times, receiving in double blind fashion, placebo, cimetidine 400 mg bd or cimetidine 800 mg nocte whilst smoking and placebo or cimetidine 400 mg bd after abstention.

There was no significant difference between nocturnal intragastric acidity, acid or pepsin output on smoking or non-smoking days when placebo was given. Cimetidine 400 mg given at 11 pm produced equal suppression on both nights for all variables studied. Cimetidine 800 mg nocte produced a further and more sustained reduction.

These results do not support the hypothesis that smoking leads to an increase in basal acid or pepsin output or to a failure of pharmacological inhibition of gastric secretion.

T20
Changing pattern of admissions for duodenal ulcer (DU) in the Trent region 1972–1983

K D Bardian, G Cust, R F C Hinciliffe, M Williamson, C Lyon, and K Bose (District General Hospital, Rotherham; Trent Regional Health Authority, Sheffield) The admission rates for duodenal ulcer (DU) and the effect of H2 receptor antagonists (H2-RA), introduced in 1977, were examined. The data are expressed as rates per million. Overall admissions for perforation and for haemorrhage have not changed, on average 100±3 (range 96-5 to 113-9) and 134±8 (range 121-9 to 151-3) respectively but this conceals a rise of 32% and 59% in those ≥65 years, in the H2 era. Emergency admissions for uncomplicated DU were unchanged (average 87-6, range 77-6 to 96-1) but the operation rates fell by 55% in 1977–83. Waiting list (WL) admissions for uncomplicated DU fell 40% from 187 (1972–76) to 112-4 (1977–83) and the proportions operated upon from 87% to 72%. This accounted for a 50% reduction in WL surgery.

In one town, proportionately twice as much H2-RA, was used compared with Trent, generally intermittently in 1976–78 and then for maintenance and high dose treatment subsequently. Yet emergency admission for DU complications was unchanged; and it rose 39% for uncomplicated DU although operation rates fell in the latter group from 20% to 6%. Compared with the pre H2-RA period (1972–75), WL admissions fell in 1976–78 by 29% and in 1979–83 by 70%.

The proportions operated upon in the three periods fell from 75% to 50% and 25% respectively, leading to an overall reduction in WL surgery by 50% (1976–78) and 90% (1979–83).

Thus H2-RA have not reduced emergency admissions in DU patients. It is associated with a marked decrease, however, proportional to the intensity with which the drugs are used. On WL admissions and on the numbers operated upon for uncomplicated DU.

T21
Alterations in mucus glycoprotein biosynthesis by cultured human gastric mucosa in gastric cancer

G M Roberts, H I Young, G T Williams, and P J Winterburn (Departments of Surgery and Pathology, University of Wales College of Medicine, Cardiff, and Department of Biochemistry, University College, Cardiff) Although there is indirect evidence of altered gastric mucous glycoprotein production in carcinogenesis this has not been established biochemically. We have studied glycoprotein synthesis in cultured mucosa from 22 gastrectomy specimens for carcinoma. Mucosal blocks from the tumour edge and from a remote site within the same gastric region were used for tissue culture, histology, and mucin histochemistry. Tissue was cultured for six hours with structural preservation and incorporation of [3H]serine. [3H]Fucose or [3H]glucosamine into high molecular weight glycoproteins. [3H]Sialic acids were purified after release by dilute acid hydrolysis. Labelled O-linked oligosaccharides were released by alkaline NaBH4 and fractionated by gel chromatography. The oligosaccharides ranged in size from 3–20 glucose residue equivalents. Statistical analysis of the chromatographic profiles revealed that the oligosaccharide units synthesised by the tumour edge samples were smaller than those from the controls by a mean of approx 0-5 glucose residues, for both [3H]fucose (p=0.006) and [3H]glucosamine (p=0.007). In addition, this decrease occurred throughout the size range of oligosaccharides produced by the tumour edge tissue. Surprisingly the extent of sialic acid labelling showed a poor correlation with the presence of intestinal metaplasia or the histochemical identification of sialomucins. The results confirm biochemically the previous observations by immunocytochemistry and lectin histo-
Long-term prognosis in childhood duodenal ulcer (DU)

J S A Collins, T G Troughton, R J McFarland, and J F T Glasgow (The Department of Medicine and of Child Health, of The Queen’s University of Belfast and the Ulster Hospital, Dundonald) Duodenal ulcer is uncommon in childhood and few long term studies have been reported. Of 47 children, median age eight years, in whom the diagnosis was made radiologically 1961–70, 31 were questioned 13–29 (median 21) years later using a standard protocol along with 56 controls, median age 24 years. Admitted to hospital for dental extraction. In the DU cases intermittent GI symptoms had occurred in 22 (72%) — abdominal pain in 17 (54%), GO reflux in 10 (33%). Fifteen out of twenty two symptomatic patients had consulted their family doctors, five had required treatment in hospital and 11 considered that life had been seriously disrupted. In only four (males) had a persistent or recurrent DU been shown at surgery or endoscopy; two of these had had GI bleeding and one other had perforated. No statistical differences were found between the nine asymptomatic and the 22 symptomatic patients since 16 years of age regarding — family history of DU, frequency or severity of initial symptoms, consumption of alcohol or tobacco. Compared with controls, the frequency of abdominal pain the in the DU cases was significantly greater since 16 years of age (p<0.005); there were no differences in the occurrence of other symptoms.

It is concluded that few patients, so diagnosed, seem to have persistent/recurrent DU at long-term review. Nonetheless, recurrent abdominal pain may persist.

Effect of treatment for one year with ranitidine (Ran) and of truncal vagotomy and pyloroplasty (TV) on intragastric pH, total and nitrate-reducing bacteria (TB & NRB), and nitrite and N-nitroso compounds in patients with peptic ulcer

J Meyrick Thomas, J J Misiewicz, N Schaub, Hui Wai Mo, A Cook, M J Hill, C Gooding, P L R Smith, C L Walters, L E Martin, J K Forster, and D F Woodings (Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London; PHS Centre for Applied Microbiology Research, Porton Down, Wilt; Food Research Association, Leatherhead, Surrey, and Glaxo Group Research Labs, Ware, Herst) Previous studies of vagotomy or short term H₂ receptor blockade have shown that intragastric N-nitrosation is not facilitated by treatment-induced hypopacidity, but there are no data on effects of long term medical therapy. In this experiment each of 15 peptic ulcer patients was studied for 24 hours on five occasions: before (study R₄) and after (R₅) initial healing (Ran 150 mg bd for six weeks), during (R₆) and upon completing (R₇) one year of maintenance treatment (Ran 150 mg nocte) and one month after stopping Ran (R₈). Eleven patients with TV (eight patients 16–38 months after and three both before and three months after TV) were also studied after verifying completeness of TV by strict Hollander criteria. During each 24 hours patients ate identical diets and smoked and exercised similarly and in hourly gastric aspirates the pH, counts of TB and NRB and nitrate, nitrite and N-nitroso compound concentrations were determined. The median percentage of samples at pH>4.0 rose from 0% (R₄) to 30% (R₅) (p<0.001) and 23% (R₆) (p=0.02) and was 15% after TV (p=0.28 compared with R₅), pH correlated, as expected with nitrite concentration and with counts of TB and NRB, but not with N-nitroso compound concentration. Compared with R₄ median pH, nitrate concentration, TB and NRB counts were increased in R₅ (p range <0.001–0.02); median pH and nitrite concentration alone were increased in R₆ (p=0.066, p=0.02) and no variable remained increased in R₇. After TV median values of all variables were not significantly different from R₅ (p range 0.37–0.80).

We conclude that prolonged maintenance treatment with Ranitidine results in decreased intragastric acidity and increased concentration of nitrite (but not of TB, NRB or N-nitroso compounds), which return to normal one month after stopping treatment. Truncal vagotomy produces changes similar to those due to prolonged medication with Ran.

An attempt to resolve the nitrosamine controversy in hypochlorhydric subjects

C N Hall, P Smith, C Walters, J S Kirkham, and T C Northfield (Norman Tanne Gastroenterology Unit, St James Hospital, Balham, London) Measurements of N-nitroso compounds in gastric aspirate from subjects with medically or surgically induced hypochlorhydria have given conflicting results. Increased levels have been reported as being associated with high pH or low pH or of being unrelated. In order to resolve this controversy, we have assessed endogenous nitrosation by the in-
dependent N-nitrosopropylene excretion test. Ten Polya gastrectomy (PG), 10 pernicious anaemia (PA) and nine matched control (NC) subjects were fed 380 mg of nitrate in beetroot juice and 500 mg of propline. N-nitrosopropylene (N-Pro) synthesized intragastrically from these precursors, and quantitatively excreted by the kidneys, was measured in 24 hour urine samples (collected checked by creatinine clearance). N-Pro excretion (mean ± SEM in ngm per day) was reduced (p<0.01) in PA (1.1±0.8) compared to NC (18±0.7), and also tended to be lower (NS) in PG (3.2±2.3). Twenty four intragastric pH was monitored on a separate occasion in 23 subjects; 13 were hypertonic (pH<4.50% of 24 hours) and 10 were acid. N-Pro yields were reduced (p<0.01) in the hypertonic group (0.9±0.6) compared with the acidic group (17.9±6.6), and N-Pro was negatively associated with mean intragastric pH (τau = -0.53, p=0.001). We conclude that endogenous synthesis of this specific N-nitrosocompound is favoured by low rather than high pH. This suggests that the nitrosation is chemically rather than bacterially mediated, and is contrary to the nitrosamine hypothesis of gastric cancer.

T26 Distribution and molecular forms of galanin in the human intestine

F E BAUER, N D CHRISTOFIDES, A E BISHOP, G L FEEN, N YANAIHARA, K TATEMOTO, J M POLAK, AND S R BLOOM. (Departments of Medicine and Histochernistry, Royal Postgraduate Medical School, Du Cane Road, London W12 OHS, Shizuoka, Japan and Karolinska Institute, Sweden) Recently a novel neuropeptide – galanin – containing 29 amino acids was isolated from the porcine upper intestine. Early pharmacological studies showed that galanin contracts smooth muscles of the fundus, ileum, and colon and produces a significant rise in plasma glucose. In the present study we have investigated the presence of galanin-IR in tissue samples of human intestine by radioimmunoassay and immunochemistry using an N- and C-terminal specific antibody. Furthermore, the galanin-IR was characterised chromatographically. The highest galanin-IR concentration was found in the duodenum (12±1 pmol/g, x±SEM) followed by fundus (9±0.5 pmol/g), antrum (7±0.6 pmol/g) and jejunum (7±1.3 pmol/g). Only moderate concentrations could be shown in the colon (3±0.2 pmol/g). Gel chromatographic analysis revealed two molecular forms eluting at Kav values of 0.66 and 0.82 respectively but the galanin standard (porcine intestine) eluted at Kav 0.70. On HPLC galanin-IR eluted in two peaks 33% and 34% acetonitrile (standard 34%). By radioimmunoassay only the N-terminal specific antibody detected galanin-IR in the human intestine. No galanin-IR was measurable using the C-terminal specific antibody. Immunochemistry localised galanin-IR to nerves mainly in the muscle layers and ganglionated plexus. These results suggest that although galanin-IR is present in the human intestine, this immunoreactivity is not identical to porcine galanin. In view of its distribution and contractile function galanin may have a possible role on smooth muscles, probably regulating muscle tone, motility and blood flow.

T27 Early gastric cancer – the case for long term surveillance

P W J HOUGHTON, A ALLAN, N J MCC MORTENSEN, AND J DAVIES (Departments of Surgery and Pathology, Bristol Royal Infirmary, Bristol) Since 1965 we have treated 35 patients (14 women, 21 men) with histologically proven early gastric cancer (EGC). The number of cases diagnosed has doubled in the last 10 years. The crude five and 10 year survival was 50% and 41% respectively.

Sixteen survivors have been reviewed for up to 10 years (median three years) after surgery (Billroth I 8, Polya 5, Roux en Y 2, Ivor Lewis 1). Gastroscopy and BIDA scintigraphy were undertaken to assess the potential risks to the gastric remnant. Multiple biopsies in 12 patients taken at six months to 10 years (median 18 months) postoperation revealed gastritis (five), atrophy (two), intestinal metaplasia (three), dysplasia (two) and were normal in four. One patient was found to have developed a metachronous EGC 10 years after resection and underwent successful oesophagectomy. BIDA scanning in 13 patients revealed mild duodenogastric reflux in three patients and more severe reflux in 10. Visick grading was I(11), II(2), III(1).

Potential risk factors such as duodenogastric reflux and achlorhydria are increased following partial resection leading some surgeons to advocate total gastrectomy for EGC. We have shown that partial resection is a suitable treatment for EGC although long term surveillance of the gastric remnant is mandatory.

T28 Short term treatment of acute duodenal ulcer. A comparison of cytoprotection with sucralfate and acid reduction with cimetidine.

H GLISE, L CARLING, B HALLBERG, J KAGEVI, J H SOLHAUG, L E SVEEDBERG AND L WAHLBY (INTRODUCED BY M RB KEIGHLY, BIRMINGHAM) (Departments of Medicine and Surgery, Hospitals of Vänersborg, Bolnäs Skövde and Torsby, Sweden) Enhancement of the mucosal defence mechanisms or a reduction of intraluminal acidity are the two general principles of medical ulcer therapy today. A multicentre, randomised double blind-placebo study was performed to evaluate these treatments.

Sucralfate (Antepsin, 1 g×4) or cimetidine (Tagamet 400 mg×2) was supplied to patients with endoscopically confirmed acute ulcerations in the pyloric ring or the duodenal bulb. All patients were controlled with endoscopy at four weeks and if not healed also at eight weeks. Symptom relief, antacid intake side effects and smoking were registered throughout the study on a special protocol.

A total of 386 patients were included at 15 centres, 371 completed the trial. The patient groups were comparable in all respects (29 parameters), except for taking snuff (tobacco under the lip), which did not affect ulcer healing. At four weeks 71% of 177 patients on sucralfate were healed compared with 77% of 194 on cimetidine (ns Fisher's exact test). The corresponding figures were 86% (Suc) and 92% (Cim) at eight weeks (ns). The 95% confidence interval for the difference concerning ulcer healing capacity for sucralfate compared to cimetidine extends from −12% to +5% – that is, may be 12% worse to 5% better than cimetidine.

Antacid intake and symptom relief did not differ significantly except for week five concerning symptoms (p<0.05, 20 pat with symptoms day 35) and week seven (day 49) concerning antacid intake (p<0.05, 11 pat) when cimetidine was superior in both. Side-effects did not differ between the groups.

It is concluded that sucralfate and cimetidine are approximately equal concerning ulcer healing, symptom relief and side effects in the short term treatment of acute duodenal ulcers.
Short term treatment of gastric ulcer – a comparison of sucralfate and cimetidine

B HALLEBæk, O ANKER-HANSE, L CARLING, H GLISE, J SOLHAUG, L E SVEDBERG, I WÄHLBY, INTRODUCED BY M R B KEIGHLEY, GENERAL HOSPITAL, BIRMINGHAM, DEPARTMENTS OF SURGERY AND MEDICINE, HOSPITALS OF VÄNERSBORG, BOLLNäs, MOTALA, SKOVDE, AND TORSBY, SWEDEN. A multicentre, randomised, double-blind study was performed to compare sucralfate and cimetidine in short-term treatment of gastric ulcer. Only patients with acute, endoscopically confirmed benign gastric ulcers were included. All ulcer were biopsied. Prepyloric ulcers in a range 0–2 cm from the pyloric ring were excluded. The patients were randomly allocated to treatment either with sucralfate (Antepsin 1g×4) or cimetidine (Tagamet 400 mg×2). Acid tablets (Novalucol nevir cap 12.5 mmol) were permitted for acute symptomatic relief. Ulcer healing was endoscopically controlled at four-week intervals.

One hundred and fifty patients entered the study. Ten patients had neoplasms and were excluded. Six patients did not fulfil the study. Of the remaining 134 patients 68 were treated with sucralfate and 66 with cimetidine. The groups were comparable except for mean ulcer size which was significantly smaller in the sucralfate-treated group (8 mm diameter for sucralfate and 12.5 mm for cimetidine group). Healing rates did not differ significantly at any time during the study (Fishers exact t). Cumulated healing rates for sucralfate are 61%, 94%, and 98% after four, eight, and 12 weeks of treatment. Corresponding figures for cimetidine are 69%, 94%, and 94%. The healing rates after four weeks of treatment have been calculated with statistical considerations taken to the initial difference in ulcer size between the two groups (Mantel test). The confidence interval for the difference in healing rates after 12 weeks is calculated between +11% and –%. This means that healing capacity for sucralfate can be 11% superior or 2% worse than for cimetidine. No significant differences were noted on side effects, antacid use of symptom relief.

Sucralfate and cimetidine are effective and well comparable in the treatment of gastric ulcer.

Slowing of gastric emptying after ingestion of calcium ions in normal subjects.

T30 Therapy for the dumping syndrome?

A J L BRAIN, R G FIDDIAN-GREEN, AND M HOB-SLEY, THE MIDDLESSEX HOSPITAL, LONDON, AND THE UNIVERSITY OF MICHIGAN, ANN ARBOR, USA. Rapid gastric emptying of hypertonic solutions results in a fluid shift from the whole extra-cellular space into the gut lumen; giving rise to the dumping syndrome. Agents that slow gastric emptying should therefore ameliorate the symptoms. Gastric emptying was measured in healthy volunteers by an aspiration technique during intragastric titration at pH 7. This was carried out with mannitol (261 mOsm/l) for 40 minutes, followed by isosmolar CaCl2 (120 mM, 500 ml). A pronounced slowing of gastric emptying was observed 27 minutes after the introduction of CaCl2, reaching a nadir at 40 minutes (median –23%; range –8–2 to –33.7 ml/min). This was different from the change observed, in the same subjunctions on a different day, when intragastric titration was continued with mannitol (median 1.1, range 8–0 to –9.7 ml/min) (p<0.01); or in 10 different subjects tested with water (median 3.1, range 11.8 to –217.7 ml/min) (p<0.01). To test CaCl2 in six patients with the dumping syndrome, the dumping provocation test during 150 ml of 50% glucose labelled with Indium 113m was carried out, and repeated on a different day 30 minutes after the intragastric instillation of 500 ml of 120 mM CaCl2. Gastric emptying was measured with a gamma camera and plasma volume fall calculated from serial haematocrit measurements. Neither symptoms nor the objective measurements changed. Although in these circumstances calcium did not reduce dumping symptoms, its powerful effect of slowing gastric emptying in normal subjects merits further investigation of its therapeutic value.

Regulation of intestinal carbohydrate absorption in man by two new selective enzyme inhibitors

T32 R H TAYLOR, HELEN M BARKER, ELIZABETH A BOWEN, AND JEAN E CROUCH, DEPARTMENT OF GASTROENTEROLOGY AND NUTRITION, CENTRAL MIDDLESSEX HOSPITAL, LONDON. Two new selective irreversible inhibitors of intestinal α-glycosidases, which are the hydrolyases for all dietary carbohydrates except lactose, have been derived from deoxyribozymycin (BAY m1099 and o1248). Their effects on the absorption of starch, maltose, and sucrose test meals in man have been measured and dose-response studies done to find doses which regulate postprandial glycaemia without causing malabsorption of nutrients.

Two groups of six healthy volunteers took 50 g carbohydrate with 400 ml water after an overnight fast. Blood glucose was measured for two hours and breath hydrogen for four hours as an indirect measure of malabsorption. In study 1, sucrose, maltose or starch were taken in random order with placebo, m1099 50 mg, or o1248 20 mg. In study 2 sucrose was taken with placebo, m1099 12.5, 25 or 50 mg, or o1248 5, 10 or 20 mg in random order.
Hydrogen production from 25 g lactulose was measured in all subjects. (1) Both m1099 50 mg and o1248 20 mg caused almost total sucrose malabsorption (=38±4 and 49±8 g respectively) and reduced glycaemic rises from 3.3 to <0.2 mmol/l (p<0.001). Maltose malabsorption (16±9 g) with 77% reduction in blood glucose peak occurred with m1099 but not o1248. Both reduced post-starch glycaemic peaks significantly (p<0.001) without malabsorption. (2) m1099 12.5 and 25 mg reduced post-sucrose glycaemia (p<0.001) without malabsorption, but even 5 mg o1248 caused malabsorption (13±4 g) whilst reducing glycaemia significantly.

We conclude that these two new inhibitors each have different substrate specificity in man. They appear to have therapeutic potential at low dosage in stabilising postprandial glycaemia by slowing carbohydrate absorption without inducing malabsorption.

T33 Glucose polymers and jejunal water absorption

B J M JONES AND D B A SILK (Department of Gastroenterology, The Central Middlesex Hospital, London) Various sugar-electrolyte solutions have been advocated for rehydration in the short bowel syndrome and ileostomists. The aim of the present study was to compare jejunal water absorption from isotonic sugar-saline solutions containing substrates of different chain length. Normal subjects underwent steady state perfusion of the proximal 25 cm jejunum with a double lumen/proximal occlusive balloon technique. Test solutions isocoric with 140 mM glucose were rendered isotonic by addition of NaCl and perfused at 20 ml/min with 14C-PEG 4000 as a marker.

Water absorption (ml/h 25 cm segment ±SEM) from maltose (G2: 22.8±4.4, n=6); maltotriose (G3: 214±34, n=8) glucose oligomers (GOM: 212±28, n=10), a complete amylyse hydrolysate of starch (CAHS: 278±50, n=6) and Caloreen (270±35, n=9) was similar to that from paired 140 mM glucose controls (n=22). Net solute absorption (mmol/h/25 cm) was significantly greater from the test solutions (G2: 22.8±4.4, p<0.001; G3: 161±14.4, p<0.01; GOM: 142±10, p<0.001; CAHS: 140±17.6, p<0.001; Caloreen: 139±1.2, p<0.001) than from glucose controls (70±2.6±1), principally because of greater NaCl absorption. Test solution absorbates were thus hypertonic and glucose controls were isotonic. Luminal contents remained isotonic with all solutions.

Thus brush border hydrolysis creates local osmotic effects which offset the expected glucose stimulated H2O absorption. Despite this, water absorption is not significantly affected provided that sufficient Na+ is present and consideration should be given to this observation when assessing sugar-electrolyte solutions under clinical conditions.

T34 Increased peptide YY release in patients with ileal resection

T E ADRIAN, A P SAVAGE, A J BACARESE-HAMILTON, H S FUESSL, H S BESTERMAN, AND S R BLOOM (Department of Medicine, Royal Postgraduate Medical School, London) Peptide YY is a recently discovered hormonal peptide from the ileum and colon which is one of the most potent of the gut hormones and powerfully inhibits gastric acid secretion and emptying in man at physiological concentrations.

We have investigated the PYY response, as measured by radioimmunoassay, to a standard mixed breakfast in 18 patients after ileal resection, nine patients after colonic resection, eight patients after total pancreatectomy and 16 healthy controls.

Plasma PYY concentrations in healthy subjects showed a small but significant rise from 8.6±1.3 pmol/l to 11.5±1.4 pmol/l at 60 min after the test breakfast. Basal PYY concentrations were greatly increased in ileal resection patients 49.8±8.7 (p<0.001) and increased to 72.2±1.31 and 60 min, reflecting the loss of absorptive function. In contrast PYY concentrations were lower in patients with colonic resection (5.4±1.7 fasting, 13.8±3.2 at 60 min). In pancreactomised patients basal PYY was only moderately increased (23.4±3.5 fasting, 35.9±4.7 at 60 min, p<0.001), suggesting that digested nutrients are a better stimulus to PYY release than the undegested nutrients seen in pancreatectomy. Thus it is likely that the increased PYY release in malabsorption reflects the presence of unabsorbed nutrients in the distal intestine. PYY may be involved in mediating adaptive responses to small intestinal resection in man. PYY is likely to be important in reducing gastric acid secretion and intestinal motility in these patients.

T35 Defective neutrophil function in intestinal lymphangiectasia

R P BOLTON, K L COTTER, AND M S LOSOWSKY (University Department of Medicine, St James's Hospital, Leeds) Intestinal lymphangiectasia (IL) is a generalised disorder of the lymphatic system characterised by oedema, hypoproteinaemia, lymphocytopenia, and variable gastrointestinal symptoms. Recurrent infection may be related to the accompanying hypogammaglobulinaemia and defective cell-mediated immunity, but we are not aware of any previous reports of granulocyte function in patients with IL. We report three patients with this disease in whom standard in vitro tests of neutrophil polymorphonuclear leucocyte (PMN) function are abnormal.

Our three patients have documented lymphangiectasia on small bowel biopsy and are now aged 17, 41, and 66 years. Peripheral blood neutrophil counts were within the normal range as were serum complement levels at the time of study. Polymorphonuclear leucocyte chemotaxis towards zymosan-activated serum was measured using a modified Boyden method (leading front technique). Polymorphonuclear leucocyte phagocytic activity was determined by counting the percentage of cells ingesting heat-killed Candida albicans.

Polymorphonuclear leucocytes from the patients with IL showed reduced chemotaxis towards autologous (45±12 μm) and normal activated serum (42±23 μm) (normal range 70–110 μm), whilst patients' sera showed impaired generation of chemotactant activity for normal neutrophils (57±11 μm; normal range 70–110 μm). Patients' sera also showed a tendency towards impaired phagocytosis (patients' 35–42%; normal range: 40–60%; cells ingesting Candida). This was similar in the presence of patients' or normal serum. Patients' serum impaired phagocytosis by normal polymorphonuclear leucocytes (39±2%) compared to normal serum (52±4%).

We conclude that patients with intestinal lymphangiectasia show defective in vitro neutrophil function with impaired chemotaxis and phagocytosis due to defects at both cellular and serum concentrations, and suggest that this may be relevant in their increased susceptibility to infection.
T36
The teenage coeliac
P J KUMAR, G HARRIS, J WALKER-SMITH, P MILLA, AND M J CLARK (Department of Gastroenterology, St Bartholomew's Hospital, West Smithfield, London, and Institute of Child Health, Guildford Street, London) Coeliac disease in childhood and adult life has been well documented but there are no recent reports on how children fare in adolescent life.

One hundred and two young adults (46 males, aged 11-20 years) with proven coeliac disease were referred between 1970-1984. Eighty five of these had been closely supervised in two paediatric units. At transfer to this hospital, dietary assessment showed only 56% were on a strict gluten-free diet: the remainder taking a variable amount of gluten. Nine per cent were on an entirely normal diet. There was no difference in height of weight percentiles between any of these groups and the normal population distributions. Of six patients below the third centile in height, three had presented in late childhood with shortness of stature. All patients despite taking gluten in their diet were asymptomatic. The onset of puberty as well as haematological and biochemical indices did not differ between the groups.

Forty four patients had jejunal biopsies at transfer of which 18 had gross mucosal damage (villus heights of less than 200 μm) despite six patients claiming to be on 'strict' and seven on 'semi-strict' diets. This finding underlines the patients' reluctance to admit to gluten ingestion. This study suggests that a less restrictive low gluten-containing diet rather than a gluten-free diet is suitable for adolescents while still ensuring normal growth and development.

T37
Neurotensin infusions increase ileostomy output
H W JONES, A D MACKAY, W S PEARL, AND I CALAM (Department of Medicine, Royal Postgraduate Medical School, London W12, and The Medical Unit, St Mary's Hospital, London) The ileal peptide neurotensin stimulates defaecation in man and it seems likely that this is either due to effects on colonic motility, or effects on small bowel water and electrolyte shifts that have been observed in experimental animals. To elucidate this we gave ileostomists a 20 min intravenous infusion of neurotensin at either 2.3 (n=5), or 6.3 (n=6) pmol/kg/min, or blank infusate in random order on the same day. Subjects consumed tea and biscuits at regular intervals and ileostomy effluent was collected for three hours after each infusion. Median plasma c-terminal immunoreactive neurotensin was 237 (range 82-422) pmol/l during high dose, 60 (16-108) pmol/l during low dose infusions and 22 (12-41) pmol/l at other times.

The high dose, but not the low dose caused a significant increase in ileostomy output in the first hour to 140 (51-239) g compared with 2.5 (0-33) g (p<0.01) after the control infusion, associated with a decrease in the proportion of solid material to 3.3 (2.1-4.8%) compared with 5.8 (1.6-8.6%) (p<0.05) after the control infusion. Sodium, potassium and chloride concentrations did not change and ileostomy output returned to control values in the second and third hours.

Neurotensin increased the volume of fluid leaving the ileum when plasma concentrations were similar to those seen in several diseases which are associated with diarrhoea.

T38
Intestinal function during starvation and enteral feeding
D G MAXTON, R P H THOMPSON, I S MUNZIES (Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London) Complete oral starvation and totally fluid diets induce intestinal hypoplasia in animals. Many hospital patients receive such diets (enteral nutrition; EN) after a period of starvation, so we investigated intestinal function in patients on EN with and without prior starvation, and during starvation alone.

Five patients receiving EN immediately post-maxillo-facial surgery (MF) and nine established on EN after more than three days of starvation ingested a solution containing 5 g D-xyllose (Xyl), 2.5 g 3-O-methyl glucose (3MG), 1 g rhamnose (Rh) and 5 g lactulose (Lac) after overnight fast. Blood was taken for two hours and urine collected for five hours. Six normal controls ingested similar solutions before and after 24 hour fast. Serial tests were performed on two obese patients during therapeutic fasting for 12 days.

Peak 60 min plasma Xyl concentrations in EN patients with pre-starvation were markedly below controls (0.46±0.16, n=9, vs 0.85±0.14, n=26 mmol/l, mean SD, p<0.01). The 60 min Xyl/3MG ratio was also reduced (0.87±0.15 vs 1.45±0.18, p<0.01). In contrast, in non-starved MF patients 60 min Xyl and Xyl/3MG ratios were normal. Sixty minutes Xyl/3MG ratios fell in all six controls after 24 h starvation (p<0.05), and decreased progressively in both patients fasted for 12 days to 61% and 73% of the initial level, but improved on refeeding. Intestinal permeability (urinary Lac:Rh ratio) was increased in EN patients (0.067±0.33, n=5 vs 0.025±0.0125, n=26, p<0.05), but normal in MF.

The intestinal malabsorption and hyperpermeability during enteral nutrition is probably related to prior oral starvation. Starvation, therefore, induces irreversible changes in intestinal function in man, as in animals.

T39
Do endogenous opioids regulate mouth-to-caecum transit time in man?
G BASILISCO, A BOZZANI, G CAMBONI, R PENAGNI, M RECCHIA, AND P A BIANCHI (INTRODUCED BY J J MIESCHWITZ) (Cattedra di Patologia Medica III, Istituto di Clinica Medica I, University of Milan, and Bio-statistics Unit, Istituto di Ricerche Farmacologiche 'Mario Negri', Milan, Italy) Endogenous opioids are involved in several intestinal functions in man. We have investigated their possible role in regulating mouth-to-caecum transit time (MCTT) using loperamide as a locally acting opioid agonist and naloxone as an antagonist. Mouth-to-caecum transit time was assessed by the hydrogen breath test (10 g lactulose in 100 ml water). Four male and four female healthy volunteers aged 23-34 years were studied. The subjects were divided into two blocks according to sex and randomly assigned to undergo tests during the administration of placebo capsules plus iv infusion of saline (P), loperamide capsules (12-16 mg according to body weight) plus iv infusion of saline (L), placebo capsules plus iv infusion of naloxone (40 μg/kg/h over 3 h) in saline (N), and loperamide capsules plus iv infusion of naloxone in saline (L+N), performed at intervals of one or two weeks. Statistical analysis was done with split-plot design (between-within subjects analysis of variance) followed by Tukey's test for multiple comparisons.

Mouth-to-caecum transit time (mean±SD) was significantly (p<0.05) longer after loperamide: 157.5
min±40.3 (L), 65±17.3 (P), 67.5±17.1 (N), 65±23.8 (L+N) in males and 155±54.5 (L), 97.5±40.3 (P), 85±42 (N), 95±47 (L+N) in females. The difference in MCTT between sexes was not statistically significant. The effect of loperamide was abolished by the concomitant administration of naloxone; naloxone administered alone had no effect on MCTT. No clinically important side effects were reported.

We conclude that exogenous opioids affect MCTT, but endogenous opioids seem not to be involved in its regulation in man.

T40  
**Giardia – bile salt interactions in vitro**  
PM G Inge, J P W Webb, and M J G Farting (Department of Gastroenterology, St Bartholomew’s Hospital, London)  
Intestinal fat malabsorption occurs in up to 50% of symptomatic individuals with giardiasis although its pathogenesis remains uncertain. Possible mechanisms include both enterocyte damage and associated bacterial overgrowth with bile salt (BS) deconjugation. We have examined the possibility that *Giardia* itself might metabolise or consume BS by searching for (i) BS deconjugation by TLC analysis of culture medium during growth of *Giardia* trophozoites with dilute Ox bile or pure BS, sodium taurocholate (TC), glycocholate (GC) and taurodeoxycholate (TDC) 0-20-2-0 mmol/l, and (ii) by quantifying BS uptake and metabolism by *Giardia* during exponential (24-48 h) and stationary (48-72 h) growth phases using tracer 14C-GC and pure GC 0-1-2-0 mmol/l. *Giardia* failed after 72 h to deconjugate BS substrates when provided as native bile or as individual pure BS. *Giardia*, however, did consume GC during the 72 h growth studies. Glycocholate uptake was concentration dependent with a peak uptake of 231±126 mmol/10^8 trophozoites from 2-0 mmol/l GC at 6 h. GC uptake fell during the exponential growth phase to 27-5±4-5 mmol/10^8 trophozoites but increased again during stationary phase to 96±24 mmol/10^8 trophozoites. TLC analysis of detergent solubilised *Giardia* membranes indicated that 14C-GC was taken up, but not metabolised further by the parasite. These findings suggest that *Giardia* consumes but does not deconjugate BS during growth in vitro. The physiological relevance of these observations remains to be determined although loss of conjugated BS from the intestinal lumen might contribute to fat malabsorption.

T41  
**Identification of *Giardia* surface antigens and their release during in vitro growth**  
MJ G Farting, C M Edson, J Prokopek, P M G Inge, and A J K Goka (Department of Gastroenterology, St Bartholomew’s Hospital, London, and Department of Medicine, Division of Geographic Medicine, Tufts University, Boston, USA)  
As *Giardia* surface components are likely targets for the host immune response we have begun to analyse the major surface proteins of *Giardia lamblia* (GL). Parallel studies failed to show release of BS-specific antibodies prepared from Balb/C mice immunised with axenic trophozoites. When ascitic fluids were assayed by indirect immunofluorescence three reacted with surface membrane components including flagella, seven reacted exclusively with intracellular components (excluding nuclei and median bodies) and one (5D4, IgG1) reacted with both, although primarily with intracellular components. The highest titre surface membrane monoclonal antibody (3D2, IgG1) immunoprecipitated on 88K dalton protein from detergent extracts of 125I-surface labelled or 35S-methionine metabolically labelled trophozoites. SDS-PAGE analysis showed that the 88K protein was a major iodinated surface protein. Human sera from patients with giardiasis immunoprecipitated the same 88K protein. Progressive release of the 88K protein into the culture medium during in vitro growth has been demonstrated by ELISA with 3D2, but parallel studies failed to show release of protein recognised by 5D4, a monoclonal antibody which reacts principally with intracellular components. The 88K protein was released in a soluble form and was not membrane associated. Thus the 88K surface protein of *Giardia* appears to be both a major immunogen and an exoantigen. The role of this antigen in the pathogenesis of *Giardia* infection requires further evaluation although exoantigens are known to be effective in blocking host immune responses.

T42  
**Neonatal intestinal lactase activity**  
LT Weaver, MF Laker, and RN Nelson (Departments of Child Health & Clinical Biochemistry, Royal Victoria Infirmary, Newcastle upon Tyne, UK)  
The intestinal lactase activity of newborn infants was measured indirectly from the differential uptake and urinary excretion of the disaccharides lactose and lactulose. In contrast with lactose, lactulose resists human beta-galactosidase. Both sugars may be passively absorbed intact, by the same pathways across the gastrointestinal wall, and fully recovered in the urine. The urinary ratio of lactose:lactulose is a reflection of unhydrolysed lactose and therefore lactase activity.

Forty newborn infants of 27 to 42 weeks gestation were studied sequentially for 14 days after the onset of oral feeding with an artificial milk formula containing 7 g lactose and 200 mg lactulose per 100 ml feed. Daily urine samples were obtained for disaccharide analysis which was performed by gas-liquid chromatography. A daily decline in urinary lactose:lactulose ratios was seen during the first seven days after starting feeds (p<0.01). Percentage decline was related directly with gestation: full term infants displayed a five fold greater decline in lactulosa than 28 weeks gestation infants (p<0.05).

This method offers a convenient, non-invasive means of studying sequential changes in lactase activity related to age and gestation in neonates.

T43  
**Kwashiorkor-like liver changes induced by an elemental diet can be prevented with dietary wheat bran**  
AP Jayaraj, Tina Barton, MR Lewin, and CG Clark (Department of Surgery, Faculty of Clinical Sciences, The Rayne Institute, University College, London)  
It is difficult to induce fatty liver changes similar to Kwashiorkor in experimental animals. The initial deposition of fat in Kwashiorkor is always in the periregal region with progressive involvement around central vein. Rats fed on elemental diet (Vivonex), which is nutritionally complete in every respect, develop this type of fatty infiltration, as distinct from the centrilocular fatty infiltration induced by choline deficient diets. Vivonex contains only 0.326% fat as highly purified safflower oil and is cholesterol free.

Ten female Wistar rats were fed on Vivonex powder and 10 received Vivonex powder with 5% wheat bran for 10 weeks.
Complications of ES occurred in 11 of 43 (25.6%) – haemorrhage (five), recurrence of cholangitis (four), pancreatitis (one) and gall stone ileus (one). There were no deaths attributable to ES.

We suggest that acute cholangitis should be treated with antibiotics and early ES whenever possible with emergency surgery reserved for those who do not improve. Elective cholecystectomy can often be avoided in the elderly and frail.

T45
Intestinal imaging: comparison of 111In-labelled leucocytes and 99mTc porphyrin

T BARNASON, G ZANELLI, T SMITH, N VEALL, AND S J LEVI. (MRC Clinical Research Centre, Harrow, Middlesex) 111In labelled leucocytes are widely accepted as the gold standard for radio-imaging of diseased bowel in patients with inflammatory bowel disease. The disadvantage of the technique includes a two hour preparation, high cost of 111In and a moderately high radiation dose. A new tracer has been developed for disease localisation and compared with that of 111In labelled leucocytes.

Ten patients with ileal Crohn’s disease (three ileum only, one ileocolic, four ileocaecal, two recurrences after resections) were studied. Pyrogen free 2mg doses of porphyrin (mixture of sulphonated tetraphenyl porphyrins) were made up and labelled with 2mCi 99mTc before iv administration. Labelling efficiency >97% (TLC with acetone). A ‘mixed’ 111In leucocyte preparation (2–300 μCi) was administered at the same time and scans obtained within four hours and at 20 hours at appropriate gate settings and with crossover subtraction. Scans were judged by two independent expert nuclear physicians.

One patient had normal scans. On early scans seven of nine had the same disease location, one not showing up on 111In and the other not on 99mTc. Of the seven with positive scans 99mTc showed slightly more extensive disease but in two of these the extent was difficult to assess by either technique. Scan quality was found to be equal in two 99mTc better than 111In in three and 111In better than 99mTc in two. Distal transfer of the two isotopes was identical in eight of nine patients at 20 h.

We conclude that 99mTc labelled porphyrin appears to be a suitable alternative to 111In leucocytes for intestinal imaging.

The technique requires only a few minutes preparation, estimated cost is <50 pence a patient and radiation to internal organs is reduced.

T46
Gastric surgery as a risk factor in human carcinogenesis

C P J CAYGILL, M J HILL, N HALL, J S KIRKHAM, AND T C NORTHFIELD (Bacterial Metabolism Research Laboratory, Porton Down and Norman Tanner Gastroenterology Unit, St James’ Hospital, London) An increased risk of gastric cancer has been reported after gastric surgery. It is postulated that gastric hypoaicidity leads to bacterial overgrowth, with production of carcinogens – for example, N-nitroso compounds. If this hypothesis is correct, an increased risk of cancers at distant sites would also be predicted. We have therefore examined death certificates from 4235 patients who underwent gastric surgery at St. James’ Hospital, Balham between 1940 and 1960. Mortality from cancers of various organs has been determined using a years at risk calculation in five year bands. There was no increase in mortality rate from gastric cancer during the first 20 post operative years, but an increased mortality (4-4 fold) after 20 years. Similarly, there was no excess mortality during the first 20 years after surgery from cancer of other organs, but there was a significant excess mortality rate thereafter for cancer of the biliary tract (8-6 fold), large bowel (2-5 fold), bronchus (5-0 fold), pancreas (3-2 fold) and cancer of all sites (2-9 fold).

We conclude that gastric surgery leads after a 20 year latency period to an increased risk of cancer at distant sites in addition to the stomach, as predicted by the chemical carcinogen hypothesis. This risk should be born in mind in clinical follow up of such patients.

T47
Randomised study comparing medical and surgical reflux control in peptic oesophageal stricture treated by intermittent dilatation

A WATSON (Department of Surgery, Royal Lancaster Infirmary, Lancaster) Fibreoptic endoscopic dilatation is now established in the management of peptic oesophageal stricture. An important adjunct to such management is control
of gastro-oesophageal reflux, which in Britain is most commonly attempted pharmacologically, although antireflux surgery is used more extensively in North America. The present prospective, randomised study was prompted by reports that strictures resistant to dilatation often respond to surgical reflux control, that some fibrous strictures resolve after antireflux surgery alone and a non-randomised study from our unit suggesting that antireflux surgery reduced dilatation requirements in younger patients.

Thirty two patients with peptic oesophageal stricture with a mean age of 65.2 years and no contra-indications to surgery, were randomly allocated to receive Gaviscon + cimetidine or to undergo antireflux surgery in addition to intermittent dilatation as frequently as necessary to maintain satisfactory swallowing. Dilatation requirements and adverse events were recorded in each group over a mean follow up period of 22 months. In the 16 pharmacologically treated group, seven (44%) required one dilatation only, the remainder requiring a mean of 1.8 subsequent dilatations in the follow-up period. In the surgically treated group, 12 (75%) needed only one dilatation, the mean number of subsequent dilatations in the remainder being 0-3 (p<0.01). There was no mortality or significant morbidity in either group.

It is concluded that antireflux surgery performed in conjunction with fibreoptic endoscopic dilatation significantly reduces the necessity for long term dilatation and medication and is the treatment of choice in younger patients with non contra-indication to surgery.

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T50 Influence of physical and psychological stress on fluid and electrolyte absorption in the human jejunum in vivo

G R BARCLAY, AND L A TURN-BERG (Department of Medicine, Hope Hospital, University of Manchester School of Medicine, Salford) The effect of physical and psychological stress on jejunal absorption was investigated using a triple lumen perfusion technique in healthy volunteers. In each study the stress period was preceded and followed by a control period. Psychological stress was induced by dichotomous listening during which subjects (n=14) listened through headphones to two simultaneous essays, one through the right ear and the other through the left. In control periods subjects listened to a mono recording of a single novel. Physical stress (n=10) was induced by intermittent immersion of a hand in iced water (mean 4°c). Each stress raised the pulse and BP significantly. Psychological stress significantly reduced absorption of water (control +30.3±7.3 vs stress +6.1±4.9 ml/30 cm/60 min; p<0.01; mean ± SEM) and caused net secretion of sodium (from 1.3±0.9 to −1.5±0.7meq/30 cm/60

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T48 Does super-efficient starch absorption promote colonic neoplasia?

J R THORNTON, A DRINK, J KELLEHER, AND M S LOSWSKY (Department Medicine, St James's University Hospital, Leeds) Dietary starch is incompletely absorbed. The degree of malabsorption, for a given food, shows considerable inter-individual variation. A low intake of dietary fibre may predispose to colonic neoplasia. Malabsorbed starch is likely to function as dietary fibre in the colon and thus may help to protect against colonic carcinogenesis.

We tested the hypothesis that super-efficient starch absorption favours colonic neoplasia. Adenoma, rather than carcinoma, patients were studied in view of possible disturbances to the colonic flora by a carcinoma and recent investigations. Ten patients who had had an adenoma removed endoscopically at least three months earlier were compared with 10 age- and sex-matched controls. On separate days, all subjects consumed, in random order, 328 g potatoes (providing 60 g starch) or 6.5 lactulose. Breath H2 was measured every 15 minutes for up to 12 hours. The relative quantities of H2 generated enabled calculation of the amount of malabsorbed potato starch. Dietary intakes of starch and fibre were assessed by one dietitian.

Patients malabsorbed less than half as much potato starch as controls (5.3 vs 10-9%; p<0.02). Mouth-to-caecum transit time of malabsorbed potato starch was similar (301 vs 287 minutes, ns) and was not significantly correlated with the amount of starch malabsorbed (r=0.186).

Consumption of starch (112 g/day patients vs 103 g/day controls) and fibre (14.3 vs 14-6 g/day) was not significantly different. Relative to fibre intakes, daily malabsorption of starch provided additional colonic carbohydrate of 6.0 g (42%) in patients vs 10-9 g (75%) in controls (p<0.05).

This study, the first demonstration of a difference in starch malabsorption in any disease, indicates that malabsorbed starch provides an important quantity of colonic carbohydrate and that super-efficient starch absorption, by reducing this provision, may promote colonic neoplasia.

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T49 Long term use of cyclosporin A (CyA) in patients after liver grafting

A BLACKBURN, J NEUBERGER, ROGER WILLIAMS, AND R Y CALNE (The Liver Unit, King's College School of Medicine and Dentistry, Denmark Hill, London and Department of Surgery, Addenbrooke's Hospital, Cambridge) Introduction of CyA in the immunosuppressive regimen of bone marrow and solid organ transplants has been associated with a significant improvement in survival, although there is concern over the toxicity of long-term usage. We have analysed the clinical course of 29 liver transplant recipients receiving CyA in the Cambridge/King’s College Hospital series followed from 10-51 months from the start of CyA therapy. Eight patients had been previously maintained on conventional immunosuppression (prednisolone and azathioprine) whereas the subsequent 21 patients were started on CyA in the perioperative period. When the dose of CyA required to maintain trough blood concentrations of 300-800 ng/l was determined, it was possible to withdraw corticosteroids in all but four patients on CyA. In only three patients were features of chronic rejection observed. The most important side effect was nephrotoxicity, with evidence of renal impairment in 21 patients (72%), manifest 1-30 (median 5) months after the introduction of therapy. Reduction in the dose of CyA was associated with a fall in serum creatinine but in nine of these patients, often presenting suddenly, necessitated withdrawal of the drug in five and institution of hypotensive therapy. Rejection occurred in two of these latter patients. Minor side effects not necessitating withdrawal and included hirsutes (four), breast fibroadenosis (two), gum hypertrophy (two), gynecomastia and severe headaches. CyA is an effective immunosuppressive agent allowing withdrawal of steroid therapy in many patients after liver grafting. Severe side effects of the drug are, however, likely to lead to its withdrawal in a quarter of the patients.
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min; p<0.025) and chloride (from +1.4±0.9 to −1.3±0.7 p<0.05). These changes were maintained during the recovery period following stress. Cold stress significantly reduced absorption of water (+27.8±5.5 vs +15.9±5.2 ml/30 cm/60 min; p<0.02), sodium (+1.7±0.9 vs +0.17±0.8 mEq/30 cm/60 min; p<0.02) and potassium (+0.17±0.4 vs +0.10±0.2; p<0.02). These changes were maintained during the recovery period.

These results suggest that psychological and physical stress can influence human jejunal absorption and indicate the possibility that activity in the central nervous system may exert some control over mucosal function.

OESOPHAGEAL

F1

Normal distal oesophageal pH profile

S Sadek, W C Haldle, G Vitale, C Cranford, N W Carter, and A Cuschieri (Department of Surgery, Ninewells Hospital and Medical School, Dundee) Prolonged monitoring of the distal oesophageal pH has become the definitive method for the quantification of acid gastro-oesophageal reflux. To date, no large series has been published which involved exclusively healthy volunteers.

Fifty asymptomatic volunteers (mean age 36-6 years, range 19-77) underwent ambulatory oesophageal pH monitoring. An integrated computerised system was used for data storage graphic display, interpretation and automatic statistical evaluation. Assessment by cumulative pH exposure (pH3-pH5) and characterisation of discrete reflux events is presented.

The baseline pH undergoes an acidic shift of one pH unit in the supine posture. Between pH3 and pH5 the pH exposure time was higher in the erect posture (significant at pH3, 4) with minimal exposure when supine. Events were more common when erect. At pH4.7 (14%) failed to show any reflux events in either posture while an additional 23 (46%) failed to reflux when supine. Although events appear shorter in duration when supine, if refluxers only are studied the events are significantly longer when supine. Prolonged events (>5 mins) constituted a higher proportion (25%) in the supine posture (decreased clearance), compared with 5% in the erect. Age had little effect on the extent of reflux. A weak correlation was found (r=0.28, p<0.05) between age and acid exposure at the pH4 level (erect).

This study has shown that normal healthy volunteers experience episodes of acid reflux predominantly in the erect position. In addition it has shown that posture dependent significant shift in the baseline oesophageal pH and indicates that evaluation of patients with reflux symptoms require separate analysis for the erect and supine periods.

F2

Prospective randomised trial of Angelchik prosthesis versus Nissen fundoplication

K Dawson, R Ryan, M Donovan, and I P J Hennessy. (Trinity College Department of Surgery, St James’s Hospital, Dublin, Ireland) In an ongoing prospective randomised clinical trial of two antireflux procedures 21 patients had an Angelchik prosthesis inserted and 19 patients had a Nissen fundoplication. All had moderate to severe oesophagitis confirmed at endoscopy beforehand. Five patients in the Angelchik group and three in the Nissen group had benign strictures. Clinical improvement was reported postoperatively by all patients in the Nissen group and all except one patient in the Angelchik group. Oesophageal manometry showed a significant improvement in LOS pressure in both groups. Twenty four hour pH studies showed a significant reduction in the total number of reflux episodes, the number of episodes greater than five minutes, and the percentage time below pH4 in both groups, but no significant difference between the two groups.

There is no significant difference between the results of the Angelchik prosthesis and Nissen’s fundoplication either clinically or on objective assessment. Both procedures provide effective control of reflux.

F3

Prospective evaluation of the Nissen fundoplication: effect on endoscopy, oesophageal pH and manometry

C Cranford, S Sadek, W Haldle and A Cuschieri (Department of Surgery, Ninewells Hospital and Medical School, Dundee) Although the Nissen fundoplication is widely practised, objective data on its ability to prevent gastro-oesophageal acid reflux are minimal. Fifteen patients with classical symptoms and endoscopic confirmation of reflux oesophagitis were evaluated prospectively by symptom score analysis, manometry, endoscopy and 24 hour ambulatory oesophageal pH monitoring. The postoperative studies were performed on average nine months after surgery (range 6-18 months). A group of 50 asymptomatic volunteers acted as control group for pH data.

Endoscopic healing was documented in the 14 patients studied. Twelve patients were rendered symptom free but three patients continued to experience occasional heartburn despite absence of acid reflux postoperatively.

Postoperatively reflux events were totally absent in 10 patients (66%) as compared with six out of 50 normal volunteers (12%). Four patients who were rendered symptom free by surgery continued to exhibit some oesophageal acid exposure when compared with controls although the number of reflux events were significantly decreased postoperatively (p<0.001).

The effect of Nissen fundoplication is a marked decrease in the number of acid reflux events which correlates with symptom relief and endoscopic healing. Contrary to previous reports this function is not related to an increase in the lower oesophageal pressure gradient (8±2.4 pre op. 8±3 post op. mm Hg), and appears to result from lengthening of the high pressure zone (3±0.7 pre-op. 5±1.2 post-op. cm; p<0.05).

F4

Role of bile reflux in oesophagitis and oesophageal stricture

A O Malu, R A Mountford, and E R Davies (University Departments of Medicine and Radiodiagnosis, Bristol Royal Infirmary, Bristol) BIDA scanning provides a non-invasive index of bile reflux into stomach and duodenum. This assessment was made in three groups of patients, each comprising 11 members. (a) Patients referred for gastroscopy without clinical or endoscopic evidence of oesophagitis. (b) Patients with oesophagitis of moderate degree showed endoscopically – that is, obviously eroded areas extending cephalad from the gastro-oesophageal junction. (c) Patients with histologically confirmed benign oesophageal strictures, considered clinically and endoscopically to be secondary to longstanding reflux.
BIDA scans were performed after endoscopic dilatation had produced symptomatic relief. All groups were matched for sex, and groups (a) and (b) were matched for age. Patients in group (c) were significantly older than the remainder. Minor grades of duodenogastric reflux were common in all three groups (17 out of 33 scans were positive – that is, 52%). Bile reflux was no commoner in patients with oesophagitis (with or without strictures), however, than in controls. No patient demonstrated duodeno-oesophageal (Grade 4) reflux.

The study provided no evidence to suggest that bile reflux is an important determinant of oesophagitis with or without fibrous stricturing.

F5 Gluten free foods: do they cause symptoms in coeliac patients?

P J CICLITIRA, R CERIO, H J ELLIS, J M MACARTNEY, AND J M NELUFER (Gastrointestinal Unit, The Rayne Institute and Department of Histopathology, St Thomas’ Hospital, London) Gluten free products based on wheat starch contain trace amounts of wheat gluten which exacerbates coeliac diseases. We wished to investigate whether a commercial gluten free bread mix that provides 0.4 mg gluten per slice of bread induces small intestinal enterotoxicity or symptoms in coeliac patients when ingested regularly for six weeks.

Ten treated coeliac patients maintained their gluten-free diet for 12 weeks. During six weeks they ingested no commercial gluten free products and during the other six weeks they continued the same diet but took in addition six slices per day of Juvela homebaked gluten free bread. The patients had a jejunal biopsy and 24 hour 51Cr-EDTA urine excretion study before the test, after six weeks without and six weeks with six slices of Juvela homebaked gluten-free bread. The patients maintained a symptom record during the study. Mean values ± 1 SD of morphometric measurements of the jejunal biopsies after no gluten free bread and six slices per day were villus height; crypt depth 3·6±0·8 vs 3·5±0·7, epithelial surface cell height 40·1±0·6 vs 38·9±2·3 and intraepithelial lymphocyte count 47±16 vs 46±19 lymphocytes per 100 enterocytes. There was no change in 51Cr-EDTA excretion. Symptoms were greater during the Juvela test period in three subjects who reported diarrhoea with the gluten free bread which resolved when the bread was stopped. Three out of 10 coeliac patients reported diarrhoea with a wheat starch based gluten free product despite no change in 51Cr-EDTA excretion or small intestinal morphometry. We conclude that wheat starch based gluten free products should be considered as a possible cause of persistent symptoms in some treated coeliac patients.

F6 Irritable bowel is marked by paroxysmal motor abnormalities

D KUMAR AND D J WINGATE (GI Science Research Unit, The London Hospital Medical College, London) A preliminary study showed that prolonged intermittent mental stress, which reduces the incidence of duodenjejunal MMCs in healthy adults, had more marked effects in five ‘irritable bowel syndrome’ (IBS) patients. Fifteen patients have now been studied following a standard protocol. Using dual intraluminal pressure-sensitive ‘radio-pills’ stationed 15 cm apart above and below the ligament of Treitz, motility was continuously recorded for a 36-hour period which included a fasting day of rest, and a fasting day of intermittent stress. Motility records were analysed to show the incidence of MMCs, and also of fasting irregular contractile activity unassociated with Phase III-type contractions that is not seen in healthy controls. Thirteen out of 15 patients showed one or more of three abnormalities. In six, MMCs were completely suppressed during stress. In 10, irregular activity was evoked under stress accompanied, in four, by IBS symptoms; in one of these patients, and in two others unaffected by stress, spontaneous symptom-associated irregular activity was observed, starting six, 15 and 23 hours respectively from the start of recording. This study has shown changes in fasting enteric motility in the majority (85%) of IBS patients that are either totally (irregular fasting contractions) or virtually (abolition of MMCs during stress occurred in only one of 34 control subjects) absent in controls. The data suggest that IBS is marked by paroxysmal enteric dysrhythmias, but in 11/15 patients, these were only evoked by stress. Symptomatic symptom-associated dysrhythmias occurred in three patients, but in two patients, would have been undetected without prolonging recording techniques.

F7 Clinical controlled trial of the effect of Ketanserin in carcinoid syndrome

J GUSTAFSEN, A LENDORF, H RASKOV, AND S BOESBY (Righshospitalet, Department C, Surgical Gastroenterology, Copenhagen, Denmark) The effect of Ketanserin, a new, highly selective 5-HT receptor antagonist was evaluated in a prospective study of patients who had been on chronic treatment for different periods of time. Seven patients, four women, and three men, aged 54–74 years (median 64), were randomised to treatment with either Ketanserin or placebo for one week periods. The daily dose of Ketanserin was 40–160 mg. The study includes 13 treatment periods with Ketanserin and 13 with placebo. All patients had typical symptoms of carcinoid syndrome with flushing as their main complaint, and the diagnosis had been verified histologically 5-hydroxyindole acetic acid in urine was raised in all patients. Five patients could convincingly state whether they had been treated with Ketanserin or placebo. In these patients Ketanserin reduced the number of flushing attacks (p<0.05). Diarrhoea was reduced in two patients. No side effects were observed.

Ketanserin seems valuable for the symptomatic relief in carcinoid syndrome.

F8 Natural history of established radiation enteritis

R B GALLAND AND J SPENCER (Department of Surgery, Royal Postgraduate Medical School and Hammersmith Hospital, London) Of 69 patients presenting to a surgical unit with radiation enteritis, nine were managed conservatively (five dying). Sixty required an operation for the presenting lesion and there were 14 operation related deaths. The 50 survivors have been followed up from three months to 12 years (median 18 months). Twenty four patients had no further symptoms related to their radiation enteritis. The remaining 26 patients had either continuing symptoms, problems caused by operation, progression of the radiation disease, or a combination of these. Four patients who presented
initially with rectal bleeding continued to bleed intermittently, one fatally. Eight patients developed symptoms because of stenosis of ileostomy, colostomy or anastomosis. Twenty patients developed one or more new radiation related problems, stricture (eight), malabsorption (five), fistula (one) and miscellaneous (six). Twelve of 23 patients presenting initially with strictures developed further radiation related problems compared with eight of nine patients initially presenting with either a perforation or fistula (p=0.009 Fisher’s exact test). None of the surviving patients whose initial problem was bleeding went on to develop further problems (p=0.001 vs perforation and fistulae combined). Of the twenty-six patients developing further problems 12 required one or more operations and five of these patients died.

We conclude that radiation enteritis is a progressive disease, further radiation related problems becoming apparent in about half of those surviving management of the initial lesion. Perforation or fistula as presenting features indicate a poorer prognosis than either stricture or haemorrhage.

F9
Experience with a $^{14}$C triolein test in the diagnosis and management of malabsorption

K MYLVAGANAM, C P WILLIAMS, AND A ROSS (Wrexham Maelor Hospital, Wrexham, Clwyd) We wished to introduce a simple and efficient screening test for significant fat malabsorption in a busy district general hospital. The absorption of oral $^{14}$C triolein in a standard fat meal was measured in more than 200 subjects by sampling breath $^{14}$CO$_2$ at hourly intervals up to eight hours. All patients examined, regardless of age or respiratory function, were able to complete the test. The group included 60 patients without gastrointestinal symptoms to establish a normal range. The cumulative eight hour value for absorption was selected for analysis and a normal range of plus or minus two standard deviations of the mean calculated. Tests repeated after four to six months suggest that the procedure is reproducible. All patients tested with untreated coeliac disease, symptomatic Crohn’s disease and chronic pancreatitis had absorption values below the lower limit of normal. Serial tests repeated after the institution of treatment have proved helpful in the control of treatment of these patients. Values in patients with the irritable bowel syndrome show a similar pattern to that previously reported. Twenty per cent of our patients have subnormal values despite normal jejunal biopsies. Patients with ulcerative colitis have normal values. The difference may prove helpful in the diagnosis of food intolerance.

In our experience the $^{14}$C triolein breath test is a simple, cheap, and reliable screening test for fat malabsorption which can easily be performed in a district general hospital. It seems of value in monitoring the progress of individual patients.

F10
Effect of glucose and lactulose on superior mesenteric arterial blood flow in man

M J OAMAR, R MOUNTFORD, AND A E READ (University of Bristol Department of Medicine, Bristol Royal Infirmary, Bristol) We have previously shown that the chemical nature of the meal is a significant factor determining postprandial superior mesenteric artery blood flow (SMABF) measured transcutaneously by Doppler ultrasound. Other factors regulating postprandial SMABF such as absorption, however, are unknown. The present study was designed to define the effect of ingestion of glucose (absorbable) and lactulose (non-absorbable) solutions on the SMABF in man.

Superior mesenteric artery blood flow was measured in nine healthy volunteers in the resting and fasting state and serially for 60 minutes following the ingestion of 400 ml of an isotonic glucose solution. These measurements were repeated on a second occasion following the ingestion of 400 ml of an isotonic lactulose solution.

SMABF increased by 53% (p<0.05) five minutes after the end of ingestion of the glucose solution. This increase persisted at 10 minutes and declined to 47% at 15 minutes, and to 23% 30 minutes later. No significant change in SMABF was found following the ingestion of the lactulose solution. Significant differences between the two responses were found at five, 10 and 15 minutes (p<0.05).

The increase in SMABF after a glucose solution and not after lactulose suggests therefore that the process of absorption is an important factor governing postprandial SMABF.

F11
Stereological data on endocrine cells of the gastric corpus in patients treated with omeprazole

H F HELANDER, O KRYSLÄKEN, A UUSITALO, A-L KARVONEN (INTRODUCED BY M J DALY) (Research Laboratories, AB Hässel, Möln达尔, Sweden, and Tampere University Central Hospital, Tampere, Finland) ECL cell hyperplasia and carcinoids are found in rat oxyntic mucosa after two years’ treatment with large omeprazole doses. This study aimed at detecting if any changes occurred in the amount of endocrine cells in patients treated with omeprazole.

Corpus biopsies were obtained from 12 duodenal ulcer (DU) patients before and after four weeks’ treatment with omeprazole (40 mg/day). Biopsies were also obtained from 11 untreated healthy volunteers. The biopsies which comprised the entire thickness of the mucosa were fixed in Karnovsky, embedded in Polybed 812, sectioned, stained and analysed by light microscopy. Volume densities - that is, the proportion of mucosa taken up by endocrine cells were calculated. Fasting blood samples were taken for gastrin analyses.

In the healthy volunteers the volume density of the endocrine cells amounted to 0.4±0.06% (mean±SEM). In the DU patients the corresponding figure was 0.4±0.06% before omeprazole treatment and 0.4±0.05% after four weeks’ treatment. The differences are not statistically significant. Serum gastrin increased from 92±6 pmol/l before to 152±15 pmol/l during treatment (n=10).

We conclude that the proportion of endocrine cells in DU patients does not change during omeprazole treatment.

F12
Comparison of two different doses of omeprazole versus ranitidine in duodenal ulcer (DU) healing

K D BARDIAN, G BIANCHI PORRO, K BOSE, R F HINCHLIFFE, M LAZZARONI, P MORRIS, J NAESDAL, M THOMPSON, AND A WALAN (District General Hospital, Rotherham, UK, Ospedale L Sacco, Milan, Italy, and Department of Internal Medicine, University of Linköping, Sweden) In

GASTRODUDENAL

F11

F12
Clinical assessment or A558

The three were
or by 53%, 82%/e, 36 mg four, and H'K
had omeprazole to two days: median all
days was to prazole mg twice
Omeprazole heals duodenal, but not gastric, ulcers more rapidly than ranitidine
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With both studies it was shown for the first time that 20 mg/day omeprazole is superior to 300 mg/day ranitidine in the short term treatment of duodenal ulcer and equivalent in the short term treatment of gastric ulcer. According to these results a stronger acid inhibition seems to be more important to accelerate healing in duodenal than in gastric ulcer.

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Relation of plasma gastrin concentrations and oxyntic mucosal ECL cell density during inhibition of gastric acid secretion in the rat
H Larsson, E Carlsson, R Hakansson, H Mattsson, F Sundler (introduced by Dr Mike Daly) (Department of GI Pharmacology, AB Hässel, S-831 83 Malmö, Sweden, and Departments of Histology and Pharmacology, University of Lund, Lund, Sweden) In rats treated with high doses of omeprazole (OME) for two years a general and focal hyperplasia of enterochromaffine-like (ECL) cells and ECLomas were found in the oxyntic mucosa. It is anticipated that hyperplasia resulted from high plasma concentrations of gastrin, which in turn are caused by a sustained inhibition of acid secretion over long time periods. Intact or antrectomised rats were treated with OME (400 μmol/kg) or vehicle for 10 weeks. In addition intact rats were treated with a low dose of OME (10 μmol/kg) and with ranitidine (RAN, 175+175+350 μmol/kg). After 10 weeks the plasma gastrin concentration, oxyntic mucosal histamine concentration, histidine decarboxylase (HDC) activity and ECL cell density were determined.

Plasma gastrin, oxyntic mucosal histamine, HDC activity and ECL cell density were increased in intact rats treated with the high dose OME and with RAN. These parameters were decreased in antrectomised controls and were maintained on DAMMANN, R. 1985. The British Society of Gastroenterology, 265: A541-543.

Omeprazole treatment results in elevation of antral gastrin and reciprocal reduction in somatostatin concentrations
J M Allen, J C Yeats, A J Bacarese-Hamilton, H Larsson, E Carlsson, and S R Boman (Departments of Medicine, Royal Postgraduate Medical School, London, and AB Hässel, Malmö, Sweden) Somatostatin-secreting cells in the gastric mucosa have been postulated to play a role in control of gastric acid secretion as morphological studies suggest close interactions between gastrin and somatostatin secreting cells. The ratio of number of these two cell types in antral mucosa have been suggested to depend on acid secretory status. Omeprazole is a potent new drug which in high doses completely inhibits gastric acid secretion. Ten rats received orally 400 μmol omeprazole/kg daily, and a further 10 rats received vehicle alone. After 10 weeks, the stomach was resected and the peptide content extracted separately from antrum and fundus. Concentrations of nine regulatory peptides of the gastrointestinal tract were determined. Omeprazole treatment resulted in a rise of antral gastrin concentrations (control 3.2±0.3, treated 10.8±1.0 nmol/l) and this was associated with an increase in plasma gastrin concentration (control 35.3, treated 35.3±28 pmol/l). Significant reductions in antral...
and fundic concentrations of somatostatin were found in the rats treated with omeprazole (antrum: control 363±38, treated 96±9 pmol/g; fundus: control 365±33, treated 229±21 pmol/g). Fundic and antral content of the remaining regulatory peptides were unchanged by omeprazole treatment. These results show a clear reciprocal relationship between gastrin and somatostatin concentrations in the stomach following hypochlorhydria induced by omeprazole therapy, and further suggest a physiological role of somatostatin.

F16 Evaluation of large single night-time doses of cimetidine using continuous 24-hour ambulatory gastric pH monitoring

B KAPUR, JANE G MILLS, HELEN GLENNY, W L BURLAND, M LUNT, AND K D BARDHAN (Rotherham District General Hospital, Rotherham, and Smith Kline & French Research Limited, Welwyn, Herts). In order to determine whether high doses of cimetidine given at bedtime will suppress intragastric acidity for longer than a conventional dosage regimen, the responses to cimetidine 1200 mg and 2400 mg (given at 23.00 h) were compared with those of placebo and the more usual dosage regimen of 400 mg bd.

Intragastric pH was continuously recorded over 24 hours using a combination microelectrode and a Medilog cassette recorder with subsequent computerised data analysis. Eight healthy subjects received their four treatments double blind and in random order. Intragastric pH during placebo treatment was <2.0 for 48±8% (mean±SEM) of the night-time (24.00 to 08.50 h) and was >PH 4.0 for 38±9% of the time. On cimetidine 400 mg bd, cimetidine 1200 mg and cimetidine 2400 mg, pH was <2.0 for 22±4%, 11±4%, 2±1% of the night and was >PH 4.0 for 47±6%, 71±6% and 86±4% respectively. Thus there was a significant (p<0.05) and dose related shift to longer periods at higher pH, with 2400 mg producing virtually complete anacidity overnight. The day time (08.50 to 24.00 h) pH on placebo was <2.0 for 66±7%, and >4.0 for only 61±6% of that time. For the three doses of cimetidine, the corresponding values were: pH<2±0 for 49±8%, 56±2%, 44±11% and pH>4±0 for 15±3%, 10±3%, 19±2%, respectively.

During the following day the 2400 mg dose caused a significant increase in the period of time at higher pH’s (p<0.05) compared with placebo and 1200 mg but not with the 400 mg bd dose. For the same period, the effect of 1200 mg was not significantly different from either placebo or 400 mg bd. In conclusion, the effects of cimetidine 1200 mg at bedtime are primarily confined to the night; in contrast cimetidine 2400 mg has a significant effect the following day.

F17 Beta-blockers can protect human upper gastrointestinal function from disturbance by stress

JOHN O’BRIEN, D. G. THOMPSON, J HOLLY, W BURNHAM, AND E WALKER (The Department of Gastroenterology and Chemical Pathology, The London Hospital, London) Stress, induced experimentally in man, by immersion of a hand in cold water (CW), disturbs gastric function and delays orocaelal breath hydrogen (H2) transit. The following studies were performed to investigate the role of the sympathetic nervous system in this effect and to identify the adrenoceptor subtypes involved.

A series of orocaelal H2 Transit studies in individual using a variety of adrenoceptor blocking drugs during stress, suggested a beta, but not an alpha, receptor mediated pathway. To test this hypothesis, nine healthy volunteers each performed four orocaelal H2 transit studies. A standard mixed nutrient meal (containing the transit marker, lactulose) was ingested on each occasion during either: 20 minutes stress (CW) or control (hand in warm water, WW); and after pretreatment with either placebo or atenolol 100 mg (peripheral beta-1 blocker), according to a randomised, double-blind study design. The mean control transit was 58±7±4 (SEM) mins. Atenolol itself exerted no effect (mean 56±6±4 mins, p>0.5). Cold water induced stress consistently delayed transit (mean 82±2±10 mins, p<0.02 vs WW) and raised plasma noradrenaline, adrenaline, and corticosterone (mean increase 166±2±297 pg/ml, p<0.05) and adrenaline (mean increase 45±1±14 pg/ml, p<0.05). Atenolol abolished the CW induced delay (mean 56±5±4, p<0.02 vs placebo + CW) without changing either the severity of the stress (p>0.5), or plasma catecholamines (p>0.5). These results show a peripheral beta-1 adrenoceptor mediated pathway in the gastrointestinal response to stress, and introduce a possible role for beta-blockade in the therapy of patients with stress-related upper gastrointestinal symptoms.

F18 Non-acetylated salicylate is absorbed faster and causes less disruption in the gastric mucosal electrical potential difference than aspirin in man

B J Z DANESH, B REEVES, G MITCHELL, AND R I RUSSELL (Gastroenterology Unit and Department of Pharmacy, Royal Infirmary, Glasgow) The gastric mucosal damaging effect of acetylsalicylic acid (ASA) is known to be associated with a decrease in gastric electrical potential difference (EPD). Choline magnesium tri-salicylate (CMT), a non-acetylated salicylate, is reported to have a similar therapeutic effect to that of ASA but to induce less gastric mucosal damage than ASA. In a controlled double blind study, we compared the absorption, and the effect of these two compounds (at equivalent salicylate doses and pH values) on gastric transmucosal EPD in 10 healthy volunteers, who attended fasting on two occasions, 10 days apart. The EPD (mean±SEM), after a control period with 154 mM NaCl, was decreased from −42.7±0.8 to −20.8±0.9 mV (p<0.001) by oral administration of ASA (652 mg in 50 ml 154 NaCl) and from −42.6±0.7 to −32.0±0.6 mV (p<0.001) by CMT (655 mg in 50 ml NaCl). The fall in EPD was significantly less and occurred much earlier with CMT (~10±8±0.5 mV and 15.5 minutes respectively) than with ASA (~21.9±0.8 mV and 28±8 minutes respectively) (p<0.001). A full recovery of EPD was achieved at 60 minutes with CMT, whereas with ASA, the EPD remained −7.9±0.8 mV below the control level at 90 minutes (p<0.001). The peak serum salicylate level was higher and was achieved earlier (mean±SEM) with CMT (39.4±5.3 μg/ml and 57±5.0 minutes respectively) than with ASA (31.6±3.2 μg/ml and 120±12 minutes respectively) (p<0.05 and <0.001 respectively). Thus, replacing the acetyl moiety of aspirin by choline and magnesium molecules to form CMT, improves the absorption of salicylate and markedly reduces the aspirin induced disruption in the gastric EPD in man. These findings suggest that CMT may be a safer drug for therapeutic use than ASA.
a cytoprotective agent versus a histamine-2-antagonist

L-E Svedberg, L Carling, L Guse, B Halterback, I Kagen, I Solhaug, and L Wahlen (Hospitals of Vänersborg, Bollnäs, Skövde, and Torshy, Sweden)

The study was performed in order to compare a cytoprotective agent (sucralfate) with an established histamine-2-antagonist (cimetidine) on prepyloric ulcers. It is known that after surgery of prepyloric ulcers (selective proximal vagotomy) follows high recurrence rates and it seems to be important to separate prepyloric ulcers from ulcers with another location even when studying medical treatment. A randomised double-blind multicentre study (16 centres) was performed. One hundred and forty two patients with endoscopically confirmed ulcers within two centimetres of the pylorus completed the study. The patients were randomised to get either sucralfate (Antepsin 1 g) qid or cimetidine (Tagamet 400 mg) bid. Endoscopic control was performed after four weeks and if not healed after eight weeks.

At four weeks 68% in the sulcrate group were healed compared with 70% in the cimetidine group. After eight weeks the corresponding figures were 83 and 92% respectively. Statistical analysis (Fischer’s exact test + Mantel test) show that sulcrate cannot be less than 13% and not more than 17% effective than cimetidine at four weeks, at eight weeks 4% and 19% respectively when using a 95% confidence interval. Symptomatic relief, antacid consumption and side effects did not differ between the two groups.

The study shows that sulcrate is safe and as effective as cimetidine when treating prepyloric ulcer. The healing rate of PPU follow what is reported for gastric ulcer and duodenal ulcer in short term treatment.

F20
Adaptation of gastric mucosa to chronic acetylsalicylic acid treatment measured by gastric microbleeding and cell exfoliation in man

H-J Hagel, H Wild, H Ruppen, W Domshke, and D N Croft (University of Erlangen-Nuremberg, West Germany, and St Thomas Hospital, London) Adaptation of gastric mucosa to chronic acetylsalicylic acid (ASA) treatment has been shown recently in the rat. Gastric epithelial cell damage caused by different preparations of ASA is dose dependent and can be quantified by measuring DNA (or cell) loss from gastric mucosa. As another indicator of epithelial injury, microbleeding after ASA therapy can be measured using the method described by Hunt et al.

Sixteen volunteers (eight women, eight men) participated in the study. They were treated with 0.5 g ASA three times per day for four weeks. In the first group of eight volunteers gastric microbleeding was determined before and during treatment on days 3, 14, 28, and 29. In the second group gastric cell shedding was measured before and after four weeks ASA treatment, by irritation with 0.5 g microencapsulated ASA followed by 10 g of soluble aspirin.

Microbleeding increased during aspirin treatment significantly on day 3 and 14, but was nearly normalised on day 28. Gastric cell shedding after irritation with 0.5 or 1.0 g aspirin, respectively, was significantly less (p<0.01) after four weeks.

These data indicate that human gastric mucosa adapts to chronic aspirin treatment within four weeks as expressed by normalisation of gastric blood loss and increased resistance of gastric surface epithelium leading to reduced cell loss after aspirin challenge. So, both methods appear to provide equally sensitive evidence of the state of human gastric mucosal integrity.

F21
Reduction by enprostil of aspirin induced bleeding from human gastric mucosa

C J Hawkey, G Simpson, and K W Somerville (Department of Therapeutics, University Hospital, Nottingham) Enprostil is a synthetic dehydro prostaglandin E2 with potential as a once or twice daily ulcer healing agent. We have investigated its ability to protect human gastric mucosa against aspirin induced damage in a double blind double dummy placebo controlled study.

Each of 20 healthy male volunteers was studied four times at weekly intervals after receiving, over 48 hours, five doses of real (35 µg) or placebo enprostil followed 20 minutes later by real (600 mg) or placebo aspirin. Treatment order was randomised by Latin square design. Two hours after the final dose mucosal damage was quantified as blood loss into gastric washings aspirated every 10 minutes via an orogastroscope. Blood was estimated spectrophotometrically using orthotolidine in the presence of hydrogen peroxide. Phenol red was used to correct for recovery rates.

Preliminary studies showed that basal blood loss in the absence of aspirin was near the limits of detection and blood added to samples in vitro could be quantified accurately. Aspirin increased blood loss in all subjects (from median 0.9 to 7.8 µl/10 minutes). Enprostil led to a reduction in aspirin induced bleeding in 15 subjects (overall to median value of 4.2 µl/10 minutes, p=0.05).

This sensitive technique can detect moderate reductions in aspirin induced microscopic bleeding and has shown that enprostil has mucosal protective properties in man. Evaluation of its ulcer healing potential is warranted.

F22
Prostaglandin E2 in normal and abnormal upper GI endoscopic biopsies

S Pugh, S E Williams, M R Lewin, T P Barton, P R Salmon, and C G Clark (Department of Surgery, University College, London, and The Rayne Institute, London) The ability of prostaglandin E2 to be cytoprotective to the gastroduodenal mucosa has led to its use as an ulcer healing agent. Attempts to assess prostaglandin E2 activity in upper GI ulceration, however, have failed to show any deficiency. We have developed a reproducible method (based on that of Whittle et al 1983) for use with endoscopic biopsies.

We now present out results in 29 patients who had biopsies taken from duodenum, antrum, oesophagus, and ulcer rim (where present) at diagnostic endoscopy. None were on drug treatment. Ten were endoscopically normal, eight had oesophagitis, seven had duodenal ulcer and four had gastric ulcer. Both normals and abnormalities had similar ages and sex ratios. Mean wet weight of the biopsies (±SD) was 8.1±2.3 mg. Our results for prostaglandin E2 activity are expressed as (mean±SD) pg PG E2/mg wet weight and were, normal duodenum 106±49 vs duodenal ulcer 45±16 (p<0.005); normal antrum 108±54.2 vs gastric ulcer 40.3±34 (p<0.02); normal oesophagus 96.8±40.6 vs oesophagitis 39.2±15.1 (p<0.001).
Areas not affected by inflammation in patients with ulceration did not differ significantly from normal.

These significantly reduced levels may be relevant pathologically and provide the rationale for treatment with prostaglandin E₂ and other drugs which may work via increased prostaglandin activity. Whether reduction in mucosal prostaglandin E₂ activity is the cause of ulceration or merely associated with it remains to be ascertained.

**LIVER**

F23

**Non-neoplastic bile duct strictures simulating a malignant lesion at the hilum of the liver**

N S RADHS AND L H BLUMGART (Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London) Nine patients with biliary obstruction and a preoperative diagnosis of a neoplastic stricture at the hepatic duct bifurcation were found postoperatively to have benign disease. The cholangiographic appearance of the strictures was indistinguishable from a malignant stricture. Visceral angiography had indicated that the lesions were potentially resectable. Eight of the nine patients had had no previous biliary surgery at the time of diagnosis. Eight patients underwent elective surgery; in seven the confluence of the hepatic ducts including the lesion was removed, without mortality. Seven patients are alive, six of them totally asymptomatic, in a median follow up of 26 months.

As it is difficult to obtain histological proof of the nature of a hilar bile duct lesion, many patients with such strictures are treated on the assumption of malignant disease made on clinical and radiological grounds. Because these strictures are often treated by a percutaneously or endoscopically inserted endoprosthesis or the obstruction they cause is bypassed surgically without excision of the lesion, it is likely that some of these patients with benign disease will be treated inappropriately unless they are considered for a curative resection.

F24

**Cholesterol gall stone pathogenesis: morphology of cholesterol nucleation on calcium salt crystals**

B W A WILLIAMSON, J L ANDERSON, AND J W PERCY-ROBB (University of Birmingham Department of Surgery and Pathology. The Royal Infirmary, Glasgow and Department of Pathological Biochemistry Western Infirmary, Glasgow) We have previously provided biochemical evidence that the incubation of calcium salt crystals in biliary lipid systems supersaturated with cholesterol, results in nucleation and subsequent growth of cholesterol. We now report direct morphological evidence showing the nature of these processes.

Pure crystals of calcium carbonate (calcite) and calcium phosphate (hydroxyapatite) were separately added to biliary lipid systems containing sodium glycocholate, phosphatidyl choline, and cholesterol. After 21 days the crystalline material was prepared for scanning electron microscopy. Electron probe analysis of the two calcium salts indicated the presence of calcium with carbonate or phosphate respectively; no other elements were detected before incubation with biliary lipid. After the incubation new aggregates were seen adherent to some areas of the hydroxyapatite (x 50 000). Electron probe microanalysis of these areas revealed the almost total absence of calcium and phosphate, the new additions having the appearance of crystalline cholesterol. These took the form of two-dimensional plates and of spiral dislocations, each of which infer growth under different levels of cholesterol supersaturation. Similar morphological and analytical data were obtained with calcium carbonate; in this case there were also areas of dendritic growth.

These morphological and analytical data support our previous conclusion that calcium salts nucleate cholesterol from biliary lipid systems and may therefore be one important phase in the initial stages of gallstone formation.

F25

**Poor sulphoxidation status in patients with primary biliary cirrhosis could explain the high incidence of adverse reactions to D-penicillamine therapy**

A OLOMU, D CLEMENTS, R WARING, AND E ELIAS (Department of Medicine, Queen Elizabeth Hospital, Birmingham and Department of Biochemistry, University of Birmingham, Birmingham) Sulphoxidation status of an individual can be a significant factor in determining the toxicity of a drug. The incidence of D-penicillamine (D-PCA) toxicity in patients with rheumatoid arthritis has been found to be significantly greater for poor sulphoxidisers (51-4%) than for extensive sulphoxidisers 17-25%. Major complications necessitated the withdrawal of D-PCA in 20-31% of primary biliary cirrhosis (PBC) patients being treated with the drug, and fatalities are also recorded caused solely by D-PCA. In one series 31% had severe and a further 46% less severe side effects. We have investigated the sulphoxidation status in patients with PBC (n=13) and liver disease controls (n=23; 17 with cirrhosis and six with cholestasis). The sulphoxidation index (SI) for each subject was determined as the ration of parent compound and other non-sulphoxidation metabolite: sulphoxide metabolite in urine (0-8 hours), after a single 750 mg oral dose of S-carboxymethyl cysteine (SCMC). The ability to sulphoxidise SCMC has been suggested to reflect the ability to remove D-PCA from the body and hence reduce its toxicity. In controls 14/23 (61%) were good sulphoxidisers (SI<6) and 5/23 (21-7%) were poor sulphoxidisers (SI>18), four being intermediate, the same frequency distribution as for a normal population. There was a significantly greater proportion 12/13 (92-3%) of poor sulphoxidisers (SI>18) among PBC patients (p<0.01). Sulphoxidation did not correlate with other indices of liver function.

Toxicity to D-PCA in PBC may be explicable on the basis of poor sulphoxidation status. The basis for the strong relationship between PBC and poor sulphoxidation status remains to be determined.

F26

**In vitro and in vivo binding studies with a monoclonal antibody directed against the PLC/PRF/5 cell line**

A DUNK, K WEIDMANN, J WATERS, AND H C THOMAS (Department of Medicine, Royal Free Hospital, London) A monoclonal antibody RHK-K1 has been produced by immunising mice with PLC/PRF/5 cells, a cell line derived from a human hepatocellular carcinoma (HCC). Using indirect immunofluorescence, this antibody produces membrane staining of 3 HCC cell lines, and it has positively stained all eight human HCC's that it has been tested against. In vitro 125I-labelled RHK-K1 binds specifically to PLC/PRF/5 cells, as
shown by a competitive inhibition assay. Tumours derived from the PLC/PRF/5 cell line were grown in the nude mouse. Groups of mice were then injected with either 125I-RFH-KI, or a similar amount of 125I-mouse IgG. Mice were killed one, four, and seven days postinjection. The liver, spleen, kidneys, heart, lungs, and tumour were removed and bound radioactivity counted. Tumour: liver ratios for RFH-KI were greater than those for mouse IgG at each time point and the difference was greatest at day four (ratio RFH-KI 4.4±0.93, ratio IgG 1.53±0.60, mean ± SD, p<0.005). The amount of 125I-RFH-KI bound was greater in the tumour than in any other organ studied, the differences again being maximal at day four. Treatment of PLC/PRF/5 cells with Interferon produced a significant increase in RFH-KI binding in vitro, suggesting that the display of the tumour associated antigen recognised by RFH-KI may be therapeutically manipulated. This may have great clinical significance.

F27

Digoxin reduces portal hypertension and liver blood flow in patients with cirrhosis

R M Valori, D B Jones, S Somers, and S C Pappas (Intestinal Disease Research Unit and Department of Medicine, McMaster University Medical Centre, Hamilton, Ontario, Canada) Digoxin has been shown to cause splanchnic vasoconstriction in several animal models and to reduce hepatic blood flow in healthy humans. We examined the effects of 0.5 mg digoxin given intravenously on portal haemodynamics in patients with alcoholic cirrhosis and portal hypertension. Six patients with compensated chronic liver disease underwent hepatic vein catheterisation. Indocyanine green (ICG) was infused at 0.5 mg/min to steady state. Portal pressures were estimated by measuring the wedged hepatic vein pressure gradient (WHVPG). Estimated hepatic blood flow (EHBF) was calculated from the ratio of systemic clearance to hepatic extraction of ICG and corrected for haemocrit. After a 30 minute basal period, digoxin was given over a 10 minute period; the WHVPG was monitored and peripheral and hepatic venous samples were collected for a further 60 minute period. Digoxin caused a fall in WHVPG in four of six patients, and in EHBf in four of five patients in which it could be calculated. The reduction in WHVPG, which did not reach statistical significance, was from 24±3.4 to 20±5.8 mmHg (mean±SEM; 0.2>p<0.15). There was a significant reduction in EHBf, however, from 714±176 to 466±113 ml/min (p<0.05). There were no adverse reactions.

In summary, digoxin caused a 17% reduction in portal pressure and a 35% reduction in hepatic blood flow in patients with portal hypertension. These effects are similar to those seen with vasopressin therapy but without any peripheral haemodynamic disturbance. Thus, digoxin may be a useful therapeutic agent in acute varical haemorrhage. Further study of the effects of long term digoxin on portal haemodynamics is warranted.

F28

Effect of a long acting analogue of somatostatin (SMS 201–995) on hepatic venous pressures and azgos blood flow in cirrhotics

A K Burroughs, J A Santanna, T Dux, R Dick, and N McIntyre (Academic Department of Medicine, Royal Free Hospital School of Medicine, London, UK) SMS 201–995 is a new octapeptide analogue of somatostatin with a longer post intravenous infusion half-life of about 60 minutes. Preliminary published studies suggest it is a more potent compound, suppressing diarrhoea secondary to endocrine tumours (therapeutic level approximately 2 ng/ml). In view of the greater potency of SMS 201–995 we have studied its effect on free and occluded hepatic venous pressures (FHVP, OHVP) and azgos blood flow (possibly a better index of splanchnic haemodynamic effect) in six stable cirrhotic patients who had recently bled from oesophageal varices (three women, three men, five alcoholic and one schistosomal cirrhosis, three ascitic, three encephalopathic, bilirubin range 17–108 umol/l). Drug levels were measured during different bolus and infusion rates: 50 ug/30 mins (peak level 6-4 ng/ml) 100 ug/30 followed by 100 ug/15 mins (two patients, peak levels 16-6 and 24-6 ng/ml) and 100 ug bolus and 100 ug/30 mins (three patients, peak levels 17-6–20-9 ng/ml). Despite very high plasma concentrations there was no significant change and no trend in decreasing FHVP (mean 9: range 5–14 mmHg, OHVP (mean 29.8: range 20–35 mmHg) or OHVP–FHVP (mean 19.6: range 15–25 mmHg), measured in triplicate at baseline, 1, 3, 5, 10, 20, 30, 40, 50, 60, and 75 minutes from start of administration.

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Azygos blood flow measured in two patients did not change over the same time period. SMS 201–995 does not seem to be an effective portal hypotensive agent. Its different structure may account for its different haemodynamic effects from somatostatin. More evaluation is needed before use in active variceal bleeding.

F29

Haemodynamic responses to glypressin

J G Freeman, J R Barton, and C O Record (Gastroenterology Unit, Royal Victoria Infirmary, and University of Newcastle upon Tyne) Intravenous glypressin has been shown to be as effective as vasopressin in the management of acute variceal bleeding but with less side effects. There are, however, little data on the haemodynamic effects after glypressin injection. The aim of the present study was to assess the effect of glypressin on cardiac output (CO), mean arterial blood pressure (MAP), portal pressure and hepatic blood flow (HBF).

Six patients with histologically proven cirrhosis and varices were studied. Cardiac output was measured using a thermodilution technique and determined by the indocyanine green clearance method. Wedged hepatic vein pressure gradient (WHVPG) was used as an index of portal pressure. Values were obtained before and 30 minutes after 1-25 mg of intravenous glypressin. There were significant falls in WHVPG (13±2.1±40 vs 10±2±0.8 mmHg; p<0.05), and pulse rate (98±5 vs 70±4 beats/min; p<0.01) and a significant rise in MAP (95±2.5 vs 109±5±5 mmHg; p<0.05). There were no significant changes in either CO (5.2±0.7 vs 4±3±0.4 l/min/ m2; p>0.05) or HBF (993±28 vs 915±80 ml/min; p>0.05). No correlation was shown between changes in CO and WHVPG.

Thus like vasopressin, glypressin significantly decreases WHVPG probably because of splanchnic vasoconstriction and this accounts for its therapeutic efficacy.

F30

Oesophageal varix pressure measurement: the relationship to portal pressure and the response to changes in intra-abdominal pressure

D Westaby, A Gimson, and Roger Williams (The Liver Unit, King’s College Hospital and Medical School, Lon-
don) The present study was designed to evaluate a direct method of varix pressure measurement: to correlate these values with an estimate of portal pressure and to record changes in varix pressure during raised intra-abdominal pressure. The study was carried out in 11 patients with cirrhosis and recent variceal haemorrhage who were to undergo elective sclerotherapy. Before sclerotherapy the wedged (WHVP) and free hepatic venous pressures (FHVP) were estimated using a balloon occlusion technique. At the time of endoscopic sclerotherapy varix pressure was measured by direct puncture 2–4 cm above the squamo-columnar junction. Intravesophageal pressure was measured simultaneously by means of a manometer line attached to the endoscope and was used as an internal zero reference point from which varix pressure was recorded. Varix pressure (mean 27.4±2.2 mmHg) correlated closely with the WHVP (un-corrected by FHVP) (mean 28.5±2.6 mmHg; r=0.98 y=1.1+0.92 p<0.001). Direct abdominal compression caused a marked rise in varix pressure (mean rise 13.2±2.1 mmHg; p<0.001).

In summary, oesophageal varix pressure closely reflects intra-abdominal portal pressure (WHVP). Furthermore, rises in intra-abdominal pressure are transmitted to the varices leading to an increased gradient across the varix wall. This observation may have bearing upon the mechanism of varix rupture.

F31 Comparison of conventional BSP kinetics with single photon emission tomography

E M ALSTED, A J MORRIS, I T GILMORE, J WARE, J S GRIME, AND M CRITCHLEY (Departments of Medicine, Surgery and Nuclear Medicine, Royal Liverpool Hospital and University of Liverpool, Liverpool) The disappearance of BSP from blood has been used in assessment of hepatic function for years. We have developed a technique of tomographic scanning using single photon emission tomography (SPET) and 131I BSP, from which it is possible to obtain both structural and functional uptake information, and have compared it to the conventional BSP retention test. Sixty patients with histologically proven liver disease have been studied. They received 60 MBq 131I BSP intravenously. Tomography was performed 10 minutes after injection using an IGE 400 T γ-camera linked to a computer. Simultaneously, blood was sampled and counted for a conventional 90 minute BSP test. The patients were divided into groups of disease severity based on clinical, biochemical and histological criteria. There were A (severe disease), B (moderate) and C (mild dysfunction). The mean percentage uptake of 131I BSP assessed by tomography in the three groups was: (A) 36±5%±8 (mean ± SD); (B) 56±7%±8 (mean ± SD); (C) 73±±±10. There is a significant difference between groups A and B and also B and C (p<0.002 for both). Plasma 131I BSP disappearance curves were also compared. The t1 of the first exponential was (A) 13±2±5.5 min. (B) 5±6±2.4; (C) 4±4±9. There is a significant difference between A and B only (p<0.002). The t2 of the second exponential was (A) 60±3±4.9 min; (B) 48±2±6.6; (C) 41±8±2.8. There was no significant difference between these. The results show that there is better discrimination between clinical disease groups using the SPET technique, than with a conventional BSP test. The information can be obtained simply, at the same time as acquiring structural information.

F32 Impaired acetaldehyde metabolism in patients with non-alcoholic liver disorders

K MATTHEWSON, H AL MARDINI, K BARTLETT, AND C O RECORD (Gastroenterology Unit and Department Clinical Biochemistry and Medicine, Royal Victoria Infirmary and University of Newcastle upon Tyne) Acetaldehyde has been implicated in the genesis of alcoholic liver disease and its impaired metabolism has been demonstrated in alcoholic subjects. We have studied the metabolism of ethanol and acetaldehyde in subjects with non-alcoholic liver disorders in order to assess the specificity of the abnormality to alcoholic liver disease. Forty subjects were studied, of whom 14 had alcoholic liver disease, 14 had non-alcoholic liver disorders and 12 were normal controls. After an ethanol load, each subject had blood samples taken at 30 minute intervals for three hours. Each sample was assayed for ethanol and acetaldehyde using a new simplified technique. Mean blood acetaldehyde concentration was significantly greater in alcoholic liver disease patients than controls in all six hourly samples (p<0.01 on all occasions) and in all six samples (p<0.01 on all occasions) in the non-alcoholic liver disease group. Comparison of average blood acetaldehyde concentration of individual patients revealed that both alcoholic and non-alcoholic liver disease subjects had higher average levels than controls (p<0.001) and p<0.01 respectively. There were no differences in ethanol concentrations between any of the groups. The data confirm the impaired metabolism of acetaldehyde in alcoholic liver disease and suggest a similar abnormality in non-alcoholic liver disease subjects. Such an abnormality is likely to be consequent on liver disease rather than causative.

F33 Focal necrosis in liver and a fibrosarcoma in rats produced by photodynamic therapy

S G BROWN, J WIEMAN, C J TRAIAL, C COLLINS, P R SALMON, AND C G CLARK (University College Hospital, London) Photodynamic therapy (PDT) produces local necrosis with light after tissue sensitisation, which is reported to be selective for malignant tumours. Little is known of which factors determine tissue damage. We report quantitative studies of PDT with a new sensitiser, a phthalocyanine (PC). Rats (normal and with a subcutaneously transplanted fibrosarcoma) were given 5 mg/kg PC intravenously. After four hours, the liver or tumour was exposed and treated interstitially (200 micron laser fibre inserted into the tissue) with light at 675 nm from a dye laser. The rats were killed two hours to 21 days later, and the treated organs removed, fixed and sectioned. The extent of injury depended on laser power, energy (= power x exposure time) and presence of PC. With PC at 100 and 400 mW, the diameter of necrosed liver increased rapidly with energy up to 100 J, but more slowly thereafter. Without PC (necrosis due to hyperthermia only) at 400 mW, damage was comparable (above 50 J but at 100 mW was much less) (mean 1.7 vs 5.9 mm at 100 J). Maximum necrosis was seen after one to seven days with almost complete resolution by 21 days. All lesions showed sharp demarcation of damaged areas with florid proliferation of granulation tissue. Without PC, however, Kupffer cells were normal, but with PC they were markedly reduced in numbers and abnormal in form in damaged areas, which could be related to the increased damage seen with PC at low energies. Necrosis in sensitised tumours averaged 8.5
Abnormal haem biosynthesis in Gilbert's syndrome

K E L McCOLL, G G THOMPSON, M R MOORE, and A GOLDBERG (University Department of Medicine, Western Infirmary, Glasgow) Gilbert's syndrome affects approximately 5% of the population and is characterised by intermittent mild icterus due to genetically impaired hepatic clearance of unconjugated bilirubin.

In each of 13 patients examined with the syndrome, we have identified in peripheral blood cells, a characteristic abnormality of haem metabolism. The activity of the penultimate enzyme of haem biosynthesis protoporphyrinogen oxidase (PROTO.O) was reduced to 30% normal and was associated with a compensatory increased activity of the initial and rate-controlling enzyme of the pathway 5-aminolaevulinic acid synthase (ALAS). The urinary and faecal excretion of porphyrins and precursors was normal. A close negative correlation of the PROTO.O activity and the bilirubin concentration suggests that the bilirubin is inhibiting this enzyme and thus interfering with haem synthesis. Further evidence for a direct effect of bilirubin on haem biosynthesis was obtained by demonstrating similar changes in ALAS and PROTO.O when unconjugated hyperbilirubinaemia was induced in normal subjects by inhibiting hepatic bilirubin uptake with Rifampicin.

This effect of bilirubin on the synthesis of haem, its own precursor, is likely to be of both physiological and pathological importance. It may be relevant to the biochemical basis of the neurological damage caused by unconjugated bilirubin in both neonatal kernicterus and in the Crigler-Najjar Syndrome because aberrations of haem biosynthesis are an important cause of neuronal damage.

Changes in faecal bile acid excretion following promotion of colonic cancer by small bowel resection in the rat

A P SAVAGE, M S SIAN, J L MATTHEWS, S R BLOOM, and T COOKE (Department of Surgery, Charing Cross Hospital and Department of Medicine, London) Faecal bile acids have been implicated in the pathogenesis of colon cancer on both epidemiological and experimental grounds. We have investigated the role of faecal bile acids in an experimental model of colon cancer in rats subjected to small bowel resection, a procedure previously shown to promote the development of tumours.

Eighty male Wistar rats underwent either jejunal transection or 20%, 50%, or 80% small bowel resection. Colonic tumours were induced with azoxymethane 10 mg/kg for 12 weeks. Twenty four hour faecal collections were made during the period of initiation at six weeks and during the period of promotion at 16 weeks. Faecal samples were lyophilised and bile acids extracted in methanol and analysed by gas liquid chromatography in duplicate. Animals were killed at 26 weeks and the number and site of tumours recorded.

Faecal bile acid excretion fell from 10-4±2 mg/day in the transected group to 6-2±0.5 mg/day in both the 20% and 50% resected group and 4-2±0.2 mg/day (p<0.001) in the 80% resected group at six weeks. Almost identical changes were seen at 16 weeks. Colonic tumour number rose from 0.44±0.2/rat in the transection group to 1.24±0.24/rat in the 50% resection group (p<0.01) but fell in the 80% resection group to 0.86±0.3/rat. The reduction in faecal bile acid excretion seen after small bowel resection in carcinogen treated rats is probably because of the adaptation of the specific bile acid transport mechanism following resection. Promotion of colonic neoplasia by small bowel resection in the rat is unlikely to be due to changes on faecal bile acid excretion.

Ca 19-9 antibody in colorectal cancer and synchronous adenomata

N H AFDHAL, A LONG, B TOBIN, and D P O’DONOGHUE (Departments of Gastroenterology and Histopathology, St Vincent’s Hospital, Elm Park, Dublin) In order to evaluate the relationship between adenomatous polyps synchronous with colorectal cancer (CRC) we studied 56 consecutive patients undergoing surgery for CRC. All tumours and adenomatous polyps removed were stained by an indirect immunoperoxidase technique using a monoclonal antibody Ca 19-9 (kind gift of the Wistar Institute, Philadelphia).

Thirty two patients had CRC with no associated polyps (group 1). 16 patients had 30 synchronous polyps (group 2), while eight patients had invasive CRC clearly arising from a polyp (group 3). The three groups were compatible for age and sex, location and differentiation of carcinoma. Modified Duke’s classification A and B was seen in seven of eight group 3 patients whereas Duke’s C and D predominated in the other groups. Histology of the polyps showed 24 tubular adenomas, five tubulovillous adenomas and one villous adenoma varying in diameter from 0-5-4 cm. Ten of the adenomata showed moderate to marked dysplasia.
while three contained carcinoma in situ.

In all groups approximately 70% of CRC stained positively with the tumour marker and there was no correlation with tumour differentiation or location. Approximately 60% of adenoma stained positively for Ca 19-9 and this staining was usual focal and strongest in areas of dysplasia. This is higher than our incidence of 35% for adenomas unrelated to CRC. There was poor correlation between staining of parent CRC and co-existent adenoma, suggesting that adenoma may differ in mucin secretion pattern from their associated CRC. These findings show a high incidence of CRC associated adenoma expressing both dysplasia and positive tumour marker and this would support the adenoma–dysplasia–carcinoma sequence. Colonic polyps positive for Ca 19-9 may be a better determinant for pre-malignant potential than histological typing.

F38
Cell-mediated immunity in colorectal cancer: the effect of surgery

G P MCENTRE, J P DUGNAN, S FORSTER, S J HEFFERNON, AND E O’MALLEY (Mater Misericordiae Hospital, Dublin, Eire) Cell-mediated immunity was evaluated pre-operatively and on days 1, 3, 7, and 14 postoperatively in 20 patients undergoing surgery for colorectal cancer. The absolute lymphocyte count was determined from the white cell count. Total T cell and T cell helper and suppressor subset populations were evaluated using monoclonal antibody labelling techniques. Lymphocyte function studies were carried out using the in vivo delayed cutaneous hypersensitivity response and the in vitro transformation response to the T cell mitogen phytohemagglutinin (PHA).

Three patterns of immune responses were noted. Four patients were anergic pre-operatively with significant depression of lymphocyte response to PHA (p<0.05). The remaining parameters were normal. All four had extensive disease (Duke’s C). These parameters remained depressed throughout the hospital stay despite surgical excision of the lesion. The remaining 16 patients with local disease (Duke’s A and B) had normal parameters pre-operatively when compared with age and sex-matched controls. In 13 patients the depressed transformation responses and absolute lymphocyte counts that followed surgery had returned to normal by day 14. These patients had an uncomplicated postoperative course. Three patients developed major postoperative complications. A second phase of immunosuppression followed in these patients. Lymphocyte function studies may predict extensive disease pre-operatively and sequential evaluation may mirror the postoperative cause.

F39
Abnormal lectin binding in colonic carcinoma and adenoma

J M RHODES, R BLACK, AND A SAVAGE (Department of Medicine, Queen Elizabeth Hospital, Birmingham, and Department of Histopathology, Selly Oak Hospital, Birmingham) It has recently been reported that peanut lectin binds to mucins in colonic carcinoma and adenoma but not to normal colonic mucosa. To investigate this further we have studied the binding pattern of 10 peroxidase-labelled lectins selected for their differing carbohydrate specificities.

Paraffin sections from 20 ‘normal’ (irritable bowel syndrome) rectal biopsies, 19 colonic carcinoma and 20 colonic adenoma were deparaffinized, passed from ethanol into 0.1% PBS pH 7.2, pretreated with 1% H2O2 for one hour and then incubated in lectin-peroxidase (0.002 mg/ml in PBS) for 24 hours at 4°C. Sections were then stained with DAB/H2O2 and counterstained with haematoxylin. Pre-incubation of lectins with their appropriate binding sugars blocked their attachment demonstrating that the peroxidase positivity was lectin specific. Peanut agglutinin (PNA, galactose-binding), Ulex europaeus lectin (UEA1, fucose-binding) and Griffonia simplicifolia (GS II, N-Ac-glucosamine-binding) all showed specificity for carcinomatous or adenomatous mucosa with no reactivity for any normal mucosa: carcinoma, 15/19 (79%) PNA +ve, 13/19 (68%) UEA +ve, 12/19 (63%) GS II +ve, adenoma 7/20 (35%) PNA +ve, 8/20 (40%) UEA +ve (6/8 surface border only), 3/20 (15%) GS II +ve. Adjacent ‘normal’ mucosa showed similar lectin binding abnormalities in 10/17 (59%) carcinoma and 3/16 (19%) adenoma. All 20 normal rectal biopsies were negative for PNA, UEA1 and GS II binding.

Their very high specificity for abnormal mucosa makes these lectins very promising as markers for malignant or pre-malignant colonic epithelium.

F40
Relationship between mucosal structure and intestinal flora in ileal reservoirs

D G NASMYTH, P R GODWIN, M F DIXON, N S WILLIAMS, AND D JOHNSTON (The University Departments of Surgery, Microbiology and Pathology, The General Infirmary, Leeds) Stasis in pelvic ileal reservoirs has been associated with villous atrophy and impaired absorption. As the intestinal flora and their metabolites influence the kinetics of epithelial cell renewal, the relationship between mucosal structure, stasis and faecal flora was investigated following total colectomy for ulcerative colitis or adenomatous polyposis.

Ileal biopsies from pelvic ileal reservoirs (n=13, in continuity 5–31 months; median 8.5 months) and Brooke ileostomies (n=9, established 1–15 years, median 6 years) were compared with control ileum (n=10) from right hemicolecotomy specimens. Using computer assisted microscopy to determine the ratio of mucosal surface (MS) to the area of lamina propria (LP) villous atrophy was shown in the reservoirs (median MS/LP=0·119, range 0·071–0·18), compared with the ileostomies (MS/LP=0·251, 0·193–0·276) and controls (MS/LP=0·293, 0·19–0·39), p<0·01 Mann Whitney. Neither reservoir stasis, determined by measuring retention of radiolabelled stool, nor faecal bacterial counts of 14 different genera, correlated with MS/LP. There was, however, a significant correlation between faecal volatile fatty acids (VFA) measured by gas liquid chromatography and MS/LP for the reservoirs; less severe villous atrophy was associated with increased VFA (rs=0·643, df=10, p<0·03). Volatile fatty acids in the gut are generated by anaerobic fermentation of carbohydrate, and in fasted animals they decrease with a resultant increase in coliforms. A similar inverse correlation was found between coliforms and VFA in faeces after total colectomy (rs=−0·472, df=16, p<0·05). These observations suggest that production of VFA protects the reservoir mucosa, possibly by suppressing the growth of bacteria with toxic metabolites, and that dietary manipulation might be beneficial where villous atrophy is severe.
The British Society of Gastroenterology

F43 Abdominal tuberculous in the urban Britain – an underestimated clinical problem?
K R PALMER, D H PATEL, J F RIORDAN, G S BASRAN, AND D B A SIlk (Departments of Gastroenterology and Nutrition and Thoracic Medicine, Central Middlesex Hospital, London) Between 1973 and 1983 abdominal tuberculosis was responsible for the admission of 90 patients to a North West London district general hospital. Over the same period Crohn’s disease was newly diagnosed in 102 hospitalised patients. In contrast with Crohn’s disease, the majority (75%) of tuberculous patients were Asian immigrants. Mean duration of residence in the United Kingdom was 4±0.9 (SD) years, and mean age at presentation was 34.9±1.1 years. Forty per cent of tuberculous patients presented as an acute emergency to physicians, surgeons, or gynaecologists while the remainder present a more insidious, chronic picture.

Five groups of tuberculous patients were recognised. Forty two subjects had intestinal tuberculosis characterised by pain (100%), abdominal mass (47%) and abnormal contrast radiology (100%). Ten of these underwent emergency laparotomy for intestinal obstruction or perforation. Twenty seven patients had tuberculous peritonitis although only 16 had ascites. Eight patients presented with pyrexia and granulomatous hepatitis. Five had pulmonary and abdominal tuberculosis. The remaining eight patients represented a miscellaneous group.

The diagnosis of abdominal tuberculosis was established histologically (60 cases), bacteriologically (six cases) or radiologically (24 cases). Chest radiography, tuberculin skin testing and paracentesis were usually unhelpful. Five severely ill patients died. The remainder recovered completely after specific triple chemotherapy and response to treatment was usually evident within 14 days.

In urban Britain tuberculosis is an important cause of abdominal disease; in areas with a large immigrant population it may be as common as Crohn’s disease.

F44 Iatrogenic ileoacaeitis due to non-steroidal anti-inflammatory drugs (NSAID’s)
I BJARNASON, G ZANELLl, P WILLIAMS, P PROUSE, B ANSELL, J M GUMPEL, AND A J LEVI (MRC Clinical Research Centre, Harrow, Middlesex) We have recently shown that NSAID’s disrupt intestinal integrity in man with subsequent development of ileoacael inflammation. This study assesses the prevalence of intestinal inflammation in long term (>2 years) NSAID users and the rate of recovery following their withdrawal.

Abdominal scintigrams were obtained one to four and 20 hours after injection of 111Indium labelled leucocytes followed by a four day faecal specimen in estimation in 28 patients with rheumatoid and osteoarthritis.

Three untreated patients with active rheumatoid arthritis were normal. Three of six patients off NSAID’s for 2–24 months had localisation of radioactivity in the ileoacael region and one in addition increased faecal excretion of 111Indium. Ileoacael inflammation was found in 11 (58%) in 19 NSAID treated patients with rheumatoid and osteoarthritis and an additional four (79%) had increased faecal excretion of 111Indium. All the abnormal scintigrams were obtained at 20 hours. High dose indomethacin was most consistently associated with the highest faecal excretion of 111Indium but there was no clear correlation with NSAID dosage, duration or activity of disease and faecal 111Indiums.

F42 Role of metronidazole in the management of severe ulcerative colitis
R W CHAPMAN, W S SELBY, AND D P JEWELL (Gastroenterology Unit, John Radcliffe Hospital, Oxford) The role of intravenous corticosteroids in the treatment of severe ulcerative colitis (UC) is well established. It is unclear, however, whether the addition of antibiotics such as metronidazole increase the number of patients going into remission. The purpose of this double blind controlled study was to examine the role of metronidazole in the management of severe UC. Thirty nine patients with severe UC were randomised on admission to hospital to receive either 500 mg of intravenous metronidazole eight hourly (19 patients) or an identical intravenous placebo preparation (20 patients). The two groups were similar with respect to age, sex and the extent of colitis. In addition, all patients received a standard intravenous regimen consisting of 16 mg methyl prednisolone six hourly and parenteral nutrition together with a twice daily enema containing 100 mg hydrocortisone. Treatment was continued for five days when patients were formally assessed. Fourteen of 19 patients (74%) receiving metronidazole and 15/20 (75%) receiving placebo were regarded as substantially improved or in remission at the end of five days. Five patients from each group had made no improvement and all proceeded to urgent colectomy with no operative mortality.

The results of this study do not support the use of intravenous metronidazole in the treatment of severe UC.
It is concluded that long term NSAID treatment causes ileocaecal inflammation in a substantial number of patients with rheumatoid and osteoarthritis and the majority of patients had increased faecal excretion of 111Indium. Inflammation may persist for over a year after discontinuing NSAID's.

F45
Healed colonic anastomoses remain susceptible to experimental carcinogenesis

R ROE, P W DAVIES, J B BRISTOL, AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Colonic anastomoses are common sites for 'recurrent' carcinoma in man and for chemically induced carcinomas in the rat. The possibility that fully healed anastomoses might no longer be susceptible was tested in male Sprague-Dawley rats (n=128) of initial weight 150 g. Rats received the first of a 5-week course of azoxymethane injections (total dose 50 mg/kg sc) either immediately after transplantation and resection of the descending colon or at 2, 4, 8, and 12 weeks thereafter. Control groups at each time point had laparotomy and handling of the bowel without transection. All animals were killed 28 weeks after the first injection of azoxymethane. The total colorectal tumour yield was greater in rats receiving carcinogen immediately postoperatively (4.0×0.8 tumours/rat) (mean±SEM) than in the other four groups (1.9±2.9 tumours/rat). The yield of anastomatic tumours (2.1±0.4) was also greater in the immediate carcinogen group than in rats receiving azoxymethane from eight weeks (1.1±0.2, p<0.05) or from 12 weeks (0.9±0.20, p<0.02).

Carcinogens received during the immediate postoperative period may have an enhanced effect. Healed anastomoses remain favoured sites for tumour development but to a lesser extent than freshly created anastomoses. These phenomena may reflect increased cell proliferation in the vicinity of the suture line, which diminishes with time.

F46
Faecal impaction in the elderly

J J BANNISTER, L ABOUZEREK, AND N W READ (Department of Surgery, Royal Hallamshire Hospital, Sheffield, and Tickhill Road Hospital, Doncaster) In a study of the pathogenesis of faecal impaction, tests of anorectal physiology were carried out on 55 elderly patients (F28:M27), who on admission had impacted masses of faeces in the rectum. The findings were compared with similar studies in 36 age matched (F18:M18) patients with normal bowel habit. Mental state and mobility were similar for both groups.

Tests of simulated defaecation, maximal basal and squeeze sphincter pressures showed no significant differences between the two groups. The minimum rectal volume required to elicit a reflex anal relaxation was lower in the constipated group (p<0.05). Rectal sensation in the impacted subjects was markedly blunted for the perception of a rectal balloon (p<0.05), pain (p<0.05) and the desire to defecate (p<0.05). Finally, anal and perianal sensation were impaired (p<0.01) in the constipated patients.

These findings are suggestive of a neuropathy which reduces the perception of faeces in the rectum, blunts the desire to defecate and decreases the ability of rectal distension to elicit rectal contractions, resulting in the accumulation of a mass of faeces in the rectum of such a size and consistency that it cannot be passed.

F47
Primary biliary cirrhosis in men

M R LUCY, J NEUBERGER, AND ROGER WILLIAMS (Liver Unit, King's College School of Medicine and Dentistry, Denmark Hill, London) Eighty five per cent of cases of primary biliary cirrhosis (PBC) occur in women. A recent study, albeit without follow-up data, has compared 30 men with PBC with 30 age-matched women with PBC and emphasised their similar hepatic histology (Rubel et al. Hepatology 1984; 4: 671–766). There is no report, however, comparing the presentation and clinical course of the disease in men and women followed at one centre. From 1970 to 1984 38 men and 191 women with PBC were diagnosed and followed at this Unit. Of the men the mean age at diagnosis was 55 years (range 32–70): 45% of the men presented with pruritus and/or jaundice, 18% with GI haemorrhage, 13 with malaise and/or weight loss, while 24% had no liver-related symptoms. At diagnosis 39% were histological stage I or II, 61% histological stage III or IV. Anti-mitochondrial antibody titres were present in 95%. The median duration of follow up of the male patients was 37 months (range 1–598) and 22 (58%) died, with a 50% survival period of 65 months. In comparison, presentation differed significantly among female patients. 17% describing pruritus and/or jaundice (p<0.01 vs males). Fifteen per cent had no liver-related symptoms. There were no significant differences compared with male patients in histological stage at diagnosis (42% stage I or II, 58% stage III or IV), median duration of follow up 42 months (range 6–216), mortality 49%, or survival as estimated by life table analysis, with a 50% survival period of 72 months.

It is concluded that while the mode of presentation of PBC may differ between men and women the clinical course of the disease is similar in both groups.
tion was excessive (>20 mmol per day on a 70 g daily fat intake) in 40% of patients tested.

Small bowel disease must now be considered in addition to bile secretory failure and pancreatic dysfunction as a cause of weight loss and malnutrition in PBC.

F49
Factors determining response rate to antiviral therapy

L J SCULLY, R SHEIN, A S F LOK, A DUNK, AND H C THOMAS (Academic Department of Medicine, Royal Free Hospital, London) The records of all male patients with chronic hepatitis B, treated with either ARA-AMP (minimum four weeks) or lymphoblastoid interferon (IFN) (Wellferon) (minimum 12 weeks) were reviewed to identify factors which predict response or non-response to either therapy. A response was defined as a sustained loss of HBeAg and HBV-DNA from the serum within one year of completion of treatment. All patients were HBSAg, HBeAg and HBV-DNA positive for >6 months before treatment. ARA-AMP was given at a dosage of 10 mg/kg/day for five days, and then 5 mg/kg/day IM 12-hourly for four to seven weeks. Interferon was given at a dose of 5–10 μm²/IM daily for five days, then 7.5–10 μm²/thrice weekly for a minimum of 11 weeks. One Arab patient, lost to follow up, was excluded as was one patient who discontinued IFN therapy after five weeks. Four IFN-treated patients had received ARA-AMP more than two years before.

The results showed that 0/24 homosexual responders to ARA-AMP, whereas 9/18 responded to IFN (p<0.001). In contrast, heterosexuals responded to both ARA-AMP (10/22) and IFN (5/8). The pooled response rate was significantly greater in Caucasian (ARA-AMP 7/10; IFN 4/4) than non-Caucasian (ARA-AMP 3/12; IFN 2/6) heterosexuals (p<0.05). Eighty and 87% of responders to ARA-AMP and IFN, respectively, had a previous history of acute hepatitis, compared with 38 and 17% in the non-responder group (p<0.05).

We conclude that heterosexual male Caucasian carriers of HBV have a high response rate to either ARA-AMP (70%) or IFN (100%). In contrast, IFN is superior to ARA-AMP in homosexual carriers (50% vs 0% response). Non-Caucasians (predominantly SE Asians) respond poorly to both forms of therapy.

F50
Comparative studies of non-invasive investigation of Budd-Chiari syndrome

S BARTEO, S GUPTA, R N GIBSON, AND H J F HODGSON (Departments of Medicine and Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London) The presentation of Budd-Chiari syndrome may mimic chronic liver disease. The value of isotope liver scans as a non-invasive investigation has been emphasised. In contrast our experience suggests that ultrasound is the most valuable such investigation. We have reviewed studies on nine patients with Budd-Chiari syndrome (four of recent origin, five with chronic disease), in whom the diagnosis was confirmed eventually by full angiographic studies. In only one out of seven isotope liver scans was the characteristic central uptake reflecting caudate lobe accumulation seen. In six patients CT scanning showed an enlarged caudate lobe with low attenuation elsewhere, in one patient an enlarged caudate lobe with normal attenuation and in one patient the study was normal. In contrast ultrasound was abnormal in all nine cases, with failure to show normal outflowing hepatic veins. In the five chronic cases, a prominent hepatic venous collateral network of tortuous small vessels was shown, and in the four patients studied acutely, this developed in follow up scans performed two to four weeks from presentation. The inferior vena cava was shown to be narrowed by caudate lobe expansion in seven out of nine patients, and occluded in two out of nine. In three patients studied recently with Doppler ultrasound, abnormal dilated intrahepatic channels with blood flow away from the site of hepatic vein ostia, were visualised. Non-specific findings included ascites, and enlarged umbilical, azygos, and hemiazygos vein. We believe ultrasound to be the non-invasive investigation of choice in Budd-Chiari syndrome.

F51
Diagnosis of Budd Chiari syndrome by liver ultrasound and colloid scintigraphy

P POWELL-JACKSON, J KARANI, R EDE, H MEIRE, AND ROGER WILLIAMS (Liver Unit and Department of Radiology, King's College School of Medicine and Dentistry, Denmark Hill, London) Since 1972, nine patients with unsuspected Budd Chiari syndrome (BCS) have been mistakenly op-

erated on before referral for specialist investigation, and in each instance the laparotomy was followed by considerable deterioration and four deaths. In no instance had ultrasound examination (US) or 99Tc sulphur colloid scintigraphy been carried out pre-operatively, and to determine the diagnostic value of these non-invasive investigations we have examined their use in 17 patients referred to this Unit in whom BCS was also confirmed by histology and hepatic venography. Ultrasound appearances were considered diagnostic in 14 of 17 (82%) with relatively low reflectivity and/or hypertrophy of the caudate lobe in 13 (76%) and failure to visualise normal hepatic veins in 12. Additional findings of relevance included ascites in 15, compression of the inferior vena cava in nine, portal vein block in one and intra-caval tumour in one. In comparison scintigraphic appearances were considered diagnostic in five out of 14 (36%) with increased uptake and/or enlargement of the caudate lobe. In one of three with non-diagnostic US however, scintigraphy gave a positive diagnosis.

In conclusion, US provides diagnostic information in a high percentage of BCS and is not only more sensitive than scintigraphy but may provide further information regarding portal vein block, intra-luminal tumour and malignancy within the hepatic parenchyma, and should always precede more invasive investigations including exploratory laparotomy.

F52
Effect of methionine loading and endogenous hypermethioninaemia on blood mercaptans in man

H A MARINTI, K BARTLETT, J LEONARD, AND C O RECORD (Gastroenterology Unit, Royal Victoria Infirmary, and University of Newcastle upon Tyne, and Institute of Child Health, London) The mercaptans methane thiol and dimethyl sulphide have been implicated in the pathogenesis of hepatic encephalopathy and may be derived from the amino acid methionine. Oral methionine loading can cause neurological deterioration in patients with chronic encephalopathy and it has been suggested that this is because of a toxic breakdown product of methionine other than ammonia. In the present study blood mercaptan concentrations were determined after an oral challenge of methionine (5–10 g) in five patients with stable cirrhosis and one patient who exhibited chronic
ultrasound. There were 50 (94%) patients with alcoholic liver disease had evidence of either steatosis or fibrosis on ultrasound.

Routine clinical ultrasound accurately detects hepatic steatosis but is less reliable in recognising fibrosis. As hepatic steatosis is the earliest change in alcoholic liver disease and may be of prognostic importance for the development of cirrhosis; ultrasound provides an effective screening procedure particularly in the occult alcoholic who often presents with non-specific gastrointestinal complaints.

F54 High lipid parenteral feeds raise plasma branched chain amino acid concentrations – a possible therapeutic approach to portasystemic encephalopathy?

M J GLYNN, J POWELL-TUCK, D REAVELEY, AND I M MURRAY-LYON (Gastrointestinal Unit and Department of Chemical Pathology, Charing Cross Hospital, London) In portasystemic encephalopathy (PSE) the low plasma concentrations of branched chain amino acids (BCAA) have been thought to be related to hyperinsulinism. Some workers have shown that plasma concentrations of BCAA may be raised in patients without liver disease by using Intralipid as the sole non-nitrogen caloric source for parenteral feeding, and this technique might therefore be of value in treating patients with PSE. In feeding such patients, nitrogen given as parenteral amino acids seems to be better tolerated than protein given enterally, and the energy source is usually carbohydrate alone. Before trying a high lipid parenteral feed in patients with PSE we have studied patients without liver disease.

Seven patients established on a regimen of total parenteral nutrition for enterocutaneous fistula, oesophageal rupture, total dysphagia or pancreatitis were entered into a crossover trial. For each patient the feeding regimen was constant throughout the 10 days of the study except that for five days the non-nitrogen caloric source was all glucose and for the other five days it was Intralipid with only 100 g of glucose – the two periods being in randomised order. On day two and five of each arm of the study plasma samples were taken and 24 hour urine sodium excretion measured. On day two of the fat infusion mean plasma glucose and insulin concentrations were lower (5.0 mmol/l and 10 μU/ml respectively) than on the glucose infusion (7.5 mmol/l and 39.2 μU/ml, p<0.01).

Similar significant changes were seen on day five. On day two of the fat infusion mean plasma concentrations (μmol/l) of valine (296), leucine (135) and isoleucine (117) were significantly higher than they were during glucose infusion (250, 111, and 89 respectively) and similar significant changes were seen on day five. The concentrations of other amino acids, including the aromatics and glutamine, were not significantly altered by varying the energy substrate. Mean urinary sodium excretion was significantly higher on day 5 of the fat infusion (85-7 compared with 56 mmol/24 h, p<0.05).

A parenteral feeding regimen with all but 4000 non-nitrogen calories supplied as Intralipid (sufficient glucose to prevent hypoglycaemia) looks promising for trial in patients with PSE and sodium retention.

F55 Endocrine liver: identification of the classical cytosolic androgen receptor in rat liver

P BANNISTER, P SHERIDAN, AND M S LOSOWSKY (University Department of Medicine, St James’s Hospital, Leeds) The liver is not classically considered a site for the genomic (receptor mediated) action of steroid hormones. There are, however, a number of steroid sensitive processes in both rodent and human liver. Previous studies have claimed the presence of a cytosolic androgen receptor (AR) in rat liver, but in all reports the characteristics of the receptor differed from the classical AR seen in prostate tissue. We have used a new radioactive testosterone derivative, mibolerone (17α, 17α dimethyl nortestosterone) to identify a cytosolic AR in rat liver with the characteristics of the classical receptor.

Male rat liver cytosol contains AR which binds mibolerone with a high affinity (association constant = 1·02±0·27 nmol, mean±SD, n = 10) and a low capacity (8·0±0·9 fmol/mg protein). Competition studies with androgens, oestradiol and hydrocortisone shows a high specificity for androgens. Initial column chromatography analysis shows a high molecular weight component (m wt = 60 000) and a low molecular weight component (m wt = 50 000), comparable with the 8S and 4S components seen on sucrose density analysis of the prostatic receptor.

Our data suggest that mammalian liver contains classical AR and as such may be
Sex hormones and sex hormone binding globulin in postmenopausal women with non-alcoholic liver cirrhosis

P Bannister, P Sheridan, and M S Losowsky (University Department of Medicine, St James's Hospital, Leeds) Men with alcoholic liver disease are feminised and show abnormalities of their sex hormones – low testosterone (T), raised oestradiol (E2), raised androstenedione (Δ4), low dehydroepiandrosterone sulphate (DHEA-S) and raised sex hormone binding globulin (SHBG). These changes may be secondary to liver disease or to direct ethanol toxicity on the hypothalamic pituitary axis. The majority of previous studies have concentrated on studying men with alcoholic liver disease, and little information is available on non-alcoholic liver disease or in women with liver disease. We have investigated post menopausal women with non-alcoholic cirrhosis (n=25), and a control group of healthy women (n=21) to assess whether women with liver disease show hormone abnormalities and, if so, to see if the pattern of change is different from that in men with alcoholic liver disease. Plasma oestradiol was raised: 102±97 pmol/l vs 45±9±20±4 (mean±SD) p<0.01. Plasma SHBG was raised: 16±5±7±4 mg/dl vs 12±±2±3±2, p<0.02. Plasma DHEA-S was low: 0.74±0.5 μmol/l vs 4.45±2.41, p<0.001 as was plasma Δ4: 4.56±2.53 nmol/l vs 6.3±±2.13, p<0.05. There was no significant difference in T levels. These data show that postmenopausal women with cirrhosis have abnormalities of sex hormone and SHBG levels. Our finding of a low Δ4 is at variance to that seen in males, and may reflect the absence of an effect secondary to ethanol toxicity.

Faecal incontinence in the elderly impacted patients

J J Bannister, I Abozekry, and N W Read (Department of Surgery, Royal Hallamshire Hospital, Sheffield and Tickhill Road Hospital, Doncaster) Fifty five elderly patients (28 women, 27 men) who had impacted masses of faeces in the rectum and a history of faecal soiling underwent extensive investigation of their anorectal physiology and radiology. The results were compared with those obtained from 36 age matched controls (18 women, 18 men) with no anorectal problem.

The sphincter pressures were similar, but the minimum rectal volume required to cause reflex anal relaxation was lower in the constipated subjects (p<0.05). Similar results were obtained with the faecal mass in situ and at least one week after disimpaction, suggesting that soiling was not caused by mechanical stretching of the anal ring or by prolonged reflex inhibition of the anal tone by the faecal mass.

Radiology showed a more obtuse anorectal angle in the impacted patients (p<0.01). Perception of a balloon in the rectum (p<0.05) and anal sensation (p<0.01) were reduced in the constipated patients. In the impacted patients the minimum rectal volume which causes reflex anal relaxation is less than the threshold for perception, in contrast to controls. This factor combined with an obtuse anorectal angle and reduced anal sensation may help to explain the incontinence seen in the impacted patients.

Effect of timed exposure of cytocidal agents on colorectal cancer (HT29) cells

M Crowson, P Light, J Griffin, and N S Ambrose (Surgical Immunology Unit, Queen Elizabeth Hospital, Birmingham) The use of cytocidal agents in colorectal cancer operations to prevent live cell exfoliation and possible local recurrence is controversial. The time of application of agents either topically or luminally is variable. We have cultured a colonic cancer cell line (HT29) and investigated the effect of six cytocidal agents (Povidone iodine 5% and 100%, Eusol, Cetrimide 30% and 100%, water, mercuric perchloride, Nystatin) on the viability of cells at different exposure times.

Cells have been brought to confluence, and incubated for 2, 5, 10, 15 minutes with each agent, washed, and cultured for 24 hours. Cells were trypsinised and assessed for viability. Control cells showed between 79–76% viability. Only Cetrimide 30% and 100% and Povidone iodine (5% and 100%) achieved <10% viability after a two minute exposure. Only Cetrimide 30% and 100% achieved 0% viability at all exposures. Eusol and mercuric perchloride required five and 10 minutes exposure to achieve 0% viability. Water and Nystatin allowed 40% and 19%, 60% and 89% viability at 5 and 15 minutes respectively. Only Cetrimide achieved 100% kill rate of cells at all times of exposure. This should be the agent of choice for topical or luminal use.

Anterior posterior rectopexy: a new treatment for solitary rectal ulcer syndrome in patients without overt rectal prolapse

J E Simson and R J Nicholls (St Mark’s Hospital, City Road, London) The treatment of solitary rectal ulcer syndrome without overt rectal prolapse is unsatisfactory. Conventional operations fail to support the anterior rectal wall where intussusception and ulceration commonly occur. A combined anterior and posterior rectopexy was therefore developed. The rectum is mobilised to the pelvic floor and polypropylene (Marlex) sheets placed on...
the anterior and posterior aspects. Nine patients (four men, five women, ages 19-46 years) with solitary rectal ulcer without overt rectal prolapse were treated between three and 45 months (mean 23 months) previously. Improvement of tenesmus was most marked: the mean number of attempts to defaecate/24 hours fell from 10.0±6.7 to 4.5±2.6.5 postoperatively, and the mean time spent in the toilet/24 hours fell from 176±98.5 to 163±15.0 minutes. Other symptoms were cured or greatly improved as follows: mucus 8/9, bleeding 9/9, straining 6/8, pain 6/7 and incontinence 2/4. Two patients complained of constipation without sensation of rectal fullness postoperatively and two patients have experienced recurrence of symptoms of solitary ulcer syndrome. Seven patients (78%) remain well and are most satisfied with the result.

Combined antero-posterior resection may be effective treatment for solitary ulcer syndrome when conservative management fails.

F61
Is ‘simple constipation’ a myth?

S N MARCUS and K W HEATON (University Department of Medicine, Bristol Royal Infirmary, Bristol) Constipation and spastic colon are usually regarded as separate entities. Patients with ‘simple constipation’ receive scant sympathy and less interest. The symptomatology of documented and induced constipation has not been reported. We administered a questionnaire about colonic symptoms to 45 volunteers with definite and unremitting constipation (BO<3/week and/or mean whole-gut transit-time 68 hours, actually 13.3±5.2 hours); (a) when untreated or ineffectively treated and (b) in 28 cases after effective treatment for six weeks with Senokot (n=14) or Trifyba, a wheat-fibre concentrate (n=14). We also questioned 13 healthy volunteers before and after induction of constipation with loperamide for six weeks (transit-time prolonged from 48±10 to 102±31 hours).

In spontaneous constipation symptoms of spastic colon were common, one or more occurring in 96%. Passage of mucus occurred in 60% (regularly in 20%), feeling of incomplete evacuation in 80% (regularly in 40%), bloated feeling in 80% (regularly in 36%). Lower abdominal pain occurred >6 times/year in 51%, and was relieved by defaecation in 70% (regularly in 43%). All four symptoms occurred in 31%. Mucus, bloating and incomplete evacuation were common even in 22 who denied pain. Effective laxation reduced the frequency of all these symptoms. Trifyba abolished pain more often than did Senokot. bloating tended to remain with Trifyba, while Senokot usually relieved it. With loperamide-induced constipation most subjects developed bloating and incomplete evacuation while five developed colonic pain. Mucorhoea developed once.

We conclude that it is artificial to distinguish constipation from spastic colon.

F62
Large intestine as an accessory organ of K excretion in chronic renal failure (CRF)

G I SANDLE, E GAIGER, AND S TAPSE (Departments of Medicine and Clinical Biochemistry and Metabolic Medicine, University of Newcastle upon Tyne) Faecal K excretion rises in patients with CRF, suggesting that the large intestine plays a role in homeostasis as renal function declines. To investigate possible controlling factors, a rectal dialysis technique was used to measure net K secretion (mmol/cm²/h) and transmural potential difference (pd in mV, lumen-negative). Rectal solutions contained KHCO₃, 45 mmol/l, NaCl 105 mmol/l and PEG 4000 (5 g/l) as a water marker. Groups studied were: (I) normal controls (n=14), (II) normotensive CRF patients not requiring haemo- or peritoneal dialysis (n=8), (III) normotensive haemodialysis patients pre- and post-dialysis (n=7), and (IV) normotensive patients undergoing chronic ambulatory peritoneal dialysis (n=10). Compared to net K secretion in group I (1.9±0.2), secretion was greater in group II (3.1±0.6, p<0.005), group III (3.7±0.4, p<0.001) predialysis and 2.4±0.5, p<0.05 post-dialysis, and group IV (2.4±0.4, p<0.02). Plasma K concentrations (mmol/l) in groups I, II and IV were similar (4.1±0.1, 3.9±0.2, and 4.3±0.3, respectively), but compared with controls (I), haemodialysis patients (III) were hyperkalaemic predialysis (5.3±0.1, p<0.001) and hypokalaemic postdialysis (3.5±0.2, p<0.005). There was no significant difference in plasma aldosterone (pmol/l) between groups I (313±34) and II (272±33) and the concentrations in the dialysis patients (groups III and IV) were within normal limits. Rectal pd's in groups I-IV were also similar (46±3, 45±4, 43±5 predialysis and 47±3 postdialysis, and 39±3, respectively). Thus, large intestinal K secretion increases in CRF as renal excretion declines. This change is independent of plasma aldosterone and K, and rectal pd, and may reflect an active K secretory process.

F63
Perioperative assessment of colonic perfusion as a predictor of anastomotic healing

M E FOSTER AND D J LEAPER (University Department of Surgery, The Bristol Royal Infirmary, Bristol) Colonic anastomotic leaks are common in the elderly and also after emergency operation when adequate tissue perfusion and oxygenation may be impaired because of hypovolaemia. Perioperative assessment of perfusion is crude and can at best only differentiate between viable and non-viable bowel.

We examined the effect of hypovolaemia on colonic healing in 40 Sprague-Dawley rats. Colo-colic anastomoses formed in hypovolaemic rats, following 10% depletion of blood volume, healed less well at 3 days than normals: hypovolaemic (n=10) 5.8 (4.1-9.9) mg/mg hydroxyproline; (median and range) vs normal (n=10) 7.8 (4.6-11.8); p<0.05. Similarly after right hemicolectomy collagen content was reduced in ileo-colic anastomoses: hypovolaemic (n=10) 4.8 (3.0-6.4) vs normal (n=10) 5.8 (4.3-6.9); p<0.02.

Colonic perfusion was assessed using a multwire oxygen electrode to measure tissue oxygen tension (pTO₂) in seven half-lap rabbits with monitoring of arterial pressure and blood gases. pTO₂ from 950 readings in normal colon was 37±18 mmHg (mean±SD) and fell to 33±12 mmHg after a 10% blood volume loss (p<0.001). Small bowel pTO₂ (42±18 mmHg) was higher than colon (p<0.001) but did not fall following hypovolaemia. High inspired pO₂ failed to improve pTO₂ colon but raised pTO₂ in small bowel in hypovolaemic rats.

Hypovolaemia compromises healing in colonic anastomoses. Hypoxia may be the causative factor and poor perfusion may be predicted by the pTO₂ electrode.

F64
Why do patients with slow transit constipation have no postprandial defaecation response?

A M ROE AND N J MCC MORTENSEN (University Department of Surgery, The Bristol Royal Infirmary, Bristol) Patients with slow transit constipation have no post-
prandial call to stool. We have investigated three possible hypotheses for this phenomenon: (1) an abnormality of rectosigmoid motility (2) abnormal rectal sensation and compliance (3) abnormal sampling reflex and anal sensation. Seventeen patients with radiologically defined slow transit have been studied group A (n=10) post hysterectomy, group B (n=7) no surgery and 12 controls. Motility was recorded at 15, 20 and 25 cm for ½ hour fasting and ½ hour after a meal. The meal significantly increased the motility index in both patient groups and controls (p<0.01). The motility index was significantly lower in group B patients than controls both fasting (p<0.004) and postprandial (p<0.005). But in group A it was not. Rectal sensation and compliance were assessed by proctography. Rectal compliance, DV/DP was controls 4-02 (2.25-7.90) ml/cmH.O, group A 4-86 (2.15-8.10) and group B 4-65 (1.20-6.80) p=NS. Threshold of anal mucosal electro-sensitivity was measured in the lower, middle and upper anal canal. Results (medians and ranges in mA) were controls 5-0 (3-0-6-0), 3-6 (2-0-5-3) and 5-0 (3-3-7-0), group A 5-0 (2-0-6-6), 5-0 (3-0-7-0) and 7-0 (3-3-11-0) p=NS and group B 4-0 (3-0-5-0), 4-6 (3-0-6-0) and 7-8 (5-0-10-5) p=NS. The study has failed to confirm any of the three hypotheses in group A but in those constipated patients without previous surgery a motility disorder may be implicated.

F65
Increased crypt number is a feature of colonic adaptation to jejunoileal bypass in rats

J B BRISTOL, H AOKI, AND R C N WILLIAMSON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Compensatory hyperplasia of the small bowel involves increased cell proliferation within an unchanged population of crypts. Colonic adaptation is poorly documented, though crypt cell production rate (CCPR) is accelerated 30 weeks after an 85% jejunoileal bypass (JIB) in rats. The early response of the large bowel to JIB and its effect on total crypt number was studied in 12 adolescent Sprague-Dawley rats. Controls (n=12) had sham bypass. When killed four weeks later JIB rats weighed 84% of controls (p<0.001). The total crypt number in each rat caecum and colon was estimated by counting crypts on representative photomicrographs. CCPR was determined for the same sites by a stathmokinetic technique and whole crypt microdissection. Mean total caecal crypt number in JIB rats increased by 25% over control values (34058±16106 vs 269509±14235, p<0.01). In the proximal, middle and distal thirds of the colon crypt number was unchanged. JIB enhances CCPR throughout the large bowel: caecum 16±7±0.8 vs 8±7±0.6, p<0.001; proximal colon 14±7±1.0 vs 5±1±0.4, p<0.001; mid-colon 10±3±1.4 vs 4±8±0.4, p<0.01; distal colon 8±4±1±0 vs 4±0±0.3, p>0.001. These results indicate that large bowel responds to massive enteric bypass with an early increase of CCPR throughout, with additional enhancement of total crypt number proximally.

F66
Razoxane (ICRF 159) delays appearance of colorectal liver metastases

R H TAYLOR, J M GILBERT, M G C EVANS, AND H G LANE (Department of Gastroenterology, Central Middlesex Hospital: University College Hospital and ICRF, London and Wexham Park Hospital, Berks) Razoxane is a well tolerated cytostatic agent with an antimetastatic effect in experimental tumours. This study was designed to evaluate the benefits of razoxane as long term adjuvant therapy in patients who had had Dukes' stage A, B or C colorectal tumours resected successfully and to monitor the development of liver metastases.

At the time of operation 126 patients were allocated randomly to treatment with razoxane 125 mg bd 5 days/week (n=61) or no treatment (n=65) and had regular clinical follow up as outpatients. Serial grey scale ultrasound scans of the liver were done prospectively every three months by the same operator and reported immediately without knowledge of other results or treatment. Liver function tests were done routinely and isotope scans when indicated.

After a median follow up of three years, 28 patients developed liver metastases, 12 on razoxane and 16 in the control group, of which 72% were diagnosed first by ultrasound. Median time to recognition of liver metastases was 87±10 weeks on razoxane and 60±8 weeks untreated (p<0.05). Twelve on razoxane had probable metastases seen on ultrasound of which eight subsequently regressed completely, compared with only one of eight control patients. Among survivors, the survival was greater on razoxane (>30 months) than not (>20 months). Razoxane was well tolerated by all treated patients.

We conclude that razoxane may delay development of colorectal liver metastases, that some metastases may regress on treatment and that razoxane is a well tolerated, acceptable adjuvant therapy for patients with colorectal tumours.

F67
Food intolerance and atotic status in the irritable bowel syndrome (IBS)

M A SMITH, G R YOUNGS, R M R BARNES, AND R FINN (Gastroenterology Unit, Chester Royal Infirmary; Departments of Immunology and Medicine, Royal Liverpool Hospital, Liverpool) Dietary management in the treatment of IBS remains controversial. We have investigated the value of elimination diets (ED) in a double blind crossover study. Subjects were also tested for atopy, serum IgE, and the presence of serum antibodies to wheat, gluten, milk, and ovalbumin.

Twenty eight patients with IBS were treated with ED for either two or four weeks. In addition they consumed either a neutral (rice) or mixed food (egg, milk, corn, wheat) powder in a double blind crossover fashion with an intervening washout period. Improvement was assessed in terms of change in eight cardinal symptoms of IBS.

Seventeen patients received ED for four weeks. Of 12 diarrhoeal subjects, eight were significantly improved compared with one of five constipated patients. When 11 patients were treated for two weeks there was little overall improvement with no difference between diarrhoeal and constipated subjects. Overall there was little difference between scores achieved when consuming the neutral and mixed food powder. Seven of the nine improved patients in the four weeks study remained well at one year follow up and had identified a number of foods exacerbating their symptoms at reintroduction. Atopy was more common in IBS patients (60%) compared with controls (23%), p<0.01. Serum food antibodies were similar in the two groups and only one IBS patient had a raised IgE level.

We conclude that ED help a proportion of subjects with the diarrhoeal IBS and the increased atopy rate in these patients suggests a true food allergy may be responsible.
Colorectal function in the elderly constipated

J S Varma, A N Smith, R G Smith, and J Bradnock (University Departments of Surgery/Urology and Geriatric Medicine, Edinburgh) Rectal function and colonic motility were studied in patients with chonic constipation from a geriatric unit (n=15) and compared with an asymptomatic control group (n=10). Rectal distension studies were performed to measure volume at sensory perception (SP, ml air), maximal tolerable volume (MTV, ml H2O) and rectal compliance (RC, ml/cm H2O). Anal sphincter pressures and pudendoanal reflex latency (ms) were also determined. Sigmoid colon motor response to surface bisacodyl stimulation was determined by pressure monitoring of small intraluminal balloons.

Reduction in SP was apparent (constipation of controls, mean±SEM. Wilcoxon’s rank sum test; 114±16.8 cf 54±8.5, p<0.05). Four patients showed a functional megalon. The remaining 11 showed a significant reduction in MTV (355±34 cf 492±25.3, p<0.01) and RC (5.5±0.5 cf 9.0±0.5) and 10 extruded the balloon at the MTV. Differences in the resting sphincter pressures and rectal distension reflex were not significant. Four patients had an absent pudendoanal reflex and the remainder significant prolongation (43±7.2±6 cf 39.4±2.1, p<0.02). In two patients bisacodyl failed to elicit a sigmoid motor response.

Constipation in the elderly is not simply caused by delayed transit or dyschezia. Deficits of rectal sensory perception and sacral cord function and hypertonicity of the distal bowel may also be responsible. The latter feature may also explain the phenomenon of balloon extrusion and tendency to incontinence in this group.

Changes in blood lipids related to the presence of dimethylhydrazine (DMH) - induced colon cancer in rats

M R Lewin, Tina Barton, and J P Cruse (Department of Surgery, University College, London and Department of Histopathology, Royal Free Hospital, London) Those people at risk from coronary heart disease and large bowel cancer are drawn from the same urbanised Western populations, but these conditions generally do not coexist. Whilst blood lipid changes are well recognised in heart disease, little is known of their role in large bowel cancer. This study investigates this in a rat colon cancer model. Seventy female Wistar rats received a colon cancer producing regimen of DMH (40 mg/kg BW. sc for five weeks) and were sequentially killed from week 10 in groups of 10 at five weekly intervals. Blood was collected and assayed for total and free cholesterol, phospholipids, and triglycerides. All animals were autopsied and all colonic tumours were histologically examined and classified either as adenomas or carcinomas. Groups were divided into tumour free or tumour bearing animals, the latter group being further subdivided into those animals with adenomas and those with carcinomas. There was no difference in total cholesterol or triglycerides between tumour free and tumour bearing rats, but there was a significant increase in free and per cent free cholesterol (p<0.005) and a significant decrease in phospholipids in the tumour-bearing rats (p<0.001). There was no difference in any lipid between tumour free and adenoma bearing rats, but in the carcinoma-bearing rats, whilst there was no difference in total cholesterol or triglycerides, there was a significant increase in free (p<0.002) and per cent free cholesterol (p<0.005) and a significant decrease in phospholipids (p<0.001) compared to tumour-free rats.

These data show for the first time a clear relationship between blood lipids and the presence or absence of large bowel disease.

Postirradiation diarrhoea

J H Meerwaldt and M Van Blankenstein (Rotterdamsch Radio-Therapeutisch Instituut/Dr Daniel den Hoed Kliniek Groene Hilledijk, Rotterdam; Academic Hospital Dijkzigt Rotterdam, The Netherlands) Diarrhoea, often accompanied by faecal incontinence, is a common complaint after pelvic radiotherapy (PRT). In order to evaluate the role of bile acid spillover (BAS) and continence mechanisms a prospective study was conducted in 196 women undergoing PRT. Stool weight (SW), intestinal transit time of solid markers (ITT), fasting and postprandial serum bile acids (SBA) were measured before, during and after PRT with stool frequency (SF) and incontinence (IC) being evaluated simultaneously by a questionnaire. In a subgroup facal excretion of radioactive labelled cholic acid was measured. A rectal saline continence test was performed before PRT.

During radiotherapy 75% of patients reported an increased stool frequency (mean 3x) with SW rising from 120 g to 210 g/24 h but ITT remained unchanged. Fasting and postprandial SBA were significantly reduced. At six weeks and six months after PRT 32 and 36 patients reported diarrhoea (SF 3 x/24 h) and/or incontinence. SBA however, the faecal labelled cholic acid excretion. SW and ITT before and after PRT, were unchanged both in symptomatic and asymptomatic patients. The pre-PRT continence test failed to predict the subsequent occurrence of incontinence.

We conclude that although bile acid spillover may influence diarrhoea during pelvic radiotherapy, neither bile acid spillover as reflected in serum bile acids and stool weight nor prepelvic radiotherapy continence test, determines postpelvic radiotherapy diarrhoea and incontinence, suggesting that decreased compliance of the rectosigmoid reservoir may be responsible.
American criteria demonstrate, however, an increasingly reciprocal relationship between adenomas and carcinomas, with progressive accrual of in situ and intramucosal carcinomas and a decline in the adenoma/carcinoma ratio from 2:1 at 10 weeks to 1:4 at 35 weeks.

These results provide experimental support for the concept of an adenoma-carcinoma sequence, provided colonic neoplasms are classified according to American criteria. If the same discrepancies exist in the diagnosis and classification of human colonic tumours, then the current British histopathological criteria will need revision.

F72
Structural explanation for the invasive behaviour of signet ring cell carcinoma of the colon

C ROWLATT, A A SADRUDIN, AND J P CRUSE (Imperial Cancer Research Fund and Department of Histopathology, Royal Free Hospital School of Medicine, London) Signet ring cell carcinoma (SCa) is an uncommon gastrointestinal tumour with a poor prognosis due to widespread early dissemination. In a rat model, ten SCa were unusually invasive. An ultrastructural explanation of this behaviour has emerged. Colonic epithelial tumours were induced in 56 Wistar rats by dimethyldihydrazone (200 mg/kg sc in five divided weekly doses). Animals were sequentially killed, autopsied and colonic tumours processed for histology. Tumours were classified histopathologically and staged according to Dukes. Some SCa were studied by transmission electron microscopy. SCa were uncommon, comprising only 10 of 220 colonic tumours (4%). They were found earlier and had a different accrual rate from classical adenocarcinomas. Histologically, SCa formed endophytic masses of dissociated cells lacking glandular structures, occurred within mucosal lymphoid tissue and had no associated adenomas. By Dukes' staging, SCa were more invasive, accounting for a greater proportion of deeply invasive B and C tumours (p<0.001).

Ultrastructurally, SCa cells lacked polarity, causing the characteristic mucin retention. The cytoplasmic basis for the cellular dissociation and invasiveness of SCa is attributable to the complete absence of intercellular junctional complexes necessary for gland formation, aided by an absence of stromal desmoplastic reaction.

OESOPHAGUS
F73-77
F73
Effect of oesophageal pH sensors on patterns of swallowing

D F EVANS, M S PRIEST, A G CLARK, AND J D HARDCASTLE (Department of Surgery, University Hospital, Nottingham) Long-term oesophageal pH monitoring using a glass pH electrode or a tethered radio-telemetry capsule (Sietens Ltd) has been widely used in the diagnosis of gastro-oesophageal reflex (GOR). The frequency of swallowing which is known to be important in the clearance of acid from the oesophagus may be affected by the presence of such devices.

Swallowing rates were measured in five normal subjects during an eight-hour period using surface submental EMG electrodes and a piezo-electric swallow sensor (Siemens Ltd). Subjects were studied on three occasions, once as a control and then with either a 3-5 mm diameter nasogastric tube or a tethered pH-sensitive RT probe positioned in the distal oesophagus. Swallowing was continuously monitored for a three-hour control period and for four hours after a standard meal. There was no significant difference in swallows per hour control and RT (either before or after the meal (Control pre-meal 60.48±1.68 SEM, postmeal 56.7±5.2, RT Pre-meal 54.18±4.4, postmeal 59.34±2.4). There was a significant increase in swallowing in the nasogastric tube group preprandially (72.36±11.5, p<0.01) and a decrease postprandially (51.12±10.56, p<0.05) compared with control studies. This study has shown that a nasogastric tube in the oesophagus significantly affects swallowing rates whereas a tethered pH telemetry capsule does not. Oesophageal clearance of refluxed contents is therefore likely to be altered by the presence of the tube, thus increasing errors in the assessment of gastro-oesophageal reflux.

F75
Comparison of an antacid/dimethicone mixture and an alginate/antacid mixture in the treatment of oesophagitis

C POKORYN, M LANCASTER-SMITH, R J WALKER, A J MORRIS, N KRASNER, C R HUTCHISON, M D HELLER, B J Z DANES, AND R I RUSSELL (Gastroenterology Departments of Queen Mary's Hospital, Sidcup, Walton Hospital, Liverpool, Princess Margaret Hospital, Swindon, and the Royal Infirmary, Glasgow) In an endoscopically controlled eight-week trial liquid preparations of an antacid/dimethicone mixture (Maalox plus) and an alginate/antacid mixture (Gaviscon) were compared in patients with oesophagitis. Fifty-one patients (26 women, 25 men; mean age 51, range 19–75 years) completed four weeks of the trial and 46 continued for

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eight weeks. They were randomly allocated to treatment with either Maalox plus (27 patients) or Gaviscon (24 patients). Patients recorded symptoms on diary cards and assessment was made clinically, endoscopically and histologically at 0, four, and eight weeks. The groups did not differ significantly with respect to duration of symptoms, initial severity of oesophagitis, age or sex. At eight weeks symptoms had resolved or improved in 20 of 23 (87%) on Maalox plus and in 16 of 23 (70%) on Gaviscon. Endoscopic appearances at eight weeks had improved or returned to normal in 16 of 23 (70%) patients taking Maalox plus and in 13 of 23 (57%) taking Gaviscon. Histological material from 27 patients has been assessed and showed improvement or complete healing at eight weeks in eight of 14 (57%) on Maalox plus and in nine of 13 (69%) on Gaviscon.

This study, therefore, shows that Maalox plus is as effective as Gaviscon in the management of gastro-oesophageal reflux in which condition the latter has proven efficacy.

F76 Gastrointestinal bleeding in alcoholic and non-alcoholic subjects with varices - short and long term prognosis

D W BULLIMORE (INTRODUCED BY M S LOSOWSKY) (St James's Hospital, Leeds)

Gastrointestinal bleeding in subjects with varices carries a high mortality whether treated medically or surgically. Outcome being worst in subjects with poor hepatic reserve (Child's C). The study was undertaken to determine whether the presence of active variceal bleeding at the time of initial endoscopy indicated a worse prognosis. One hundred and forty three episodes of variceal bleeding in 104 different subjects were subdivided by endoscopic appearance: (a) active variceal bleeding (62 events), (b) evidence of recent bleeding with no alternative source and no erosions or clot overlying varix (58 events) and (c) intermediate group with no active bleeding but overlying clot or erosions (23 events). Group (c) was not further studied nor were subjects whose source of bleeding was undefined or who were bleeding from sources other than varices. Survival rates were compared for distribution of Child's grade, per cent alcoholics and mean age. Transfusion requirements were greater in the actively bleeding group (16 vs nine units, p<0.001) as was the use of tamponade (47% vs 22%, p<0.01). Active bleeding at initial endoscopy was a poor indicator of the need for subsequent surgical referral (39% vs 28%, p=0.14). Survival to discharge was similar in the two groups (74% vs 78%) and mortality was related to Child's grade (B=16%, C=54%). Long term survival was relatively good (63% at 500 days and 47% at 1000 days overall, p>0.1, no significant difference between groups).

We conclude that this study indicates that active variceal haemorrhage at the time of initial endoscopy is not per se an indicator of the need for surgical referral. It also illustrates the converse - lack of active bleeding at the time of initial endoscopy is still associated with a significant admission mortality of around 22%.

F77 Is active bleeding at time of initial endoscopy a bad prognostic sign in variceal haemorrhage?

D W BULLIMORE (INTRODUCED BY M S LOSOWSKY) (St James's Hospital, Leeds)

Variceal haemorrhage is a condition which carries a high mortality whether treated medically or surgically. Outcome being worst in subjects with poor hepatic reserve (Child's C). The study was undertaken to determine whether the presence of active variceal bleeding at the time of initial endoscopy indicated a worse prognosis. One hundred and forty three episodes of variceal bleeding in 104 different subjects were subdivided by endoscopic appearance: (a) active variceal bleeding (62 events), (b) evidence of recent bleeding with no alternative source and no erosions or clot overlying varix (58 events) and (c) intermediate group with no active bleeding but overlying clot or erosions (23 events). Group (c) was not further studied nor were subjects whose source of bleeding was undefined or who were bleeding from sources other than varices. Survival rates were compared for distribution of Child's grade, per cent alcoholics and mean age. Transfusion requirements were greater in the actively bleeding group (16 vs nine units, p<0.001) as was the use of tamponade (47% vs 22%, p<0.01). Active bleeding at initial endoscopy was a poor indicator of the need for subsequent surgical referral (39% vs 28%, p=0.14). Survival to discharge was similar in the two groups (74% vs 78%) and mortality was related to Child's grade (B=16%, C=54%). Long term survival was relatively good (63% at 500 days and 47% at 1000 days overall, p>0.1, no significant difference between groups).

We conclude that this study indicates that active variceal haemorrhage at the time of initial endoscopy is not per se an indicator of the need for surgical referral. It also illustrates the converse - lack of active bleeding at the time of initial endoscopy is still associated with a significant admission mortality of around 22%.

F78 Therapeutic potential of acid resistant fungal lipase in pancreatic steatorrhea

K BALASUBRAMANIAM, C BROWN, D BENOLIEL, D FACCHINIETTI, J C BATTEN, AND T C NORTHFIELD (Department of Medicine, St George's Hospital Medical School and Brompton Hospital, London) A major problem with conventional treatment of pancreatic steatorrhea using pancreatic lipase of animal origin is that 90% of the lipase is destroyed by acid in the stomach. Current methods of avoiding this problem are only partially successful in patients with severe steatorrhea. We have therefore investigated the potential value of a fungal lipase. This was said to be resistant to acid, but inhibited by bile acids. In vitro, we checked the activity of fungal lipase at different pH values and at different bile acid concentrations. In vivo, we assessed intragastric acid resistant lipase activity for two hours after a lipid meal in 10 patients with pancreatic steatorrhea caused by adult cystic fibrosis (CF) after oral administration of fungal lipase (750 mg) or matching placebo in random order. In vitro, fungal lipase had a wide pH optimum of 2.5 to 5.5. 70–80% lipase activity was retained at bile acid concentrations of 8–12 mM (the concentration found intraduodenally in CF). In vivo, acid resistant lipase activity (mean±SEM: mmoles free fatty acid released/ml gastric aspirate/minute) at 30, 60, 90 and 120 minutes postprandially was 718, 1073, 984 and 611 on fungal lipase, compared with 499, 622, 536 and 555 on placebo (p=0.03 for area under the curve).

We conclude that acid resistant fungal lipase represents a novel and potentially valuable therapeutic approach in pancreatic steatorrhea.
F79
Optimum bile acid regimen for rapid gall stone dissolution

R JAZRAWI, A LANZINI, AND T C NORTHEFIELD
(Norman Tanner Gastroenterology Unit, St James's Hospital and Department of Medicine, St George's Hospital Medical School, London) A major problem with bile acid therapy for gall stones is the slow dissolution rate. Urso-deoxycholic acid (UDCA) causes a greater reduction in cholesterol saturation index (SI) than chenodeoxycholic acid (CDCA), but SI during UDCA may not predict dissolution rate if liquid crystal formation is involved. Both have a greater effect on SI if given as a single bedtime dose. We have therefore matched 44 patients with radiolucent gall stones into groups of four according to gall stone size, and have randomly allocated one out of each group to receive mealtime CDCA, bedtime CDCA, mealtine UDCA or bedtime UDCA (12.5 ml/kg/day for each). Reduction in gall stone volume was assessed from carefully standardised oral cholecystograms, and SI was measured in fasting gall bladder bile obtained by nasoduodenal intubation. Results are available at six months for eight matched patients on each regimen. There is a significantly greater reduction in gall stone volume for UDCA than CDCA (mean±SEM; 50±9% vs 35±8%, p<0.05), and for bedtime than mealtime administration during CDCA (46±13% vs 23±8%, p<0.05) but not UDCA (53±11% vs 37±14%). Dissolution rate correlated with SI during treatment equally for UDCA (r = -0.64, p<0.001) and as for CDCA (r = -0.61, p<0.001).

We conclude that gall stone dissolution rate over the first six months is more rapid for UDCA than for CDCA at mealtimes, but is similar for bedtime administration because this enhances the effect of CDCA more than UDCA; and that uncorrected SI is an equally good predictor of gall stone dissolution rate for UDCA as for CDCA.

F80
Compensatory increase in lingual lipase activity and intragastic lipolysis in pancreatic steatorrhoea caused by adult cystic fibrosis (CF)

K BALASUBRAMANIAM, C BROWN, D FINE, J C BATTEN, AND T C NORTHEFIELD (Department of Medicine, St George's Hospital Medical School and Brompton Hospital, London) We have previously reported that some lipolysis occurs in patients with complete pancreatic lipase deficiency due to adult CF. Hamosh et al (1984) have reported that acid-resistant lingual lipase is the predomi-

nating intra-duodenal lipase in such patients, but they did not carry out a direct comparison with healthy controls. We have therefore assessed lingual lipase activity and percentage lipolysis in gastric aspirate obtained from 10 patients with steatorrhoea caused by adult CF (confirmed by sweat test) and from 10 matched healthy volunteers. Gastric samples were aspirated fasting and for two hours following a meal consisting of long chain triglyceride in an emulsified form. For the lingual lipase assay we used 1H-triolein as substrate at pH 4.2. Lingual lipase activity (mean±SEM) remained relatively constant postprandially in both groups, but was twice as high in CF as in controls (596±25 vs 299±28 nmol of free fatty acid released/ml of gastric juice/minute; p = 0.03 for area under the curve). Mean per cent lipolysis rose to 5, 9, 7 and 10% at 30, 60, 90 and 120 minutes respectively in CF, compared with 5, 5, 5, and 5% in the controls (p=0.036 for area under the curve).

We conclude that patients with pancreatic steatorrhoea owing to adult CF have a compensatory increase in lingual lipase activity and in intragastic lipolysis.

F81
Micellar theory of fat absorption may be only half the story

D FINE, C BROWN, AND T C NORTHEFIELD (Department of Medicine, St George's Hospital Medical School, London) It is believed that the products of fat digestion (fatty acids and monoglyceride) are absorbed solely from a micellar solution. This belief stems from the classical observation of Hofmann and Borgstrom that ultracentrifuged chyme displays only three phases - an oil phase, a clear aqueous 'micellar' phase and precipitate. We have noted visually two additional aqueous phases, immediately above and below the micellar phase, and have termed them the upper and lower intermediate phases (UIP and LIP). We have analysed these two new phases physically and chemically in postprandial jejunal chyme from each of six normal subjects. Samples were immediately lipase-inactivated before ultracentrifugation overnight. Phases were then separated by tube-slicer. Lipids were extracted by partitioning, and fatty acids (FA) measured colorimetrically. Physical analysis revealed liquid crystals by polarising microscopy in UIP, and giant liposomes by electron microscopy in LIP. Chemical analysis showed that FA mass was higher in the 'micellar' phase (32±6% of the total FA mass in sample) than in UIP (12±3%, p<0.05), or LIP (9±1%, p<0.01). 15±2% was in the precipitate and 36±7% in the oil phase. But FA concentration was lower in the 'micellar' phase (4±2 mM/l) than in UIP (26±4 mM/l, p<0.05) or LIP (12±2 mM/l, p<0.01). We conclude that two additional aqueous phases can be identified in jejunal chyme, consisting of liquid crystals and giant liposomes; and that these two new phases contain almost as much fatty acid as the 'micellar' phase but at a considerably higher concentration, suggesting that they may play an important role in fat absorption.

F82
Pancreatic enzyme synthetic rates in 'mild chronic pancreatitis'

J HAMILTON, E J S BOYD, M R JAYCNA, J PENSON, J S SOUTAR, I A D BOUCHIER, AND K G WORMSLEY (Departments of Medicine, Therapeutics and Radiology, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland) The significance of the pancreatographic abnormality of 'mild chronic pancreatitis' (MCP) is uncertain. To determine the functional correlates of these radiological changes pancreatic enzyme synthetic rates were measured by measuring the incorporation of 3H-se-methionine into enzymes during stimulation of pancreatic secretion. We have compared pancreatic exocrine function and enzyme synthetic rates with pancreatography in patients suspected of pancreatic disease. Pancreatograms were assessed blind by two experienced observers according to the Cambridge criteria. Twelve patients had a normal pancreatogram and six had MCP. Duodenal contents were aspirated for eight consecutive 15 minute sample periods during intravenous infusion of secretin and cholecystokinin containing 3H-se-methionine. Concentrations of trypsin and bicarbonate were measured in each sample, and the specific activity of TCA precipitated protein determined, and expressed as a percentage of the specific activity of TCA-precipitate of the same patient during the final 15 minute collection period. In MCP, trypsin and bicarbonate output were normal in four patients, trypsin was reduced in one and bicarbonate in one. Both trypsin and bicarbonate out-
puts were normal in all patients with a normal pancreatogram. Incorporation of 
75Se-methionine into pancreatic enzymes was significantly greater in MCP than 
normal at all times between 30 and 90 minutes. Despite normal outputs of pan-
creatic enzymes and bicarbonate in MCP, pancreatic enzyme synthesis rates are in-
creased, indicating acinar damage. The radiological abnormalities of MCP there-
fore imply pancreatic disease.

_F83_  
Right upper quadrant pain: the early di-
agnosis by prolonged infusion cholecysto-
graphy  
K R POSKITT, A D TAYLOR, I F LANE, T COOKE  
(Introduced by J Powell Tuck) (Department of Surgery, Charing Cross Hospi-
tal, London)  
Ultrasonography can give a reliable diagnosis in gall bladder disease but its ac-
curacy is operator dependent. As it is suggested prolonged infusion cholecysto-
graphy (PIC) is useful in diagnosing acute cholecystitis, we have compared ultraso-
nage to PIC in the diagnosis of right upper quadrant pain.  
Fifty consecutive patients admitted with 
right upper quadrant pain had ultraso-
nography and PIC performed within 72 
hours of admission. Prolonged infusion 
cholecystography involved an overnight 
infusion of 1 litre of dextrose saline con-
taining 100 ml of meglumine iothixate 
(Biliscopin) with standard and tomog-
raphic radiography performed the follow-
ning morning. 

Gall bladder disease was present in 28 
patients; 25 of these were shown to have 
 bile disease with PIC compared with 27 
cases with ultrasound. In the 22 patients 
with no proven biliary disease, PIC pro-
tected two false positive results compared 
to three with ultrasound. PIC is reliable in 
 diagnosing gall bladder pathology with an 
overall accuracy of 90% compared with 
92% with ultrasonography. The addition 
of tomography to anteroposterior and oblique 
views proved effective in increasing its 
accuracy. Two cases with apparently nor-
mal opacifying gall bladders on anteropo-
sterior/oblique radiographs were shown to 
 have radiolucent gall stones on 
tomography.  

Prolonged infusion cholecystography is an 
accurate aid in the diagnosis of right upper quadrant pain and has the advan-
tages of not requiring skilled radiologists 
and avoids operator dependency.

_F84_  
An initial assessment of the value of serum 
carbohydrate antigenic determinant (CA19-
9) concentrations in patients with pancrea-
cancer  
P K BUAMAH, C CORNELL, C W VENABLES, 
AND A W SKILLEN (Departments of Clinical 
Biochemistry and Surgery, Freeman Hospi-
tal, Department of Clinical Biochemistry, Royal Victoria Infirmary, 
Newcastle)  
Serum CA19-9 concentrations were 
measured in healthy controls, patients 
with pancreatic cancer, benign pan-
creatic disease or malignancy involving the 
 liver, colon, or rectum. In all cases of 
malignancy the diagnosis was proven histo-
logically. The immunoradiometric techni-
que used had a coefficient of variation of 
both within and between batch precision of 
less than 10%.  
The CA19-9 concentrations of 20 healthy 
adult controls were all less than 40 μ/ml 
 with a median of 5 μ/ml. CA19-9 concen-
trations greater than 40 μ/ml were found in 
15 of 15 patients with pancreatic cancer, 
eight of 10 with primary liver cell cancer, 
five of eight with metastatic liver disease, 
five of nine with colorectal carcinoma and 
seven of 15 with benign pancreatic disease. 
CA19-9 levels greater than 120 μ/ml were 
found in 15 of 15 patients with pancreatic 
cancer with no variation in level according 
to the site or extent of the tumour. No patient 
with benign pancreatic disease or 
colorectal carcinoma had CA19-9 levels 
greater than 103 μ/ml, but three of 10 
patients with primary liver cell cancer and 
five of eight patients with metastatic liver 
disease had CA19-9 levels greater than 120 
μ/ml.  
Raised serum AFP concentrations were 
found in eight of 10 patients with primary 
 liver cell cancer and raised serum CEA in 
 all patients with metastatic liver disease, 
but none of the 15 patients with pancreatic 
cancer had raised AFP. Thus simultaneous 
measurement of CA19-9, AFP and CEA 
may assist in the diagnosis of pancreatic 
cancer.

_F85_  
Dietary antioxidants, cytochrome P450, 
and non-alcoholic pancreatitis  
D W K ACHENOS, P ROSE, E FREANE, L HUNT, 
AND J M BRAGANZA (The University De-
partment of Gastroenterology, the Dietetics 
Department and the Faculty of Medicine 
Computation Group, Manchester Royal In-
firmary, Manchester)  
The microsomal 
cytochrome P450 system is involved in the 
detoxification of drugs and chemicals: oxygen 
free radicals are generated and may 
initiate peroxidation of lipid membranes 
unless antioxidants are sufficient. Our 
finding of P450 induction in patients with 
pancreatic disease, together with increased 
lipid peroxidation products in their bile 
suggested an imbalance between produc-
tion and quenching of reactive metabolites. 
The diet is a potential source of inducers 
(caffeine, Brassica, barbecued foods) and 
antioxidants (glutathione precursors; sele-
nium; vitamins A, C, E) and we have 
therefore analysed: the diet of 13 patients 
with non-alcoholic pancreatitis who had 
not altered their eating habits, except 
during attacks. In the week following the 
assessment of enzyme activity (theophyl-
line kinetics) each patient, and seven 
controls, completed a seven-day weighed diet-
ary intake at home. The data were pro-
cessed on a microcomputer using a program 
based on published food tables. Theophyl-
line clearance in patients (median 120 
ml/kg/h, range 59–326) exceeded that in 
controls (median 69 ml/kg/h, range 50–106, 
p<0·05) indicating induction of 
cytochrome P448, but there was no differ-
ence in their intakes of the commoner 
dietary inducers. The patients ingested less 
selenium (p<0·05), vitamin E (p<0·05) and 
vitamin C (p<0·02) than controls; there 
was a trend towards even lower selenium 
p<0·001) and vitamin C (p<0·01) intakes in the subgroup of pa-
tients whose theophylline clearances were 
within the normal range.  
We conclude (1) enzyme induction in 
our patients cannot be explained by diet; 
(2) a relative deficiency of antioxidants 
may be as damaging as a relative excess of 
reactive metabolites generated via 
cytochrome P450 induction.

_F86_  
Bile and bowels: the effects of a new, 
concentrated wheat fibre product  
S N MARCUS AND K W HEATON (University 
Department of Medicine, Bristol Royal 
Infirmary, Bristol)  
When the cholesterol saturation index of bile is reduced by wheat 
bran there is generally a fall in the deox-
cycholic acid (DCA) content of bile. 
Because the same effects occur with senna, 
bran might act on bile simply via its 
laxative properties. We have studied the 
effects of a new, concentrated, wheat fibre 
product (Trifyba, 80% dietary fibre) on
bile composition, DCA metabolism and bowel function, and assessed whether these effects are related.

Twenty constitutively volunteers were prescribed Trifyba in doses (10-32 g/day) sufficient to relieve their symptoms for at least six weeks. Before and at the end of this period, duodenal bile was sampled to enable measurement of DCA pool (by isotope dilution), total bile acid pool, bile acid composition and cholesterol saturation index (CSI).

Whole-gut transit time fell in all but one subject, from 120±35 to 68±35 hours. At the same time, biliary %DCA fell from 26.6±12.0 to 23.0±11.8 (p=0.002), the total bile acid pool expanded from 2.36±0.77 to 2.75±0.90 g (p<0.001), and CSI fell from 1.13±0.32 to 1.07±0.29 (p=0.04). In subjects with initial CSI>1.0 (n=12), CSI fell from 1.33±0.25 to 1.22±0.21 (p<0.008). There were no significant correlations between change in CSI and change in %DCA or DCA pool, nor between change in transit time and change in %DCA or DCA, pool, nor between change in transit time and change in CSI.

We conclude that bran, Trifyba reduces the CSI of supersaturated bile but this action appears to be independent of its laxative properties and of changes in DCA metabolism.

INFLAMMATORY BOWEL DISEASE

F87 Methods of assessment of small bowel strictures in Crohn’s disease

P MOREL and J ALEXANDER-WILLIAMS (General Hospital, Birmingham) Most of the indications for surgical intervention in Crohn’s disease are caused by stenosis or its sequelae. Many patients with small bowel Crohn’s disease have long narrow segments shown on contrast radiographs (Cant’s string sign) without necessarily requiring early operation. The decision to operate is dictated more by the frequency and severity of symptoms than by the radiographic appearances. Therefore, we undertook a prospective study to compare the apparent radiological diameter of the small bowel before operation with the observed diameter at operation and by measurement of the resected specimen.

Twenty patients with small bowel Crohn’s disease requiring operation for active disease with luminal stenosis, who had radiograph contrast studies within one month of operation, had the narrowest diameter of the bowel measured directly on the radiograph: at operation the length and diameter of the narrowest part of the bowel was measured by a variable volume balloon catheter being pulled through the gut from an enterostomy. In those patients having gut resection the diameter of the resected bowel was measured again with graduated bougies before fixation. The x-ray picture overestimates both the diameter and length of the stenosis, while the balloon measurement correlates closely with the measurement of the specimen. The diameter ratio x-ray:balloon:specimen is 1:4:3.8 with the discrepancies resulting from the estimation of the length of strictures being 1:2:1:0.

We conclude that assessment of stricture length and diameter in conventional x-ray contrast studies may measure spasm rather than true fibrous stenosis.

F88 Technetium-99m-sucralfate isotope scanning. A new technique to detect active inflammatory bowel disease?

D J DAWSON, A N KHAN, AND D R SHREEVE (Departments of Diagnostic Imaging and Gastroenterology North Manchester General Hospital, Manchester) Sucralfate labelled with Tc-99m-human serum albumin has been used to detect peptic ulceration by isotope scanning. We have now studied the ability of this technique to detect the ulceration of inflammatory bowel disease. Scans were obtained in 18 patient controls (peptic ulcer), 13 patients with active Crohn’s disease (four ileal, seven ileocolonic, two colonic) and six with active ulcerative colitis. Extent of disease was assessed by barium studies or colonoscopy. Two hundred and fifty milligrams Tc-99m-sucralfate (130–200 MBq) was taken orally with metoclopraamid and manntul to hasten transit, and serial analog images of the abdomen obtained from two to 24 hours. Scans were regarded as positive if localised activity persisted in the small bowel at five to six hours or colon at 20 hours.

All controls had negative small and large bowel scans. Twelve of 13 Crohn’s subjects had positive scans: In seven, isotope distribution matched known abnormalities; in four, additional colonic lesions not seen on barium enema were detected; in one, three of four known colonic lesions were detected. All six ulcerative colitic subjects had positive scans, which in three, suggested more extensive disease than the barium enema.

The isotope scan was cheap, easy to perform, well-tolerated by patients and visualised small and large bowel sequentially. It involved less radiation dosage than barium studies and appeared more sensitive in detecting mucosal lesions. Theoretically, it could prove useful in differentiating active from inactive disease.

F89 Carcinoma-type mucus glycoprotein abnormalities in ulcerative colitis and Crohn’s disease demonstrated by altered lectin binding

J M RHODES, R BLACK, P PATEL, AND A SAVAGE (Department of Medicine, Queen Elizabeth Hospital, Birmingham and Department of Histopathology, Selly Oak Hospital, Birmingham) A specific alteration in colonic mucus glycoprotein structure has been reported in ulcerative colitis. Lectins have specificity for different carbohydrates and can be used to detect changes in glycoprotein structure. We have therefore studied the lectin binding of normal, ulcerative colitis (UC) and Crohn’s disease (CD) rectal mucosa using 10 peroxidase-conjugated lectins chosen for their differing carbohydrate specificities. Paraffin-embedded rectal biopsies from 20 normal subjects (irritable bowel syndrome), 20 with histologically inactive UC without dysplasia and 18 with ileocolonic Crohn’s disease were studied. Sections were incubated in lectin-peroxidase conjugates (0.002 mg/ml) for 24 hours at 4°C. Pre-incubation of lectins with binding sugars demonstrated specificity of lectin-binding. Peanut agglutinin (PNA, galactose binding) which is known to bind carcinomatous but not normal rectal mucus, bound to 8/20 (40%) UC biopsies, 10/18 (56%) CD biopsies and 0/20 normal biopsies. Several UC and CD biopsies also bound Ulexeuropaeus lecin (UEA1, fucose binding) and Conyza simplex folia lectin (GS II, N-Ac-glucosamine binding). Both lectins which we find bind to carcinoma mucins: UEA1, UC 4/20 (20%) +ve, CD 2/18 (11%) +ve, normal 0/20 +ve; GS II, UC 5/20 (25%) +ve, CD 5/18 (28%) +ve, normals 0/20 +ve. No lectin binding pattern was found that was specific for either ulcerative colitis or Crohn’s disease.

This carcinoma-like lectin binding of non-dysplastic rectal mucosa in ulcerative colitis and Crohn’s disease may represent...
very early pre-malignant change and could be valuable for screening patients with longstanding disease.

GASTRODUODENAL

F90

A two year audit of gastroenterology clinics

M A Ivers, S Piper, and D Rowley-Jones (Smith Kline & French Laboratories Limited, Mundells, Welwyn Garden City, Hertfordshire) In order to characterise the management of patients with dyspeptic symptoms in gastroenterology clinics in the United Kingdom, data were collected on four occasions between May 1983 and November 1984. One hundred and fifty hospitals were surveyed and information was obtained from a representative sample of 50. The data base at each survey was around 1000 patients representing up to 20% of the workload of an individual clinic. Of the population surveyed 43% had peptic ulcer disease, while a quarter of the remainder had oesophagitis. About one third of patients were attending a clinic for the first time whilst the remainder had been attending for an average of 11-4 months. As expected the shortest follow-up period of 5-5 months was for patients with gastric cancer. In general up to 10% of patients had attended for more than five years, whilst a quarter of patients with stomal ulceration had been followed up for this length of time.

Although it was not possible to define the overall frequency of upper gastrointestinal endoscopy it was ordered on about one third of patient visits and yielded a positive result in about three-quarters of instances. On the other hand barium studies were requested on less than 10% of occasions and were positive in slightly more than half the patients. Routine haematology and biochemistry was normal in more than four-fifths of patients and was more commonly requested by junior doctors. Almost half the consultations did not result in drug treatment and often (208/473, 44%) the reason for this was unavailability of results of previous investigations. Only about one fifth of patients were discharged from a clinic, more commonly by a senior doctor, and only a fifth were referred for further investigation.

We conclude that upper gastrointestinal endoscopy is the most productive investigation in patients attending a gastroenterology clinic, laboratory investigations are requested too frequently and possibly too few patients are discharged to the care of their general practitioner. There also appeared to be inefficiency in the running of clinics, the results of investigation should be available when the patient is seen.

F91

Earlier diagnosis and improving prognosis of patients with carcinoma of the stomach

D C Ward, D Johnston, A T R Axon, and J Wyatt (Departments of Surgery, Gastroenterology and Pathology, The General Infirmary, Leeds) The prognosis of patients with gastric cancer in England and Wales remains appalling, only one patient in 20 surviving for five years. We have reviewed 324 consecutive cases of gastric cancer, treated between 1968 and 1984, to see if more ‘early’ cases were being diagnosed, whether this led to longer survival, and whether even earlier diagnosis seemed feasible for the future.

In the three five year periods, numbers of ‘node negative’ patients constituted nine (10%) 10 (10%) and 25 (18%) respectively, and early gastric cancer (EGC), 0%, 5%, and 7%, of all cases. The mean duration of symptoms before referral for investigation was 43 weeks in node negative patients, 37 weeks for EGC and 49 weeks for small malignant ulcers. A high proportion of patients were thus being treated for ‘benign’ peptic ulcer disease for months or even years before being investigated.

Corrected five year survival in patients with uninvolved lymph nodes was 71% in the first five year period and 82% thereafter; in EGC, 88%, and in patients with small (<2.5 cm) malignant ulcers, 67%.

These results show that gastric cancer is curable here, as in Japan, and that success depends on early diagnosis. We calculate that even a modest improvement in diagnosis of ‘early’ cases in Britain (to, say, 10% EGC, 25% node-negative and 40-50% ‘resectable for cure’), would raise crude five year survival to approximately 20% and save 2000 lives per year.

F92

Is gastric stump cancer a separate clinical entity? Analysis of 799 patients

O Søreide, A Viste, E Glattre, G E Eide (Department of Surgery, University of Bergen, Bergen, and The Cancer Registry of Norway, Oslo, Norway) Seven hundred and ninety nine patients with cancer of the gastric stump treated during 1970-1979 have been studied. Median age was 69 years (range 31–91) the male to female ratio 4:4:1. The median time interval between primary resection and stump cancer diagnosis was 30.2 years (range 6–61) with younger patients having longer intervals than older patients. Staging of the disease showed that advanced metastatic disease was as common as in the general stomach cancer population. The dominating symptoms were abdominal pain and general weakness, and the median duration of symptoms was four months. A tissue diagnosis was obtained in 88%.

Five hundred and fifty three patients (69%) were operated on, the resectability rate being 40%. The postoperative mortality rate varied from 11% in resected patients to 38% in those with a by-pass operation. The overall five year survival was 10.3% but was 40% for those resected. Patients younger than 40 at the time of primary resection had a better survival than those over 40, whereas the length of interval had no effect on survival.

In conclusion, gastric stump cancer patients have characteristics similar to the general gastric cancer population with a fairly similar stage distribution, stage of disease, postoperative mortality and survival, whereas the resectability rate tends to be lower.

F93

Campylobacter-like organisms (CLO) in the duodenal mucosa and the effect of ulcer treatment on their presence

B J Johnston, M H Ali, K Haines, and P I Reed (Departments of Gastroenterology and Histopathology, Wexham Park Hospital, Slough, Berkshire) Campylobacter-like organisms have been observed in the gastric and to a lesser extent in the duodenal mucosa of patients with various gastrointestinal disorders, but their role is unclear. While a positive correlation has been established with chronic antral gastritis, their role in duodenal inflammation and the effect on their presence of ulcer treatment is less certain. Routine endoscopic duodenal and antral biopsies were examined histologically for CLO by light microscopy both retrospectively and prospectively. Duodenitis was diagnosed when increased plasma cells and lymphocytes were seen in the lamina propria and activ-
ity was determined by the presence of polymorph infiltration, oedema of the lamina propria and degeneration and or regeneration of the surface epithelium. Duodenal biopsies from 67 patients were studied retrospectively and duodenal and antral biopsies from 64 patients prospectively. CLO were found in 33% of the retrospectively studied duodenal biopsies and 67% examined prospectively and in 76% of antral biopsies. No CLO were found in histologically normal duodenum (n=37) or in duodenitis without signs of activity (n=19). CLO were found in 97% of biopsies showing active inflammation (n=30). In duodenal biopsies from active ulcers (DU), CLO were found in 81% (n=43). In 10 patients studied before and after standard treatment (eight ranitidine, two carbenoxolone), CLO were present in all duodenal biopsies before treatment but were demonstrated after treatment only in the five patients in whom histological evidence of inflammation persisted. CLO were located on the surface epithelium of duodenum and antrum and within the superficial antral glands and in association with areas of activity. When CLO were present in the duodenum they were also present in the antrum but not the reverse. While a strong association of CLO presence with active duodenal inflammation was demonstrated, absence of CLO after ulcer treatment only occurred with complete histological healing. CLO were never seen in histologically normal duodenum.

F94
Causes of dyspepsia in general practice
B J RATHBONE, J J WYATT, R V HEATLEY, AND M S LOSOWSKY (Department of Medicine, St James's University Hospital, Leeds and Department of Pathology, The General Infirmary, Leeds) Patients suffering dyspeptic symptoms represent a considerable proportion of the workload in general practice. Little information is, however, available as to the causes of these symptoms as studies have concentrated on patients referred to hospital outpatient departments or 'open access' endoscopy units.

In order to study a representative sample of dyspeptic patients in the community, 112 patients attending their GP with symptoms believed to be arising from the upper GI tract have been investigated. All patients were interviewed and a structured history taken and clinically examined and endoscoped. Biopsies were taken from standard sites and examined by one histopathologist without knowledge of clinical details. Abdominal ultrasound examinations were also carried out.

Fifty eight per cent of the patients were women (mean age 49 years, men 46 years). Nineteen patients had peptic ulceration (six oesophageal, six gastric, and seven duodenal). Seven patients were considered to have symptoms unrelated to the upper GI tract and endoscopic examination was inadequate in seven patients. Eighty one per cent of the remaining patients had endoscopic abnormalities, histological examination showing evidence of inflammation in 80%. Antral gastritis was present in 69%, body gastritis in 53% oesophagitis in 39% and duodenitis in 29%. Four patients had gall stones at ultrasound.

In this study of primary care dyspeptic patients we have shown a high incidence of both mucosal inflammation and peptic ulcer disease affecting >75% of the patients. Our data suggest that careful use of a short course of 'ulcer healing' drugs may be warranted in the treatment of dyspeptic patients in general practice without prior investigation, because the majority of patients will have lesions which would be expected to improve on such treatment.

F95
Differentiation of acute pancreatitis from surgically correctable abdominal emergencies by peritoneal lavage
M J McMAHON and A D MAYER (University Department of Surgery, General Infirmary, Leeds) An investigation of the role of peritoneal lavage for the determination of severity of acute pancreatitis (AP) suggested that the occasional patient with a false diagnosis of AP could be identified. Further experience has revealed six more surgically correctable intra-abdominal lesions first recognised by peritoneal lavage; an incidence of 3% amongst all 'pancreatitis' and 4% of lavaged patients.

The patients presented with clinical features consistent with severe AP and a plasma amylase between 1200 and 9500 IU/l. One had both Cullen's and Grey Turner's signs. Features of peritoneal fluid which identified the diagnostic error were colour (cloudy or bile stained), faecal odour (absent in AP) and presence of bacteria or fibres on microscopy. The diagnoses were perforated peptic ulcer (2) bile peritonitis (3) and mesenteric infarction. Two patients received conservative management and died, two underwent immediate laparotomy and survived and two (peptic ulcer and bile peritonitis) were deemed too ill for immediate surgery and were initially treated with therapeutic peritoneal lavage (2 litres per hour). Both improved clinically, and successfully underwent a subsequent laparotomy.

Irrespective of its prognostic role, peritoneal lavage can identify intra-abdominal emergencies masquerading as AP and can assist in the management of the conditions.

F96
Impaired gall bladder response to intravenous caerulein in patients with coeliac disease
A BROWN, M J BRADSHAW, R RICHARDSON, C MORRIS, A P ARLAMAN, AND R F HARVEY (Department of Medicine, Frenchay Hospital, Bristol) The peptide hormone cholecystokinin (CCK) is released from the mucosa of the upper small intestine after meals, and constitutes the major stimulus to postprandial emptying of the gall bladder. It is believed to act directly on specific receptors in the smooth muscle of the gall bladder wall.

In patients with coeliac disease there is decreased gall bladder contraction after meals. It has been suggested by several studies that impaired release of CCK does not entirely explain this phenomenon, and that the gall bladder may be resistant to the effects of CCK. We have tested this hypothesis by comparing minute-by-minute gall bladder contraction in coeliac patients and control subjects using a computer-linked gamma camera to monitor expulsion from the gall bladder of the radioactive compound $^{99m}$Tc-HIDA, in response to intravenous infusion of the pure and stable CCK analogue caerulein.

Patients with untreated coeliac disease required a considerably larger dose of caerulein to initiate gall bladder contraction (55.6±16.2 vs 17.4±6.6 ng/kg, p < 0.01), and gall bladder emptying was slower than in controls and also less complete (percentage emptying at end of caerulein infusion 32.6±9.0 vs 72.0±4.6 p < 0.001).

We conclude that in patients with untreated coeliac disease the gall bladder is for some reason resistant to the action of caerulein, and therefore presumably also...
endogenous CCK. The degree of abnormality is sufficient to explain the abnormal gall bladder contraction seen in coeliac patients after meals.

F97 Relaxation of the sphincter of Oddi by glucagon-(1-21)-peptide applied locally to the periamillary mucosa

J F REY, M GREFF, J PICAZO (INTRODUCED BY
R F HARVEY) (Institut Arnauld Tzanck, St
Laurent du Var, France) Glucagon-(1-21)-peptide is an analogue of glucagon which has been shown to have a relaxing effect on the sphincter of Oddi when given parenterally. We have studied the effects of locally applied glucagon-(1-21)-peptide on motility of the sphincter of Oddi in man.

In five volunteers undergoing ERCP with manometric recordings, the sphincter of Oddi pressure (basal and peak), choleodochal pressure, duodenal pressure, and wave frequency were measured. Then 1 mg of glucagon-(1-21)-peptide in 2 ml of saline was flushed around the papilla through the recording catheter, and the pressure recordings repeated.

The basal pressure of the sphincter of Oddi decreased by between 39 and 44% after local administration of glucagon-(1-21)-peptide. Phasic pressure, wave frequency, and choleodochal pressure were also decreased. This effect started 90 seconds after local application and lasted for nine to 13 minutes in different individuals.

We conclude that glucagon-(1-21)-peptide has a relaxing effect on the sphincter of Oddi when applied locally. How this direct effect on the sphincter is exerted is still unclear and is presently under investigation. Local application of glucagon-(1-21)-peptide might in some patients aid cannulation of the sphincter of Oddi for ERCP.

F98 Alcohol and gall stone related acute pancreatitis; prospective comparison of clinical and biochemical features of the attack

A D MAYER, M J MCMAHON, M G SHEARER, A P DIXON, C W IMRE, A P CORFIELD, M J COOPER, AND R C N WILLIAMSON (Departments of Surgery, General Infirmary, Leeds, Royal Infirmary, Glasgow and Royal Infirmary, Bristol) Attacks of acute pancreatitis due to gall stones (GAP) and alcohol (AAP) have different clinical and biochemical characteristics but precise comparisons have been prevented by heterogeneous diagnostic criteria and a marked preponderance of one aetiological variant in most studies. AAP and GAP were compared in a prospective multicentre study of acute pancreatitis (AP) in which diagnostic criteria and data collection were standardised.

Of a total of 439 attacks of AP, 75 were classified as AAP (>50 g ethanol per day; no gall stones, no other cause of AP) 219 as GAP (stones shown by radiology, or at laparatomy or autopsy), and 145 as 'other'. Alcohol acute pancreatitis occurred in younger patients (median age 38 cf 67 for GAP) who were usually male (91% male cf 58% female for GAP), but severe AP was equally common (AAP 20.1%, mortality rate 7%; GAP 20.0%, mortality rate 6%). Pseudocyst or abscess complicated 13% of AAP and 10% of GAP attacks.

Admission concentrations of amylase, bilirubin, alkaline phosphatase and transaminase were significantly greater in GAP, but there were no differences in calcium, albumin LDH or WBC. During the first week, alkaline phosphatase remained high in GAP and LDH in AAP, but bilirubin and transaminase became similar in both groups, and amylase fell more rapidly in GAP.

Thus AAP and GAP were similarly lethal, but possess differing biochemical characteristics which may need consideration in diagnostic and prognostic criteria.

F99 Effect of pancreatic spasmolytic polypeptide (PSP) on the sphincter of Oddi

J F REY, M GREFF, J PICAZO (INTRODUCED BY
R F HARVEY) (Institut Arnauld Tzanck, St
Laurent du Var, France) Pancreatic spasmolytic polypeptide (PSP) is a new gut peptide which has recently been isolated from the porcine pancreas. In laboratory animals it inhibits gastrointestinal motility after parenteral or oral administration. Little is known of the effects of PSP on the biliary tract in any species. The effect of local application of PSP to mucosa of the ampullary area on motility of the sphincter of Oddi was therefore studied in man.

Sphincter of Oddi pressures (basal and peak) were recorded during manometric ERCP in 15 volunteers. After this, different doses of PSP were applied locally through the cannula to the mucosa around the papilla. Sphincter of Oddi motility was then recorded until the action of the peptide disappeared.

A 42% decrease of the basal sphincter of Oddi pressure was recorded after local application of PSP. This effect, which is statistically significant (p 0.001), was associated with a slowing of wave frequency and a decrease of the peak pressure. The inhibitory effect appeared 60 seconds after administration of the peptide, reached a maximum after five minutes and its duration was dose dependent. Duodenal and choledochal pressures were also decreased.

We conclude that PSP (1) significantly decreases sphincter of Oddi pressure, (2) reduces pressure wave frequency, (3) its effects on different levels of the human gastrointestinal tract should be investigated further.

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F100 Obstetric factors in damage to the innervation of the pelvic floor musculature in childbirth

S J SNOOKS, P R H BARNES, M M HENRY, M SWASH (INTRODUCED BY PROF J LENNARD-JONES) (The Sir Alan Parks Physiology Unit, St Mark's Hospital, City Road, London) Vaginal delivery can damage the pudendal innervation of the external anal sphincter muscle. We studied 122 women, 51 before and after delivery and the remainder only after delivery, to assess pudendal nerve function in relation to various obstetric risk factors. The methods included measurement of the pudendal nerve terminal motor latency (PNTML) and the fibre density (FD) of the external sphincter muscle. High birth weight, forceps assistance and an increased duration of the second stage of labour were associated with damage to the pudendal nerves (increased PNTML and FD). Epidural anaesthesia, episiotomy, and perineal tears (1st and 2nd degree) had no significant effect on pudendal nerve function after delivery.

F101 Abnormalities of colorectal function in intractable constipation after hysterectomy

J S VARMA, AND A N SMITH (University Department of Surgery/Urology and Wolfson Gastrointestinal Laboratories, Western General Hospital, Edinburgh) Rectal
function and colonic motor activity were studied in women with profound chronic constipation and asymptomatic control female subjects (n=8). Barium enemas had demonstrated megacolon in one and dolichocolons in two patients. Only one patient was free of urinary symptoms. Continuous fluid-infusion proctometrography was used to measure rectal volumes (ml H2O) and pressures (cm H2O) at sensory threshold (TV), constant sensation (CV) and maximal tolerance (MTV), and rectal compliance calculation (RC, ml/cm H2O). Triple-lumen fluid-perfused tubes were used to obtain colonic motility indices (MI) at 25, 20 and 15 cm from the anal verge.

Proctometrograms showed functional megacolons in four patients. There was a significant increase in all the volumes and RC in the hysterecctomy patients (hysterectomy cf controls, mean±SEM, Wilcoxon’s rank sum test; TV: 429±40 cf 241±36-6, p<0-01; CV: 465±32-2 cf 308±26-8, p<0-01; MTV: 690±51-4 cf 476±27-6, p<0-01; RC: 20-7±3-3 cf 9-2±0-5, p<0-05). Motility indices at 25 cm was significantly reduced in the hysterecctomy group (n=7) (462±89, cf 3280±936, p<0-01). Furthermore, the MI at 15 cm in the hysterecctomy group was greater than that at 25 cm (1028±189 cf 462±89), while in the control group the MI at 15 cm was less than that at 25 cm. (3280±936 cf 1226±246).

These functional abnormalities may represent autonomic nerve damage at hysterectomy which can result in colon inertia, sensory deficits and severe constipation. Barium enema and sigmoidoscopy are often unhelpful in the investigation of these patients.

F102
Discomfort after double contrast barium enema: a prospective study of carbon dioxide and air for gas contrast

R A FROST, C COBLENZ, AND G W STEVENSON (Department of Radiology, McMaster University Medical Centre, Hamilton, Ontario, Canada) Radiologists are aware that patients suffer transient abdominal discomfort and pain during air insufflation for double contrast barium enema (DCBE). It is not, however, generally appreciated that some patients suffer pain and discomfort for some hours after leaving the department. Carbon dioxide is absorbed from the gut many times more rapidly than air, so that if the discomfort is due to retained gas, patients insufflated with carbon dioxide should suffer less discomfort. To test this hypothesis 151 consecutive patients presenting to the Department of Radiology for barium enema were entered into a double blind, prospective trial. Each patient was randomised to receive either air or carbon dioxide. DCBE was performed by our standard technique, the radiologist being unaware which gas was being supplied from one of two cylinders. The patients were telephoned within 24 hours of completion of the enema by an interviewer who completed a standard questionnaire. The enemas were assessed for quality by two radiologists.

Pain experienced after the procedure was graded from 0 (none) to four (severe). Thirty per cent of patients had significant (grade 2–4 pain following DCBE with room air compared to 11% when CO2 was used (p<0-005). The mean pain score for CO2 was 0-4 and for room air, 1-2 (p<0-005). Five patients suffered grade four pain with air, but no patient had severe pain with CO2. Post evacuation films confirmed that there was considerably less residual gas in the CO2 group. There was no difference in enema quality between the two groups. The authors recommend the routine use of carbon dioxide in DCBE.

F103
Effect of a thromboxane synthetase inhibitor on oxygen tension and intestinal healing

A SHANDALL, R LOWNDES, H L YOUNG, E O CRAWLEY, AND K G LEACH (Introduction by J V PSALIDAS (Departments of Surgery and Medical Physics and Bioengineering, University of Wales College of Medicine, Cardiff) A number of vasodilators are now available but little data exist regarding their effect on the intact intestinal circulation. Interest in thromboxane synthetase inhibitors has recently occurred because of their effect on the microcirculation. We have studied the effect of a thromboxane synthetase inhibitor (UK 38,485) on intestinal O2 tension and healing. Intestinal oxygen tension (TO2) was measured using a Clark oxygen electrode and blood flow using a Xe133 clearance technique. Colonic and small intestinal blood flow and oxygen tension have been compared and the effect of suture technique on perianastomotic TO2 determined. Basal colonic blood flow and oxygen tension (36-95±2-6 ml/min/100 g; 62-3±8-9 mmHg) were significantly lower than small intestine (54-77±9-45 ml/min/100 g; 91-7±8-0 mmHg; p<0-01 Wilcoxon). Interrupted and continuous suture techniques decreased colonic perianastomotic TO2, although TO2 in the interrupted group was significantly higher than in the continuous (43-7±6-2 mmHg; 33-75±7-26 mmHg respectively, p<0-01 Wilcoxon). The leakage rate was 10% (1/10) for anastomoses with TO2 above 55 mmHg compared with 100% (10/10) if less than 25 mmHg (p<0-001 Yates corrected χ2 test). Perianastomotic TO2 correlated with the healing parameters, breaking energy, breaking length and hydroxyproline content (p<0-001, p<0-01, p<0-05) respectively. The thromboxane synthetase inhibitor, although increasing colonic TO2, did not significantly improve healing of the anastomoses. The oxygen electrode, however, may be of use to assess intestinal perfusion at the time of anastomosis in the human.

F104
Alpha-adrenoreceptor-mediated inhibition by dopamine of human isolated colonic muscle

D C CALLOW AND H L LEATHARD (Department of Pharmacology, Charing Cross and Westminster Medical School, St. Dunstan’s Road, London) Recent evidence suggests that dopamine modulates gastrointestinal motility. We have investigated further the action of dopamine on nerve-mediated responses of human colonic muscle obtained from the operating theatre following resections.

The muscle was dissected free of mucosa and thin strips, cut parallel to the longitudinal or circular muscle fibres, were suspended in Krebs’ solution at 37°C. Responses to intramural nerve stimulation (1–8 Hz; supramaximal voltage) were recorded isotonically (lg load). Contractions elicited during and after nerve stimulation were inhibited by dopamine (1–10 μg/ml) by the following maximum percentages: ascending colon circular muscle 62% (35%–83%, n=11, p<0-01) (median and quartiles as range), ascending colon longitudinal muscle 41% (31%–43%, n=8, p<0-01), left colon circular muscle 38% (28%–47%, n=43, p<0-01), left colon longitudinal muscle 34% (30%–40%, n=8, p<0-01) but dopaminergic agonists apomorphine (1–100 μg/ml) and bromocriptine (10 μg/ml) did not inhibit the contractions. Inhibition by dopamine was unaffected by specific dopaminergic antagon-
ists (domperidone, 2 μg/ml; pimozide, 2 μg/ml; metoclopramide 40 μg/ml) or by β-adrenoreceptor blockade with propranolol (2 μg/ml) but the α-adrenoreceptor antagonist phentolamine (2 μg/ml) reduced inhibition of responses to 2 Hz (p<0.05) and 4 Hz (p<0.01) in 15 circular muscle strips.

Thus our results are consistent with the suggestion that dopamine may contribute to colonic ileus although it appears to act by stimulating α-adrenoreceptors.