The British Society of Gastroenterology

The 1979 Spring Meeting of the British Society of Gastroenterology together with the British Society for Digestive Endoscopy was held at Hull on 29-30 March 1979 under the Presidencies of Dr C. C. Booth, President of the BSG, and Dr M. Atkinson, President of the BSDE. Following a teaching half-day on the Thursday a scientific programme of 101 papers was presented. The Plenary Session included the Research Medallist Lecture, given by Dr N. A. Wright and entitled 'Enterocyte turnover: homeostasis and disease'. The abstracts of the papers follow.

ENDOSCOPY

Prospective study of brush cytology in the diagnosis of carcinoma of the oesophagus

N. J. MCC. MORTENSEN AND ELIZABETH MACKENZIE (introduced by R. C. N. Williamson) (Department of Thoracic Surgery, Frenchay Hospital, and Departments of General Surgery and Cytology, Southmead Hospital, Bristol) Brush cytology (BC) may increase the accuracy of diagnosing oesophageal carcinoma. We have studied the value of BC in the diagnosis of 101 strictures of the oesophagus over a 15-month period using a cytology service with experience in gynaecological but not oesophageal cytology.

BC specimens were read 'blind' and this diagnosis was compared with that of radiology, endoscopy, and histology. BC gave a correct diagnosis in 86%, comparing favourably with biopsy (80%), endoscopy (83%) and radiology (80%). There were two false negatives (5.5%) and one technical failure. When combined with biopsy the accuracy rose to 92%. Flexible and rigid endoscopy were equally effective for adequate sampling. Of 64 benign strictures examined by BC there were three false positives, three described as suspicious, and six technical failures.

In a BC slide survey (10 benign, 10 malignant) sent to eight hospitals in the region, average false negative diagnosis was 16% and false positive 1.5%. Four of these centres had little previous experience and only one had, extensive experience of oesophageal cytology.

We conclude that brush cytology is simple and accurate in the investigation of oesophageal strictures, and within the capability of most pathology departments.

Is urgent diagnostic endoscopy justified in patients with acute upper gastrointestinal bleeding in a district general hospital?

W. G. LAMBERT, D. C. BRITTON, K. R. GOUGH, J. WALKER, AND J. S. M. BEALES (Royal United Hospital, Bath) The value of urgent endoscopy in upper gastrointestinal bleeding is controversial because recent papers have indicated that it has little effect on mortality, although diagnostic accuracy is improved. A study was undertaken to assess the benefits of this expensive, time-consuming service in a district general hospital. Two years were reviewed: 1973 when no endoscopy service was available, and 1976 when all bleeders were endoscoped. In 1976 diagnostic accuracy was achieved in 85% of 145 patients; 15 patients subsequently died (10%). In 1973, 158 patients were admitted with acute gastrointestinal bleeding. A radiological diagnosis was made (on that admission) in 54 (34%); 12 patients subsequently died (7.5%). Increased diagnostic accuracy in this hospital has not affected the numbers coming to emergency surgery, or the overall mortality. Until the management of acute gastrointestinal bleeding is modified by therapeutic endoscopy, it is difficult to justify the expense of preoperative emergency diagnostic endoscopy. In selected patients it may have a place during emergency surgery to identify a bleeding point.

Aspirin, alcohol and acute gastrointestinal haemorrhage—an endoscopic study

B. L. DEVINE, H. A. CARMICHAEL, S. T. ATHERTON, J. F. MACKENZIE, AND R. I. RUSSELL (Gastroenterology Unit, Royal Infirmary, Glasgow) A prospective study was made of patients presenting with acute gastrointestinal haemorrhage over a one year period with reference to aspirin and alcohol ingestion. One hundred and fifty-seven patients were studied. The principal causes of haemorrhage in the group were duodenal ulcer (DU) or duodenitis (77 patients, 49.0%), gastric or duodenal erosions (36, 22.9%), and gastric ulcer (GU) (22; 14%).

Fifty patients (33%) had recently ingested aspirin: the causes of bleeding in this group were: erosions 17 (34%), duodenal ulcer and duodenitis 21, gastric ulcer seven. In the other 107 patients (no recent aspirin), the corresponding figures were: erosions 19 (18%; p<0.05), duodenal ulcer and duodenitis 54, gastric ulcer 15.

Thus, 34% of patients who had taken aspirin before haemorrhage bled from erosions, but only 10.8% of the whole group appeared to have bled as a direct result of aspirin ingestion. Aspirin was not more likely to cause bleeding from DU and GU.

The incidence of bleeding in erosions, DU and GU groups was significantly
higher in patients with a recent history of alcohol ingestion, but alcohol and aspirin together did not appear to increase the risk of haemorrhage. The incidence of aspirin-induced bleeding appears, however, to be somewhat less common than has previously been considered.

Duodenitis

D. E. F. Tweedle and M. M. Ravenscroft (University Hospital, South Manchester) The frequency with which duodenitis is diagnosed at endoscopy varies greatly and there is disagreement about its significance. It has been suggested that duodenitis is part of the pathophysiological spectrum of duodenal ulcer disease. This study was performed with particular reference to the frequency of diagnosis made by different endoscopists and to the coexistence of other forms of gastrointestinal disease.

Duodenitis without coexistent duodenal ulceration (DU) was diagnosed in 185 out of 1940 patients (9.5%) undergoing oesophago-gastroduodenoscopy by nine endoscopists between January 1975 and June 1978. The frequency with which each endoscopist diagnosed duodenitis varied from 2.7 to 161%. There was no significant difference in the frequency of diagnosis between the six physicians and the three surgeons. Sixty-four (35%) of the patients who had previously suffered from DU and 17 (9%) developed DU. Of the remaining 104 patients, 76 (73%) suffered from other forms of gastrointestinal disease. Of these 104, 23 were cured by specific treatment for their coexistent disease—for example, cholecystectomy—61 lost their symptoms, two died from renal failure, 14 were lost to follow-up, and only four had persistent symptoms.

In this study there was no evidence that duodenitis appeared to be part of the pathophysiological spectrum of duodenal ulcer disease in the majority of the patients.

Reference
1 Joffe et al. BSGE Spring meeting, 1977.

Neodymium YAG laser photocoagulation in the dog stomach

S. G. Bown, P. R. Salmon, D. F. Kelly, B. M. Calder, H. Pearson, B. M. Q. Weaver, and A. E. Read (Departments of Medicine, Pathology, and Veterinary Surgery, University of Bristol, and The Rayne Institute, University College Hospital Medical School, London) Further to our initial Argon laser work, we now present the results of studies on the safety and efficacy of photocoagulation with the Neodymium YAG laser in the dog stomach. Our Messerschmitt-Bolkow-Blohm Medilas system produces a continuous wave infrared beam of up to 95W. This is transmitted via a single 600 microns quartz fibre in a 2 mm plastic catheter (providing a coaxial stream of CO₂ gas to blow blood away from the lesion) or a NATH triconic fibre fixed in a two-channel endoscope. Lesions on normal gastric mucosa show that the depth and width of damage depend mainly on the total incident energy and loss on the beam spot size on the tissue. The full extent of effects is visible histologically after four days, but not acutely.

Photocoagulation of bleeding artificial ulcers in the stomachs of heparinised animals was successful in every case with multiple 1 s pulses at powers from 25 to 95W. At 45W, three times as many pulses were required with the NATH as compared with the 600 microns fibre. With the 600 microns fibre the average energy for coagulation at 25W was 750 J and at 95W was 300 J. In all cases studied chronically full thickness histological effects were seen, but there were no perforations.

The British Society of Gastroenterology

Laparoscopy in tuberculous peritonitis

J. H. N. Wolfe, A. L. Behn, and B. T. Jackson (St. Thomas' Hospital, London) There has recently been renewed emphasis in Britain on the possibility of tuberculous peritonitis being the diagnosis in patients with obscure abdominal symptoms. Contrary to popular belief the illness may be short and the classical signs of ascites or a 'doughy' abdomen may not be present.

Diagnosis is made by either histological examination of peritoneal tubercles or, less reliably, by culture of a peritoneal biopsy or ascitic fluid. Peritoneal biopsies are traditionally obtained at diagnostic laparotomy but we believe this to be unnecessarily invasive.

In the last five years we have made the diagnosis of tuberculous peritonitis in seven patients, in each case by laparoscopy and target peritoneal biopsy without morbidity. In all cases the visual appearances were characteristic and the histology showed caseating granulomata, enabling early treatment to be given. Culture was positive in only two patients. All the patients were immigrants but five had lived in Britain for more than three years.

Laparoscopy appears to have been rarely used in patients with suspected tuberculous peritonitis. We believe the procedure to be safe, and suggest that more widespread use of this technique would reduce the need for diagnostic laparotomy and enable a rapid diagnosis to be made.

References

Mechanism and histology of argon laser photocoagulation in the gastrointestinal tract of dogs

S. G. Bown, P. R. Salmon, D. F. Kelly, B. M. Calder, H. Pearson, B. M. Q. Weaver, and A. E. Read (Departments of Medicine, Pathology, and Veterinary Surgery, University of Bristol and the Rayne Institute, University College Hospital Medical School, London) Further to our initial work on the safety and efficacy of argon laser photocoagulation, we now present the results of studies on the mechanism of haemostasis and the acute and chronic histological changes produced. The laser energy is absorbed as heat and haemostasis is induced by the thermal contraction of blood vessels and of the surrounding tissues, thrombosis only occurring as a secondary effect. Haemorrhage may be arrested from arteries up to 1-4 mm in diameter. Effects are detectable histologically up to 2 mm lateral to the irradiated spot and 2 mm below the exposed tissue surface. Some cell destruction, with the creation of holes, occurs at energies over 5J, but the critical energies required for perforation in different organs in beagles (weight 8-12 kg) are: oesophagus 40J, body of stomach 50J, duodenal bulb 90J and colon 35J. Acutely, the histological changes include oedema of the lamina propria, decreased mucosal cell staining and swelling and pallor of the submucosal connective tissue with sharp demarcation of affected areas. At one week, fibrinoid medial necrosis is seen in irradiated arteries with a marked surrounding fibroblastic response. Healing is delayed, but is complete at four weeks with some residual granulation around charred tissue fragments in the submucosa.
Endoscopic retrograde cholangiopancreatography for upper abdominal pain

J. BULL AND R. P. H. THOMPSON (Gastrointestinal Laboratory, Rayne Institute, St. Thomas' Hospital, London) Patients with undiagnosed upper abdominal pain are often further submitted to ERCP, which is frequently normal. We have studied the value of ERCP in such patients investigated over the last five years when liver function tests, serum amylase, barium meal or gastroscopy, and cholecystogram had been unhelpful.

Seventy patients had not undergone biliary surgery, ERCP opacified one or more ducts in 39, and made a diagnosis in seven: three had peptic ulcers and four pancreatic disease. In 18 of the remaining 63 psychiatric disorders were diagnosed, and 12 recovered on psychotropic drugs. In 10 the pain remitted spontaneously; in nine pain continues, and nine are lost to follow-up. Five patients responded to a high fibre diet. Of the remaining 12, in two a pancreatogram was not obtained but pancreatic disease was later diagnosed, two had gallstones at laparotomy, and two improved after the removal of a histologically normal gallbladder. The final six were given various other diagnoses.

Twenty-five patients had had biliary surgery, and fell into groups of proportions similar to those who had not undergone surgery.

In patients with upper abdominal pain, the exasperated doctor should try antidepressant tablets or bran before attempting ERCP.

ERCP after surgical trauma to the bile duct

A. G. VALLON, R. R. MASON, B. H. LAURENCE, AND P. B. COTTON (Gastrointestinal Unit, The Middlesex Hospital, London) Among more than 300 patients investigated over the last four years for problems after cholecystectomy, 21 have been shown to have suffered surgical trauma to the extrahepatic biliary tree. Ten presented immediately with jaundice and/or fistulae, and the remainder with intermittent cholangitis six weeks to three years after operation. Standard intravenous cholangiography had failed to clarify the situation. At ERCP seven patients had complete bile duct obstruction, five with a fistula; the upper part of the bile duct was shown by percutaneous cholangiography in two patients, but failed in a third. Fourteen patients had incomplete strictures, and only four showed dilatation of upstream ducts. The functional significance of strictures may be difficult to assess on radiology alone, and other criteria are necessary.

Fourteen patients underwent further surgery; four died without operation, two from portal hypertension, one from sepsis, and one from cerebral tumour. ERCP is an essential part of the management of post-cholecystectomy problems.

Endoscopic cannulation and sphincterotomy at the accessory papilla in pancreas divisum

P. B. COTTON AND B. H. LAURENCE (Gastrointestinal Unit, The Middlesex Hospital, London) Pancreas divisum occurs when the embryological ventral and dorsal parts of the gland fail to fuse in utero. Most of the pancreas then drains via Santorini's duct and the accessory papilla. Cannulation of the main papilla shows only the bile duct and the ventral part of the pancreas. We have succeeded in cannulating the accessory papilla in 17 out of 35 such patients, usually with a fine tipped catheter.

The hypothesis that this congenital anomaly can cause obstructive pain and pancreatitis is strengthened by the fact that nine patients with idiopathic recurrent pancreatitis were shown to have normal ventral duct systems, but abnormal dorsal radiographs. To improve drainage in two patients we have performed diathermy sphincterotomy at the accessory papilla. The first patient needed repeat sphincterotomy at three months because of re-stenosis, but then remained symptom free for six months before dying from myocardial infarction. The second patient had suffered virtually continuous pain for 20 years. It was necessary to snare and remove the accessory papilla before accessory cannulation and sphincterotomy was possible. This patient has been dramatically improved in the follow-up period of four weeks.
recently been suggested that in CD, a defect exists in the carbohydrate side chains of the enterocyte cell-membrane glycoproteins which allows gluten to act as a lectin and bind to the mucosa, initiating cell damage. This hypothesis is dependent upon the presence of incomplete carbohydrate side chains in the enterocyte cell-membrane glycoproteins of coeliac patients.

Fluorescein-labelled lectins provide a convenient histochemical tool for the identification of carbohydrates in membrane glycoproteins. In this study a range of lectins has been used to examine the enterocyte cell-membrane glycoproteins of jejunal biopsies from 25 normal patients and 14 patients with CD (eight untreated, six treated).

The carbohydrate staining pattern indicated α-D-mannose, N-acetyl-D-galactosamine, β-D-galactose and sialic acid residues are present in the brush border in normal patients and that goblet cell mucous contains a preponderance of sialic acid residues. A very similar pattern was observed in the patients with CD.

This study demonstrates the normality of the carbohydrate components of enterocyte cell surface glycoproteins in both untreated and treated CD and makes the previously mentioned hypothesis untenable in its present form.

References


In vitro demonstration of mucosal sensitivity to gluten

P. D. HOWDLE, G. R. CORAZZA, A. W. BULLEN, AND M. S. LOSOWSKY (University of Leeds, Department of Medicine, St. James's Hospital, Leeds) Organ culture of small bowel mucosa has been said to provide a definitive diagnosis of gluten-sensitive enteropathy, but based solely upon changes in alkaline phosphatase activity. However, gluten sensitivity has hitherto been universally diagnosed on morphological criteria and we have, therefore, used such criteria as well as enzyme activity to assess response during organ culture.

As expected, in 30 controls and 13 treated coeliacics, there was a significant (p < 0.01) increase in alkaline phosphatase (mU/mg protein) after 24 and 48 hours' culture with and without gluten fraction III (GF III). However, in complete contrast with previous work, GF III failed to prevent the rise in alkaline phosphatase in 13 untreated coeliacs after 24 or 48 hours culture.

Measurements of enterocyte height before and after 24 hours culture in 28 controls and 15 treated coeliacs showed a significant (p < 0.01) decrease after culture with and without GF III. In contrast with alkaline phosphatase activity, morphological measurement in 13 untreated coeliacs showed sensitivity to gluten, since enterocyte height increased in control culture but not with GF III.

We conclude that organ culture may be a useful in vitro system for the study of gluten sensitivity but morphological measurements appear more reliable than changes in alkaline phosphatase activity.

Reference


Local immunity in large bowel hyperplasia

P. W. BLAND, E. R. RICHENS, D. C. BRITTEN, AND J. V. LLOYD (Department of Clinical Investigation, Royal United Hospital, Bath, and School of Pharmacy and Pharmacology, University of Bath) Hyperplastic (metaplastic) polyps of the large bowel have previously been classified as phase I proliferative lesions but their relevance in the sequence of events leading to malignancy remains conjectural.

Study of freshly-resected, unfixed large bowel specimens revealed large numbers of small (0-5-3-0 mm diameter) hyperplastic lesions closely associated with carcinomata. These lesions were more common in the rectum than in the colon and histological investigation showed that they were invariably associated with lymphoid follicles. Using direct and indirect immunofluorescence techniques on frozen sections the synthesis of immunoglobulins and secretory component (SC) in the hyperplastic lesions was investigated. Synthesis of SC, IgA, IgM, and IgG was markedly reduced and in many cases completely absent in the lesions. There was a sharp demarcation line separating the defective hyperplastic tissue from the surrounding tissue producing normal quantities of immunoglobulins. The loss of immunoglobulin and SC-secreting capacity correlated well with the disappearance of mucin production.

Defects in secretory immune function in adenomatous polyps, villous adenomas, and adenocarcinomas have previously been reported but the present study reveals that these changes take place much earlier in the spectrum of dysplasia found in the human large bowel than formerly suggested.

References


White cell chemotaxis in Crohn's disease and ulcerative colitis

JONATHAN M. RHODES AND D. P. JEWELL (Academic Department of Medicine, Royal Free Hospital) Using skin window techniques previous workers have shown reduced neutrophil chemotaxis towards serum in patients with Crohn's disease. It was then suggested that Crohn's disease, like chronic granulomatous disease, might be due to a basic defect of phagocytic cells.

We have studied neutrophil and monocyte chemotaxis in patients with Crohn's disease and ulcerative colitis by measuring migration through millipore filters towards casein. Seventeen patients with Crohn's disease, 11 with ulcerative colitis, and 14 healthy controls were studied. Although there was a slight reduction in neutrophil chemotaxis in patients with ulcerative colitis (67 μ ± 20) and Crohn's disease (72 μ ± 18) compared with normal subjects (77 μ ± 11) this was not significant. Monocyte chemotaxis was slightly but significantly (p < 0.02) increased in patients with ulcerative colitis (124 μ ± 9) compared with normal subjects (111 μ ± 12). No significant difference was noted between patients with Crohn's disease (118 μ ± 14) and normal subjects. There was no correlation between neutrophil or monocyte chemotaxis and ESR, disease activity, or steroid therapy.

We have shown normal neutrophil chemotaxis in patients with Crohn's disease and ulcerative colitis. This suggests that the diminished chemotaxis towards serum previously shown may be due to serum inhibitory factors rather than to basic neutrophil defect. The slight increase in monocyte chemotaxis in ulcerative
colitis remains unexplained.

References

Antibodies to secretory IgA (SIgA) in duodenal ulcer disease

A. KWITKO AND D. J. C. SHEARMAN (Department of Medicine, Royal Adelaide Hospital and The University of Adelaide) In patients with selective deficiency of IgA, serum antibodies to IgA are common; several studies have shown that antibodies to IgA are very uncommon in controls and in other diseases.

Thirty patients with selective IgA deficiency (serum IgA < 30 mg %), 100 patients with endoscopically proven duodenal ulcer, and 192 control subjects were studied. Antibody to SIgA was measured by solid phase radioimmunoassay which detected IgG class antibody. Results were expressed as percentage of radio-labelled anti-IgG binding to this antibody.

In the controls very low levels of antibody to SIgA were detected (2.6 ± 0.9, mean ± 1 SD) and there was no significant difference in antibody levels with age, sex, or blood group. In selective IgA deficiency it was confirmed that antibody levels were raised (mean 5 ± 2.1, P < 0.0005). In the duodenal ulcer group, antibody levels were also raised (mean 3.5 ± 1, P < 0.0005) and 11 patients had levels of antibody to SIgA greater than 2 SD above the mean of the control subjects. Studies on these 11 ulcer patients revealed no cause for IgA antibodies; none was IgA deficient and only one had received blood transfusion.

This study has identified a subgroup of duodenal ulcer patients with an immunological abnormality.

Separation and purification of human large bowel mucosal lymphoid cells

P. W. BLAND, E. R. RICHENS, D. C. BRITTON, AND K. R. HARRIS (Department of Clinical Investigation, Royal United Hospital, Bath, and School of Pharmacy and Pharmacology, University of Bath) A method has been devised for the isolation from human large bowel of lymphoid cells which may be used to assess local immunological parameters.

After dissection of the mucosa and submucosa from freshly resected specimens of large bowel, the lymphoid cells were liberated by mechanical disruption of the tissue. Mucus was removed by at least six successive washes in culture medium. A final brief filtration through nylon wool removed clumps of epithelial cell debris. Linear gradients of 2-7.5-5% Ficoll w/v in culture medium were used to purify the extracted cells. Sample suspensions of 10-20 × 10^6 total cells in 3 ml were layered onto each gradient and the gradients were centrifuged for 14 minutes at 36g measured at the sample-gradient interface at 4°C.

It was possible to recover at least 90% of the layered lymphoid cells from each gradient. Highly purified small lymphocytes and plasma cells were distributed in the less dense gradient fractions, while monocytes and polymorphs were recovered from fractions of greater density. Cell viability by dye exclusion was 85-95%. Plasma cells showed typical cytoplasmic staining using immunofluorescence methods to demonstrate immunoglobulins. Functional capacities of the isolated lymphocytes were determined.

Reference

VIP innervation of salivary glands

J. M. POLAK, J. WHARTON, M. G. BRYANT, AND S. R. BLOOM (Departments of Pathology and Medicine, Royal Postgraduate Medical School, London, and Department of Gastroenterology, University Children's Hospital, Berne, Switzerland) The synthetic peptide Gly (Asp), LYS 2-naphthylamide; subcellular localisation studies in human small intestine

J. A. NICHOLSON, R. M. BATT, J. R. GREEN, AND T. J. PETERS (introduced by V. S. Chadwick) (Department of Medicine, Royal Postgraduate Medical School, London, and Department of Gastroenterology, University Children's Hospital, Berne, Switzerland) The synthetic peptide Gly (Asp), LYS 2-naphthylamide contains the substrate recognition and specificity sequence for enteropeptidase. Incubation of this peptide with enteropeptidase results in release of the highly fluorescent compound naphthylamine thus providing a sensitive and specific assay for the enzyme. Major advantages over conventional enteropeptidase assays include the absence of interference from endogenous trypsins, trypsin inhibitors, and autoactivation and degradation of trypsinogen, the traditional substrate. In the present study we have used this new substrate to investigate the subcellular localisation of enteropeptidase in the human small intestine.

Biopsies were fractionated by isopycnic density gradient centrifugation and the distribution of enteropeptidase was compared with those of organelle 'marker' enzymes. Enteropeptidase was localised predominantly in the brush border fractions but a small proportion of the enzyme was soluble. Hydrolysis of the synthetic peptide by both brush border and soluble fractions was inhibited by tryp-
The British Society of Gastroenterology


Are peptides best?

J. E. HEGARTY, P. D. FAIRCLough, D. B. SILK, M. L. CLARK, AND A. M. DAWSON (Departments of Gastroenterology, St. Bartholomew's Hospital, and Central Middlesex Hospital, London) Mixtures of small peptides may have advantages over free amino acids in the constitution of elemental diets. We have tested this suggestion by comparing amino acid, total α-amino nitrogen and salt and water absorption during intestinal perfusion of fish protein and lactalbumin hydrolysates and their equivalent amino acid mixtures. Whereas total α-amino nitrogen absorption from a lactalbumin hydrolysate (33-8±SE 5-1 mmol/h/30 cm) was greater than from its equivalent amino acid mixture (19-6±SE 3-1 mmol/h/30 cm, P<0.02), no difference in total α-amino nitrogen absorption was observed between the fish protein hydrolysate (23-8±SE 2-7 mmol/h/30 cm) and its equivalent amino acid mixture (21-9±SE 2-7 mmol/h/30 cm, P>0.5). Water and Na⁺ absorption from lactalbumin and fish protein hydrolysates was very different. Stimulation of water (70-9±SE 29-8 ml/h/30 cm) and Na⁺ (6-33±SE 4-6 mmol/h/30 cm) absorption occurred with the lactalbumin hydrolysate and its equivalent free amino acid mixture (H₂O, 67-3±SE 21-8 ml/h/30 cm; Na⁺, 3-78±SE 3-3 mmol/h/30 cm). In contrast no significant net absorption of Na⁺ or water was seen with the fish protein hydrolysate or its equivalent free amino acid mixture.

The results demonstrate that not all peptide mixtures are superior to amino acid mixtures in terms of α-amino nitrogen assimilation and stimulation of Na⁺ and water absorption. This may have important implications in terms of the effect on nitrogen balance and the production of diarrhoea by elemental diets, particularly in patients with reduced absorptive capacity.

Reference


A438

Sinogin. The sulphhydryl-binding reagent p-hydroxymercuribenzoate had no effect on either brush border or soluble enteropeptidase activity.

These data indicate that human intestinal enteropeptidase is predominantly a brush border enzyme. No evidence was obtained to suggest that the minor component of activity present in the soluble fraction is due to a different form of the enzyme.

Reference


Jejunal acid microclimate, and its effect on absorption of folic acid and propranolol

G. KITIS, M. L. LUCAS, R. E. SCHNEIDER, H. BISHOP, A. SARGENT, J. A. BLAIR, AND R. N. ALLAN (The General Hospital, Birmingham: Chemistry Department, University of Aston in Birmingham: Department of Therapeutics, University of Birmingham) The acid microclimate (AM) on the mucosal surface of human jejunum is defective in coeliac disease (CD) and Crohn’s disease. This may explain the folate malabsorption and the increased propranolol absorption in patients with CD. AM measured in jejunal biopsy specimens has been correlated with changes in folic acid (FA) and propranolol absorption in patients and healthy volunteers.

Folic acid 5 mg was given orally to 18 fasting subjects (controls: seven, untreated CD: four, treated CD: four, Crohn’s disease: three) and FA serum levels were measured (L.casei) at 0, 1, 2, 4, 8, and 24 hours. There was a significant inverse correlation between jejunal surface pH and serum FA levels at 1 (P<0.01), 1 1/2 (P<0.025) and 2 hours (P<0.005), and peak serum FA levels (P<0.02).

A 24 hour propranolol (40 mg) absorption test was done in 21 fasting subjects (controls: seven, untreated CD: seven, treated CD: seven). The mean serum propranolol levels were higher in patients than in controls at 1, 1 1/2, 2, 6, and 8 hours as reported. The difference was significant only at 1 1/2 hours and at peak values (P<0.05). Increased jejunal surface pH was associated with increased serum propranolol levels (P<0.05 at 4 and 6 hours). Alkalisation of the AM by simultaneous administration of NaHCO₃ with FA and propranolol to three healthy subjects reduced and delayed the peak serum FA and increased and advanced the peak serum propranolol levels.

We conclude that changes in the jejunal acid microclimate influence the absorption of folic acid and propranolol.

References


Tool for purification of the D-glucose active carrier

P. D. FAIRCLough, P. MALATHI, H. PREISER, AND R. K. CRANE (Department of Physiology and Biophysics, CMDNJ-Rutgers Medical School, Piscataway, New Jersey USA) The molecular basis of transport of D-glucose against an electrochemical gradient in intestinal and renal epithelia is unknown. The current concept is that active transport at the luminal membrane of the cell is mediated by a ‘mobile carrier’ able to bind both Na⁺ ion and the substrate to form a ‘ternary complex’ which can simultaneously transport both species into the cell in response to the transmembrane electrochemical gradient of Na⁺ ion.

Purification of the carrier is essential to validate this model. As an initial step we have developed a means of detecting the carrier function. Using extracts of purified intestinal or renal proximal tubular brush border membranes we have introduced stereospecific Na⁺-dependent D-glucose transport into artificial lipid membranes made from plant phospholipid. This transport is saturable (Km 0-13 mM) and shows ‘overshoot’ similar to that seen in natural membrane vesicles. The initial rate of D-glucose uptake and the magnitude of overshoot are proportional to the concentration of protein used.

This artificial system, therefore, can be used as an assay for the D-glucose active carrier, so that its purification and the eventual understanding of its function at the molecular level can be achieved.

References

Effects of vasoactive intestinal peptide on jejunal, ileal, and colonic fluid transport and cAMP levels in the rabbit

M. CAMILLERI, B. T. COOPER, S. R. BLOOM, and V. S. CHADWICK (Department of Medicine, Royal Postgraduate Medical School, London) Tumours which secrete vasoactive intestinal peptide (VIP) cause severe watery diarrhoea, and perfusion studies in patients have demonstrated small intestinal secretion but normal colonic absorptive function. VIP infusions produced diarrhoea in pigs and jejunal secretion in dogs confirming that VIP is a powerful secretagogue. In vitro VIP stimulates intestinal adenylate cyclase and cAMP production but cAMP levels were not raised in jejunal mucosa from a patient with a vipoma and diarrhoea. To assess regional differences in the secretory responses to VIP and the role if any of cAMP in vivo we studied the effects of intra-aortic VIP infusions (0-1 μg/kg/min) on fluid transport in jejenum, ileum, and colon in rabbits using steady state perfusions and measured cAMP levels in mucosal biopsies obtained at intervals from each part of the intestine.

The figures for fluid transport (control values first, followed by studies during VIP-infusion with significance levels where these were attained) were: jejenum −14 ± 5:6, 54 ± 10:4, p < 0:001; ileum −21 ± 5:6, 20 ± 12:4, p < 0:01; colon −21 ± 4:6, −21 ± 5:2 (negative values denote absorption). However, there were no significant differences in mucosal cAMP levels (pmol/mg protein) between control and VIP-infusion studies.

In conclusion: VIP produced fluid secretion in small intestine (jejenum > ileum) but not in the colon. No changes in mucosal cAMP were found in any region suggesting that VIP-induced secretion is not cAMP mediated in the rabbit in vivo.

Effect of hydrocortisone on water and sodium movement in the jejunum in coeliac disease

G. I. SANDLE, M. J. KEIR, and C. O. RECORD (Gastroenterology Unit and Department of Medical Physics, Royal Victoria Infirmary, Newcastle upon Tyne) Glucocorticoids have been used in the treatment of coeliac disease and methylprednisolone has been shown to stimulate water and sodium absorption in rat small intestine1,2. However, it is unknown whether glucocorticoids have a similar effect in man3.

To investigate this, 20 cm segments of proximal jejunum were studied by a perfusion technique (flow rate 15 ml/min) in three normal subjects and four with untreated coeliac disease (CD). Isotonic solutions perfused in sequence contained 56 mM glucose + 122 mM NaCl + PEG 5 g/l, first without (I) then with 100 mg hydrocortisone (II).

In normal subjects, water movement (ml/10 minutes ± SEM, + = absorption, − = secretion) changed from + 18-15 ± 10-58 with I to + 43-51 ± 9-60 with II and in CD from −36-56 ± 18-08 with I to −7-86 ± 11-46 with II. Simultaneously, sodium movement (mmol/10 minutes ± SEM) changed from +1-18 ± 0-97 to +4-47 ± 1-16 in normal subjects and from −4-19 ± 1-54 to −1-03 ± 1-54 in CD. In both groups hydrocortisone produced the same change in water and sodium movement (Z > 0-8).

It is concluded that hydrocortisone reduced net water and sodium secretion in CD to the same extent as it increased net water and sodium absorption in normal subjects. These changes occurred with villous atrophy and crypt hyper trophy suggesting that water and sodium movement predominately through the crypts.

Evidence for regional variation in large intestinal function

N. I. MCNEIL and J. H. CUMMINGS (Dunn Nutrition Unit Cambridge and University College Hospital Medical School, London) It has been suggested that regional differences exist in the absorptive capacity of the human colon. To investigate this we have measured short chain fatty acid, water and electrolyte absorption from different colonic regions using a dialysis bag technique in five subjects with defunctioning colostomies (three transverse, two left iliac) and in the rectum of seven normal subjects.

During one hour’s dialysis net absorption rates (μmol/sq. cm/h) were: acetate: transverse colon (T) 6-5 ± 1-7, left iliac colon (L) 6-9 ± 1-0 and rectum (R) 5-2 ± 0-5; propionate: T 2-3 ± 0-3, L 2-0 ± 0-2, R 1-8 ± 0-2; butyrate: T 2-8 ± 0-7, L 2-2 ± 0-4, R 1-9 ± 0-2; sodium: T 7-7 ± 0-9, L 6-9 ± 2-3, R 5-0 ± 0-5; potassium: T −6-7 ± 1-8, L −1-2 ± 1-1, R −1-5 ± 0-8; chorde: T −1-2 ± 0-7, L −0-9 ± 0-9, R 1-7 ± 0-3; bicarbonate: T −9-0 ± 1-7, L −5-5 ± 0-9, R −5-2 ± 1-1; water: (mg/sq. cm/h) T 26-5 ± 9-5, L 28-6 ± 9-2, R 21-4 ± 5-5. The rate of absorption of sodium and the rate of secretion of potassium are significantly higher in the transverse colon than in the rectum.

The proximal large intestine shows increased rates of absorption or secretion particularly for those ions that are probably actively transported, sodium, potassium, and bicarbonate. The high faecal potassium concentrations have their origin in the ascending and transverse colon.

References

Action of glucagon on the human and canine duodenum

G. E. FOSTER, J. D. HARDCASTLE, D. F. EVANS, J. WRIGHT, and F. JOHNSON (Department of Surgery and Medical Physics, University of Nottingham, Nottingham) Glucagon relaxes the duodenum during hypotonic duodenography in man. In the dog an infusion causes an increase in electrical fast spiking activity, a bolus dose having no effect.

We studied intravenous (1 mg) glucagon in seven volunteers using perfused tubes or a tethered radiotelemetry capsule. The duodenum was studied in 10 dogs using implanted electrodes and strain gauge transducers. Records on magnetic tape were analysed using a digital computer enabling correlations to be made between mechanical and electrical activity.

In the fasting human duodenum glucagon significantly (p < 0-001) decreased intervals between successive migrating motor complexes (MMC) from a mean of 131 minutes (± 10-2 SD) to 76 minutes (± 20 SD). In the dog a bolus intravenous injection of glucagon (0.05 mg kg−1) and an infusion (0-5 − 1-00 mg per hour) caused contraction of circular muscle (p < 0-001) together with an increase in spiking activity to a mean of
Hepatobiliary scanning in the diagnosis of acute upper abdominal pain

J. D. O'CALLAGHAN, P. W. VEROW, D. S. HOFTON, AND J. L. CRAVEN (York District Hospital, York) Confirmation of the diagnosis in acute biliary disease is important if early surgery is contemplated. In these circumstances conventional radiology is unreliable. This paper describes the new technique for hepatobiliary scanning using Tc99m labelled HIDA and its application in the management of patients with acute upper abdominal pain.

Fifty-six patients with a clinical diagnosis of acute biliary disease were scanned within 48 hours of presentation. In 36 of these there was a cholecystectomy and gallbladder pathology was confirmed in all (28 gallstones, one cholesterolosis, one chronically inflamed gallbladder). In five of the six patients too frail for elective surgery cholecystograms were abnormal. In seven of the 36 abnormal scans there was delayed transit into the bowel and stones in the common bile duct were found in six of these. Of 20 patients with six normal scans six had radiographic evidence of gallstones.

We suggest that in patients with suspected acute biliary disease and an abnormal hepatobiliary scan, early cholecystectomy may be embarked upon with the confidence of a correct diagnosis. Delayed excretion into the bowel is strongly correlated with common duct pathologies. Although normal scans do not exclude gallbladder disease, an abnormal scan indicates gallbladder pathology.

References

We conclude that iotroxamide should prove superior to IoG as a cholangiographic agent.

References

CLINICAL

Will iotroxamide replace ioglycamide as the contrast agent of choice for intravenous cholangiography?

J. DORAN, K. CLIFFORD, AND C. D. BELL (University Departments of Surgery and Therapeutics and Department of Clinical Radiology, City Hospital, Nottingham) Intravenous cholangiography is often technically unsatisfactory and carries a significant mortality. A new contrast agent, iotroxamide (IoT) has recently been produced. It is claimed that IoT is less toxic than ioglycamide (IoG) and gives better opacification of the bile ducts.

The aim of the present study was to determine the optimal method of administration of IoT and to compare the biliary excretion of IoT with that of IoG.

Biliary excretion achieved during T-tube drainage was measured after infusion of IoT at different rates. An infusion of around 4 mg/kg/min for one hour was found to give maximal biliary excretion. Comparison of biliary iodine concentrations after equimolar, one hour infusions of IoT and IoG and after the commonly used bolus injection technique showed IoT to be superior to IoG (p < 0.05).

To assess the clinical significance of these findings the two agents were compared in a double blind clinical trial. Two hundred patients referred for routine cholangiography were randomly allocated to receive either IoT or IoG. The radiographs were assessed by two radiologists independently using a scoring system previously described. IoT gave significantly better visualisation of the bile ducts (p < 0.01).

We conclude that IoT should prove superior to IoG as a cholangiographic agent.

References

Natural history of perianal Crohn’s disease

P. BUCHMANN, R. N. ALLAN, M. R. B. KEIGHLEY, AND J. ALEXANDER-WILLIAMS (The General Hospital, Birmingham) Perianal disease is a frequent presentation of regional enteritis but in our experience perianal lesions often remain quiescent for many years.

The aim of this study has been to examine the natural history of perianal Crohn’s disease from a 10 year follow-up of 109 patients with histological Crohn’s...
Disease and anal lesions. Fourteen patients (13%) have died from unrelated disorders. Ten have required excision of the rectum but only five for perianal disease (4.5%).

Of the remaining 85 patients, 60 have been followed up by proctoscopy and rectal biopsy. Anal tags were still evident in 25 of 37 patients (68%) but new tags had appeared in two patients. Only 10 of 53 fissures (19%) were still present at 10 years and there were no new fissures. Fistulae were still present in seven of 21 subjects (33%) but were asymptomatic, the remainder had healed spontaneously (n = eight) or following operation (n = six), new fistulae appeared in five patients. The one patient with a stricture still has a stricture, but anal stenosis subsequently developed in 29 patients, 27 of whom had had a fissure. None of the patients has become incontinent.

These results indicate that perianal manifestations of Crohn's disease pursue a relatively benign course and are rarely an indication for proctectomy.

Reference

Decline in the incidence of Crohn's disease

JAMES KYLE AND GAVIN STARK (Gastroenterology Research Unit, Royal Infirmary, Aberdeen) Crohn's disease was first described in Scotland by Dalziel in 1913. A continuous study has been made of new cases arising in the Aberdeen area during the 21 years 1955-76. All patients were interviewed and the population at risk has remained relatively static at 441,000. The number of new cases developing each year rose from 1.2 per 100,000 population at the beginning of the study to a peak of 4.5 in 1969. Thereafter it gradually declined, the mean incidence during the three year period 1974-76 being only 2.1 per 100,000. The decline has affected both males and females. It has been more marked in city dwellers than in the rural population. The former preponderance of city cases has almost disappeared. Disease confined to the small intestine is less common than in 1955, when it constituted 77% of the cases recorded. Today the large intestine or combined forms make up 75% of the new cases which are seen. There is no obvious explanation for the fall in incidence or change of site of Crohn's disease.

Incidence of Crohn's disease in Cardiff between 1934 and 1977

J. MAYBERRY, J. RHODES, AND L. E. HUGHES (Departments of Gastroenterology and Surgery, University Hospital of Wales, Cardiff) The incidence of Crohn's disease in Cardiff was examined between 1934 and 1977 using hospital diagnostic indices supplemented in recent years by personal records from clinicians. The records system and diagnostic index for Cardiff hospitals were intact for this period and 264 cases were identified; 256 sets of these notes were subsequently obtained. The diagnosis, based on histological and radiological criteria, was confirmed in 232 of the patients. The incidence has risen from 0.18 cases/10^4 of the population/year in the 1930s to about five cases/10^4/year in the 1970s. The increase has involved disease of the ileocaecal region, colon, small intestine, and anus, and has not been due to a major change in colonic Crohn's or disease in the elderly. The increase in incidence continues to rise and is probably real rather than apparent.

References

Naturally occurring enteropathy in the dog resembling chronic tropical sprue in man

R. M. BATT, B. M. BUSH, AND T. J. PETERS (Introduced by V. S. Chadwick) (Departments of Medicine, Royal Postgraduate Medical School, and Royal Veterinary College, London) Naturally occurring chronic malabsorption in the dog is not uncommon. Recently established techniques1,4 have been used to investigate 50 dogs referred with gastrointestinal symptoms. Of the 17 cases found by peroral biopsy to have small intestinal abnormalities five bore a striking resemblance to tropical sprue in man4.

These animals had impaired absorptive function and low levels of red cell folate, and ascorbic acid. Light microscopy of jejunal biopsies revealed reduced villus height with a chronic inflammatory infiltrate. Electron microscopy showed enterocytes with dilatation of the endoplasmic reticulum, mitochondrial disruption, and blurred microvilli alongside relatively normal cells. In one case affected enterocytes contained virus-like particles.

Subcellular fractionation on continuous sucrose density gradients showed reduced activities of brush border enzymes but little alteration in the density distribution of this organelle. In one animal brush border peptidase activity was absent. There was an increased activity of an endoplasmic reticular enzyme, consistent with proliferation of this organelle, and enhanced activities of lysosomal enzymes.

The features described in these dogs are very similar to those of tropical sprue in man. Further comparative studies may provide a better understanding of the pathogenesis of the human condition.

References

Diverticular disease—has its natural history altered?

J. M. P. HYLAND AND I. TAYLOR (Department of Surgery, University of Liverpool, Liverpool) The management of diverticular disease has altered radically with the widespread use of high roughage diet (HRD) and bran over the last 15 years. However, whether this regime has improved the prognosis in patients admitted with acute complications is still debatable.

In this study the outcome in 100 consecutive patients admitted with complications of diverticular disease between 1971-73 has been studied retrospectively. Forty-five per cent were admitted with painful diverticular disease, 6% with acute diverticulitis, 12% with perforation, and 11% with a paracolic abscess.

All 99 patients who survived this acute episode were discharged on HRD with bran and were reviewed after five to seven years. Seventy per cent adhered strictly to the diet. During the follow-up, 27 patients died of unrelated disease but 91% of the remainder were asymptomatic and only one patient died from complications of diverticular disease.

These results are an improvement on the long-term prognosis reported in previous series before the widespread use of HRD—for example, 44% symptom
free in Kyle's series1 and 62% symptom free in the series of Parks et al.3.

Thus, after acute complications of diverticular disease, HRD and bran appear to protect patients from further complications.

References

Rarity of clinical and experimental carcinoma of the ileum

R. C. N. WILLIAMSON, F. L. R. BAUER, AND R. A. MALT (Department of Surgery, Bristol Royal Infirmary, Bristol and Surgical Services, Massachusetts General Hospital, Boston, USA) Adenocarcinoma, the commonest primary malignant tumour of the small bowel, is generally confined to the duodenum and jejunum except in Crohn's disease. Ileal carcinoma is particularly rare, constituting five of 38 enteric cancers seen at Massachusetts General Hospital between 1913-573. Updating this series to 1975 has provided another 20 carcinomas affecting the duodenum (11), jejunum (seven) or ileum (two). Thus the ileum, though quite commonly the site of other types of tumour, contributed only seven of 58 cases of enteric carcinoma (12%) collected over 63 years.

Chemically-induced carcinomas of rat small intestine also tend to spare the ileum, even after proximal enterectomy, which stimulates hyperplasia of the distal bowel and promotes colonic carcinogenesis4. Since subtotal colectomy and pancreateobiliary diversion to mid small bowel cause similar adaptive growth of the ileum4, their potential role in enhancing ileal carcinogenesis was studied in male Fischer rats weighing 110-170 g and receiving weekly subcutaneous injections of azoxymethane (10-15 mg/kg/wk). Rats were killed at 30-36 weeks; control had no operation. Ileal hyperplasia was characterised by 24-102% increments in mucosal DNA and villous height (p = 0.05 - 0.001). Although pancreateobiliary diversion doubled the yield of colonic tumours (p < 0.005) and colectomy trebled the yield of rectal tumours (p < 0.05), neither operation affected the small number of ileal tumours.

Ileal mucosa is particularly resistant to developing carcinoma.

References

Ulcer-cancer of the stomach

V. H. HERNANDEZ-ANZUETO, J. S. VASSILAKIS, AND H. L. DUTHIE (University Surgical Unit, Royal Infirmary, Sheffield) Thirty-five cases of malignant transformation of a benign gastric ulcer occurring over a 14 year period (1964-77) have been analysed with a view to the assessment of diagnostic and prognostic factors.

Seventy-five per cent were men. Presentation was typically with a history of ulcer-type pain for several years (range one to 35 years). Complications were: bleeding in nine; perforation in three and pyloric stenosis in three cases.

Diagnosis was made on histology of the excised specimen. Preoperative diagnosis or strong suspicion of malignancy was established in only 19 cases (54%) despite the use of radiology and endoscopy.

In the follow-up, 14 patients (40%) have died and 13 (37%) have survived more than five years.

No clinical features correlated with prognosis. The pathological features which were shown to give a statistically significantly poor prognosis were ulcer area greater than 3 cm², serosal extension, involvement of resection margins, and lymph node spread.

Standardised endoscopic biopsy of gastric ulcers taking at least eight representative fragments is suggested to improve diagnosis and further management of these patients.

Gastritis associated with cirrhosis—a myth?

R. C. BROWN, G. J. HARDY, J. M. TEMPERLEY, K. J. A. MIŁOSZEWSKI, M. S. LOSSOWSKY, AND G. GOWLAND (Departments of Medicine and Pathology, St. James's Hospital, Leeds, and University Department of Immunology, The General Infirmary, Leeds) Up to 40% of acute gastrointestinal haemorrhages in patients with cirrhosis are from gastric mucosal erosions1. Although it has been suggested that atrophic gastritis (AG) predisposes to these erosions2, there are no satisfactory studies of gastric histology in cirrhotics. Previous reports in alcoholics either lack age-matched controls, or include patients without histologically proven cirrhosis. There are no studies in cirrhosis of other aetiologies.

We have assessed the incidence of AG by studying endoscopic biopsies from the gastric body and antrum of 85 patients with histologically proven cirrhosis, both alcoholic and non-alcoholic, and compared the findings with those of age-matched controls with 'endoscopic-negative dyspepsia'. Twelve patients were studied serially including two before and after portal decompression.

The frequency of AG in cirrhotics increased from 20% at ages 20-40, to 45% at age 60 years +, but there was no significant excess of AG in cirrhotics compared with controls in any age group. There was no significant difference in the incidence of AG in alcoholic compared with non-alcoholic cirrhosis. The presence or absence of varices did not correlate with the incidence of AG.

These findings do not suggest that the liability to bleeding from acute erosions in cirrhosis is related to a higher incidence of atrophic gastritis.

References

Hypertlipoproteinaemia, an infrequent and incidental finding in acute pancreatitis?

C. W. IMRIE, JANE THIRD, JENNIFER O'NEIL, J. LANG, A. J. MCKAY, AND F. BREMNER (Departments of Surgery and Medicine, Royal Infirmary, Glasgow) Of 310 patients with primary acute pancreatitis, only 13 (4-2%) revealed lipid abnormalities during routine screening within the first 60 hours of hospital admission. One pregnant woman suffered acute pancreatitis associated with the rare type I hyperlipoproteinaemia (HLP) and 12 men with types IV or V. All these male patients suffered alcohol abuse pancreatitis and represented 11% of their aetiopathological group. In contrast, none of the 160 patients with biliary disease had significant lipid abnormalities.

Gross rises in serum triglycerides were associated with diagnostic problems in
The measurement of serum amylase and therapeutic problems of apparently severe hyponatraemia. Two of the 12 male patients died, while follow-up studies in the remaining 10 with types IV and V HLP have revealed further attacks of pancreatitis with gross hyperamylasaemia and a minor alcohol intake with less pronounced lipid changes. It is suggested that the HLP in these patients is directly related to alcohol intake and may have a fortuitous rather than causal link with acute pancreatitis.

Pulmonary complications in acute haemorrhagic pancreatitis

P. G. LANKISCH, H. KOOP, AND G. RAHLF (introduced by C. W. Imrie) (Division of Gastroenterology and Metabolism, Department of Medicine and Institute of Pathology, University of Göttingen, West Germany) The aetiology of acute respiratory failure in haemorrhagic pancreatitis is unclear. For further evaluation histological examinations of the lungs were performed in 36 patients deceased from haemorrhagic pancreatitis. Clinically, 29 patients had had renal insufficiency (peritoneal dialysis: n = 10) and pulmonary complications were present in 25 cases (artificial ventilation (a.v.): n = 14).

Results showed interstitial and intra-alveolar oedema, an interstitial mesenchymal activation, hyperaemia, dystelec-tasis and microatelectasis in 13 patients (a.v.: n = 1) who died one to four days after the onset of pancreatitis.

In nine patients (a.v.: n = 3) who survived for five to nine days hyaline microthrombosis was additionally found.

Hyaline membranes as the predominant lung affliction was seen in six patients (a.v.: n = 4) who died nine to 17 days after the beginning of the disease.

Organisation of hyaline membranes and interstitial fibrosis was found in eight patients (a.v.: n = 6) who survived for more than 18 days.

In conclusion, morphological alterations of the lungs are frequent in fatal acute pancreatitis and were seen in cases with and without artificial ventilation. The morphological features are similar to types of damage seen in the so-called shock lung.

Biochemical and haematological indicators of excess alcohol consumption

D. M. CHALMERS, S. MCDERMOTT, C. SPICER, AND A. J. LEVI (Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex) With rising alcohol consumption in the community recognition of heavy drinkers by simple laboratory tests may be of considerable diagnostic and epidemiological importance. Mean corpuscular volume (MCV) and gammaglutamyl transpeptidase (GGTP) are frequently, but not always, raised in heavy drinkers. We have attempted to obtain better discrimination between heavy and light alcohol consumption by combining these variables with discriminant function analysis.

Three groups of patients were studied: (1) 219 patients with alcohol related problems actively drinking more than 80 g/day of alcohol; (2) 84 gastroenterology outpatients drinking less than 20 g/day; (3) 70 patients with non-alcoholic liver disease.

The best discrimination between these groups was obtained by a combination of MCV, log₁₀ GGTP, and serum alkaline phosphatase. In women, 95% of the high alcohol group, 100% of the low alcohol group, and 77% of those with non-alcoholic liver disease were correctly allocated by this method. The corresponding figures for men were 83%, 100%, and 63%. Thus over 80% of the heavy drinkers were correctly identified by the use of three simple laboratory tests. From these data a nomogram has been constructed so that results can now be obtained without the use of a computer.

Pancreas in primary biliary cirrhosis (PBC)

H. J. Klass, J. M. BRAGANZA, AND T. W. WARNES (University Department of Gastroenterology, The Royal Infirmary, Manchester) Abnormal ultrasound (US) and computed tomography (CT) scans of the pancreas have been reported in two patients with PBC. We therefore investigated pancreatic function and morphology in 11 patients with this disease.

Pancreatic secretory responses to secretin and pancreozymin were normal in six patients, in five of whom the evocative test, serum amylase, US, and CT scans were also normal. In the sixth, a positive evocative test, hyperamylasaemia and pancreatic head enlargement on US and CT scans were associated with minimal change pancreatitis on ERCP.

The post-secretin output of bicarbonate was reduced in four patients. In three of these, pancreatic secretion was otherwise normal, as were US and CT scans, but two had persistent hyperamylasaemia. In the fourth patient, a markedly reduced post-secretin bicarbonate output was associated with a reduced flow-rate and positive evocative test; CT scan showed an enlarged pancreatic head.

In one patient, the post-pancreozymin peak concentrations and outputs of amylase and trypsin were reduced and the evocative test was positive.

Thus, in six of 11 patients with PBC we have identified asymptomatic pancreatic disease; this correlated neither with the depth of jaundice nor the presence of the sicca syndrome.

References


Hypertrophic hepatic osteoarthropathy—a clinical and laboratory study

O. Epstein, R. Dick, and S. Sherlock (Royal Free Hospital, Hampstead, London) Twenty patients with histologically proven chronic liver disease and radiological features of hypertrophic osteoarthropathy have had clinical and laboratory studies performed. The syndrome was detected most commonly in primary biliary cirrhosis, but other associated diseases include benign and malignant bile duct stricture, alcoholic cirrhosis, chronic active hepatitis, and post-hepatitic cirrhosis. Patients may be asymptomatic, although bone pain, arthralgia, and arthritis may be presenting features. Ninety-five percent of patients have digital clubbing and 90% are clinically jaundiced at the time of diagnosis. The distal tibiae and fibulae are the first bones to be involved and all limb bones may be affected. The extent of the syndrome is not related to the degree of liver function impairment, portal-systemic or pulmonary arteriovenous shunting or arterial hypoaxaemia. Calcium homeostasis is normal. Hormonal imbalance has been implicated in the pathogenesis of hypertrophic pulmonary osteoarthropathy. Hypertrophic hepatic osteoarthropathy is not associated with increased urinary oestrogen excretion, or raised levels of growth hormone or parathyroid hormone. The syndrome should be considered in patients with chronic liver disease, clubbing, and bone and joint symptoms. Radiography of the
lower legs should detect all affected patients.

References

PLENARY SESSION

Rectal adaptation to colectomy and ileorectal anastomosis in the rat

W. J. OWEN AND J. A. LYTTLE (introduced by Professor I. McColl) (Department of Surgery, Guy's Hospital, London) The functional result after ileorectal anastomosis depends in part on ileal adaptation1. Less is known about rectal adaptation, although the absorptive capacity of the normal human rectum is very low when measured by perfusion techniques2. We have therefore examined morphological and functional changes in the rectum after colectomy.

Rats were subjected to either colonic transection (controls N = 8) or to subtotal colectomy and ileorectal anastomosis (N = 8). Rectal mucosal wet weight and mucosal thickness were measured and net absorption of water, sodium and potassium were measured by an in vivo intraluminal perfusion technique using 14CPEG normal saline solution.

Mucosal wet weight was increased by 89% (p < 0.005) in the colectomised group and mucosal thickness by 30% (p < 0.05) when compared with controls. There was an eightfold increase in net water absorption (p < 0.01) and net sodium absorption (p < 0.02) and a fourfold increase in potassium secretion (p < 0.001) in the colectomised group when compared with controls.

The rectum is therefore capable of a marked adaptive response to subtotal colectomy.

References

Absorption abnormalities in the jejunum of patients with Crohn's disease studied by the technique of intestinal perfusion

R. J. MORGAN, A. MAIN, M. J. HALL, L. M. NELSON, D. MWAKYUSA, J. F. MACKENZIE, AND R. I. RUSSELL (Gastroenterology Unit, Royal Infirmary, Glasgow) There is growing evidence to suggest that Crohn's disease is a diffuse rather than regional lesion of the gastrointestinal tract1. Twelve patients with Crohn's disease and 15 normal controls were studied. Only two of the patients had evidence of jejunal involvement. The absorption of water, sodium, chloride, and folic acid was measured using a triple-lumen tube perfusion system.

A significant reduction in the absorption of all four substances was found in the Crohn's group (p = 0.002; Mann Whitney U test).

The figures were as follows: water absorption (ml h⁻¹ 30 cm⁻²). Crohn's group 92.1 ± 25.4 (SEM): controls 221.0 ± 21. Sodium absorption (mmol h⁻¹ 30 cm⁻²): Crohn's group 9.6 ± 2.7; controls 25.00 ± 1.7. Chloride absorption (mmol h⁻¹ 30 cm⁻²): Crohn's group 8.8 ± 2.7; controls 23.5 ± 1.7. Folic acid absorption (%): Crohn's group 14.5 ± 4.3; controls 52.1 ± 7.4.

Four patients had normal water and electrolyte absorption; the two patients with radiological evidence of jejunal Crohn's disease had a secretory state. The remaining six patients, none of whom had radiological or histological evidence of jejunal Crohn's disease, showed a significant reduction in absorption.

The demonstration of reduced absorptive function in patients with Crohn's disease suggests that the disease process may be more extensive than was previously judged by routine methods, and it is possible that this is a factor in the widespread occurrence of malabsorption and nutritional problems in these patients.

Reference

The British Society of Gastroenterology

Stimulation of colonic mucus output

JEAN E. BRADBURY, J. W. BLACK, AND J. H. WYLLIE (Department of Surgery, University College Hospital Medical School, and Department of Pharmacology, University College, London) Little is known about physiological control or pharmacological manipulation of the secretion of mucus by the colon. A technique has been developed to explore possible actions of pharmacological stimuli on colonic mucus output.

The lumen of the colon of an anaesthetised rat was perfused at 20 ml/min by...
The British Society of Gastroenterology

recirculating 20 ml 6 mM N-acetyl cysteine in 155 mM NaCl. Mucus was estimated as the amount (mg) of total hexose recovered per hour.

In an experiment on 20 rats 5-hydroxytryptamine (10 nmol kg""·min""⁻¹), L-5-hydroxytryptophan (5 μmol kg""·min""⁻¹) and carbachol (30 nmol kg""·min""⁻¹) increased mucus output up to 3 times that produced by saline in equivalent volume. The increases were all significant (P < 0.001).

This previously unrecognised action of 5HT and 5HTP could be due to stimulation of release of pre-formed mucus or to stimulation of new secretion. The latter explanation seems more likely because (1) the increased output was sustainable over at least three hours; (2) histoology showed no differences in mucus content of mucosal cells which could be attributed to the different experimental treatments; (3) when carbon 14 labelled galactose was injected four hours before infusion of 5HT and other agonists it appeared in luminal glycoproteins in proportion to total hexose.

Reference


Cell-mediated immunity (CMI) to gluten fraction III (GF III) in the small intestinal mucosa in coeliac disease (CD)

P. D. HOWDLE, A. W. BULLEN, AND M. S. LOSOWSKY (University of Leeds, Department of Medicine, St. James's Hospital, Leeds) The demonstration of evidence of CMI in small intestinal mucosa of untreated coeliaics in the presence of gluten products provides important information about the pathogenesis of CD. We therefore set out to confirm and extend previously reported preliminary findings.

Small intestinal biopsies were cultured for five hours in the presence and absence of 1 mg/ml GF III. Culture media were removed and, after addition of 1 mg/ml GF III to the gluten-free medium, used in leucocyte migration inhibition tests with normal leucocytes. Migration index was calculated as mean migration area in medium initially containing GF III divided by mean area in GF III reconstituted medium.

Migration indices in 12 control subjects (mean 0.991) and 13 treated coeliaics (mean 1.033) were not significantly different, but were significantly lower in nine untreated coeliaics (mean 0.890) than in controls (P < 0.02) or treated coeliaics (P < 0.002). Migration indices were related to pre-culture interepithelial lymphocyte counts. In four patients rebiopsied after gluten withdrawal, the interepithelial lymphocyte count fell and the migration index rose.

These results confirm that a substance which inhibits leucocyte migration is secreted by untreated coeliec mucosa in the presence of gluten products and established gluten withdrawal reverses this abnormality. CMI to gluten may, therefore, be involved in the pathogenesis of coeliac disease.

Reference

1Ferguson, A. et al. (1975). Cell-mediated immunity to gliadin within the small-intestinal mucosa in coeliac disease. Lancet, 1, 895-897.

Prediction of gallstones in acute pancreatitis by liver function tests

I. R. PICKFORD AND M. J. MCMABON (introduced by Professor D. Johnston) (University Department of Surgery, The General Infirmary, Leeds) In acute pancreatitis (AP) jaundice has been shown to indicate that the attack is associated with gallstones, and raised levels of bilirubin and glutamic oxaloacetatic transaminase (GOT) have been associated with a poor prognosis.

One-hundred-and-twenty-two attacks of AP were classified as associated with gallstones (74), not associated with gallstones (31), or unclear (17) on the basis of subsequent radiological investigation (cholecystogram, cholangiogram, and ERCP). Levels of bilirubin, alkaline phosphatase, and GOT were measured on admission, and at 48 hours after admission during the acute attack.

We found no correlation between measured values and the severity of the AP. The majority of gallstone patients showed raised levels of bilirubin, alkaline phosphatase, and GOT on admission with a marked fall by 48 hours. GOT gave best discrimination; a level of > 60 IU/l was found in 85% of the gallstone patients but in none of those without gallstones.

We feel biochemical prediction of gallstones is sufficiently accurate to be of clinical value in the management of AP. The abrupt fall of bilirubin seen in most gallstone patients supports the concept that the attack is initiated by transient calculous obstruction at the ampulla.

Campylobacter enterocolitis

J. JEWKES, P. J. SANDERSON, AND A. B. PRICE (Northwick Park Hospital and CRC Harrow, Middlesex) Campylobacter spp. are emerging as a common cause of infectious diarrhoea. Our findings show it to be more frequent than salmonella and shigella infection.

Twenty-nine patients presenting with acute diarrhoea not due to ulcerative colitis or Crohn's disease were admitted to the infectious diseases unit during a period of five months. Campylobacter spp. were isolated by selective culture, were grown from the stools in 10 cases. Salmonella spp. in eight cases, Shigella spp. in three cases, and in nine cases no pathogens were found. Both campylobacter and salmonella were isolated from one patient. The clinical characteristics of the 10 cases from which Campylobacter spp. were grown are presented. Although fever and fluid stools were dominant features it was the severity of the accompanying abdominal pain which helped to distinguish this group from the others.

Rectal biopsies were obtained from six of the 10 patients with campylobacter. The histology showed a characteristic picture not previously documented but resembling that seen in other forms of infective proctitis and clearly distinguishable from non-specific inflammatory bowel disease.

This series emphasises the importance of campylobacter as a cause of infectious diarrhoea, the need for the routine use of appropriate culture media, and the help of rectal biopsy in diagnosis.

References


Failure of intravenous hyperalimentation (IVH) and bowel rest as primary therapy in acute colitis: results of a randomised controlled trial in 40 patients

R. J. DICKINSON, M. G. ASHTON, A. T. R. AXON, J. C. GOLIGHER, R. C. SMITH, C. K. YEUNG, AND G. L. HILL (Department of Gastroenterology and University Department of Surgery, The General Infirmary at Leeds) The place of IVH and complete bowel rest in the primary therapy of acute colitis has not been settled. To in-
investigate this we have undertaken a randomised trial, which was completed by 38 patients (27 with ulcerative and 11 with Crohn's colitis). Twenty received IVH and nil by mouth, while 18 controls received oral diet ad libitum. All received 40 mg prednisone/day and fluids, electrolytes, and blood as required. The trial was completed either at colonic surgery or when the prednisone was reduced to 10 mg/day. The rate of prednisone reduction was taken as the measure of medical success, prednisone being reduced by 5 mg every three days providing that there were three or fewer bowel movements per day, absent to mild pain or malaise, and weight loss < 1 kg during the preceding three days.

In the IVH group (eight males, 12 females, mean age 38-3 years) nine came to surgery and 11 responded to medical therapy in a mean time of 21 days. In the control group (five males, 13 females, mean age 46-5 years) six came to surgery and 12 responded to medical therapy in a mean time of 24 days. We conclude that this form of therapy does not have a primary therapeutic role in acute colitis.

Problems in diagnosis of oral contraception associated liver tumour

J. NEUBERGER, B. PORTMANN, H. MUNNERLEY, J. W. LAWS, M. DAVIS, AND R. WILLIAMS (Liver Unit of King's College Hospital and Medical School, London) During the past eight years we have seen 10 patients with oral contraceptive-associated liver tumours; women were 21-44 years (mean 34 years) and had been taking the pill for 2-15 years. Delay in diagnosis was common and symptoms preceded diagnosis by up to eight years; misdiagnosis included cholecystitis, inflammatory bowel disease, appendix, myocardial infarction, and epigastric hernia. Presentation included recurrent abdominal pain (four), a mass (three), obstructive jaundice due to partial bile duct obstruction (one), anaemia (one), and weight loss (one): only one had an intrahepatic haemorrhage. Biopsy showed hepatocellular carcinoma in six, adenoma in one, but in three it was not possible to obtain tumour tissue. Two had peliosis, in whom the operative specimen showed carcinoma arising in an adenoma. All occurred in non-cirrhotic liver and were α-fetoprotein negative. Liver scan showed a mass lesion in nine and hepatic angiography showed a vascular tumour in nine but was normal in one. Patients with either adenoma or unestablished histology underwent partial hepatectomy or tumour embolisation and are well up to three years later. Three patients with carcinoma have received transplants for recurrence; two of whom have died from secondaries; the rest are well up to three years later.

Sulphasalazine and infertility: a new association?

A. J. LEVI AND W. F. HENDRY (Department of Gastroenterology, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex, and Fertility Clinic, Chelsea Hospital for Women, London) There is no recognised association between sulphasalazine therapy for chronic ulcerative colitis and male infertility.

This report concerns four young foreign male patients with ulcerative colitis treated with sulphasalazine, and infertility associated with oligosperma. No other abnormality was found to account for the infertility either in the patients or their wives. All four patients had repeated serum analyses over months or years and had constant oligosperma, with low sperm counts and motility. In all four patients withdrawal of sulphasalazine, with replacement by other therapy that included systemic steroids and azothioprine, led to rapid improvement in total sperm count and motility. This was not related to better general health. Three pregnancies (with one early miscarriage) ensued in the spouses of two patients within weeks of sulphasalazine withdrawal. In one patient reintroduction of the drug led to rapid deterioration in the sperm count.

The mechanism of this apparent effect of sulphasalazine on spermatogenesis is not yet clear and further studies are required to assess its frequency, magnitude, and importance. The results of sulphasalazine withdrawal in these four foreign patients with infertility have been sufficiently marked to alert physicians to the possibility that the drug may play a role in reduced male fertility.

Preliminary experience with laser photoacoagulation in bleeding patients

B. H. LAURENCE, A. G. VALLON, AND P. B. COTTON (Gastrointestinal Unit, Middlesex Hospital, London) Conventional management of upper gastrointestinal bleeding is still associated with significant mortality and morbidity. Laser photoacoagulation appears the most promising of several new treatment methods. We have used an Argon-ion laser (Spectra-Physics, Model 770) with a quartz fibre light guide and coaxial gas, through a standard fibrescope endoscope, and a power output of 6-8 watts. Six patients were actively bleeding at the time of endoscopy, four from chronic ulcers (stomal, antral and duodenal), one from multiple acute gastric ulcers, and one after endoscopic gastric polyectomy.

Control of bleeding by photocoagulation was immediate in all. In two other patients with ulcers, the lesions showed stigmata of recent haemorrhage, and photocoagulation was applied to the ulcer base. There was no clinical or endoscopic evidence of re-bleeding in any of these patients within 96 hours of the treatment. We have also applied laser photocoagulation to gastric angiomata in three patients presenting with recurrent haemorrhage; all had multiple lesions and required repeated treatment. There were no complications attributable to laser photocoagulation in this series. Laser photocoagulation appears to be effective, and its true value will be tested in forthcoming controlled trials.

References


Neural activity in the abdominal vagni

P. L. R. ANDREWS, I. V. FUSSEY, D. GRUNDY, A. A. SALIH, AND T. SCRATCHERD (Department of Physiology, University of Sheffield, Sheffield) Recordings of activity were made in both the afferent and efferent vagal fibres supplying the gastrointestinal tract in the ferret, dog and rat.

The techniques used to obtain the recordings included fibre tearing, microelectrode recording from the medullary vagal nucleus, and collision. Records of the spontaneous neural activity in vagal afferents with receptive fields in the antrum and corpus, the
responses of these afferents to various types of gastric inflation (step and ramp) with physiological volumes, are illustrated.

The spontaneous discharge in vagal efferent fibres projecting to various abdominal structures are described. The influence of inputs from gastric and duodenal in-series tension receptors on the vagal efferent discharge are shown.

The results obtained from the above studies provide a general picture of the neural control of gastric motility.

Measurement of mucosal-submucosal blood flow in human colon

D. W. FORRESTER, V. A. SPENCE, AND W. F. WALKER (introduced by K. G. Wormsley) (Departments of Surgery and Medical Physics, Ninewells Hospital and Medical School, Dundee) The study of the factors affecting regional intestinal flow in man has been limited by the inaccessibility of the intestinal tract. The aim of this study was to measure colonic mucosal-submucosal blood flow by examining surgically created colostomies. A local radioisotopic clearance technique utilising a stable preparation of 131I-labelled 4-iodoantipyrine was used. This compound was found to be preferable to the inert gas 133Xenon, because it was unaffected by the fat content of the submucosa. To facilitate the interpretation of the recorded washout curves, an autoriadiographic study was carried out which showed the tracer to be cleared from both the mucosa and submucosa throughout the period of study. Mucosal-submucosal blood flow was calculated according to Kety from the monoexponential clearance curves obtained from 30 patients and amounted to 31.7 ± 11 (SD) ml per 100 g of tissue per minute.

The results from two consecutive measurements in 17 patients showed that the mean change between first and second readings was not significant (t test). The technique permits measurement of blood flow in conscious man and also by consecutive measurements, the evaluation of local changes in blood flow following reflex or pharmacological stimulation.

Control of malignant ascites by a peritoneovenous valve

A. V. POLLOCK (introduced by M. Hobsley) (Scarborough Hospital, Scarborough, North Yorkshire) The progressive loss of serum proteins into the peritoneal cavity, and the distress caused by abdominal distension and the necessity for repeated paracenteses, combine to debilitate the patient whose malignant ascites is not controllable by chemotherapeutic or hormonal manipulation. The safety and temporary effectiveness of a Holter hydrocephalus valve between the peritoneal cavity and the superior vena cava has been reported. This valve, however, is easily blocked by fibrin.

A new design of pressure-actuated silicone strut valve, with wide-bore entrance and exit tubing, was evolved by Leven and his colleagues for the treatment of resistant cirrhotic ascites. Valves of this design have been inserted in nine patients with uncontrollable malignant ascites, and their temporary effectiveness confirmed both by clinical improvement and by ultrasonic examinations. Five devices were found at necropsy to be occluded by fibrin. When the ascitic fluid contains enough fibrinogen to clot spontaneously, the results of this palliative operation are disappointing. Ancrod treatment in two patients has successfully reduced the level of the serum fibrinogen and may offer a chance of longer-term valve patency.

References


Effect of bile salts on gastric secretion

P. B. BOULOS, R. D. DANIEL, M. R. LEWIN, AND C. G. CLARK (Department of Surgery and Gastroenterology, University College Hospital Medical School, The Rayne Institute, London) Back-diffusion has been the accepted explanation for the presence of Na+ in the gastric juice. Davenport failed to reproduce his initial observation that when the gastric mucosal barrier is disrupted the luminal appearances of Na+ corresponded to the losses of H+. There is evidence, however, that duodenal contents mainly contribute to Na+ in the gastric juice.

The concentrations of Na+ and H+, the volumes of gastric secretion and duodenogastric reflux were therefore studied before and after instillation of 100 μmol h⁻¹ sodium taurocholate (STC) through the nasogastric tube, in eight duodenal ulcer patients during continuous intravenous pentagastrin infusion.
On STC instillation, the volumes of secretion were reduced (p < 0.01) and duodenogastric reflux was unaltered. While [H+] did not show a significant change, [Na+] increased (p < 0.01).

This study shows that, although the stomach was maximally stimulated, STC inhibited water and further H⁺ secretion but Na⁺ was unaffected. Thus, it seems that Na⁺ is independent of H⁺ or gastric mucosal function. Then, if Na⁺ is contributed from duodenal contents, the increased observed is not the result of excessive reflux but concentration effect following the diminution in the volume of gastric juice.

References

Influence of age on bioavailability and metabolism of paracetamol

BARBARA FULTON, M. D. RAWLINS, AND OLIVER JAMES (Departments of Clinical Pharmacology and Medicine (Geriatrics), University of Newcastle upon Tyne) Although the rate of hepatic oxidation of some drugs is reduced in the elderly, little is known about the influence of age on conjugation reactions. Furthermore, the effect of increased age on drug absorption and hence bioavailability is controversial.

We have studied the kinetics of paracetamol in 11 young (aged 23-9 ± SE 1-2 years) and 12 elderly (aged 75-8 ± SE 1-6 years) individuals. Each subject received both oral (500 mg) and intravenous (500 mg) paracetamol on separate occasions (> one week apart). None was receiving any drug known to influence hepatic drug metabolism, all had normal liver function tests, serum proteins, and urea and electrolytes. Venous blood was sampled over six hours after drug administration, plasma paracetamol concentrations were determined by gas chromatography.

A two-compartment open model was used in the analysis of the data.

The results in the elderly were as follows:

1. There was a delayed peak concentration after oral dose but bioavailability was unchanged (0.98 ± 0.03 young vs. 0.95 ± 0.11 elderly).

2. The central compartment was reduced (0.62 ± 0.06 young vs. 0.48 ± 0.04/kg elderly, p < 0.001); peripheral compartment unchanged (0.34 ± 0.05 vs. 0.42 ± 0.08/kg).

3. Clearance was diminished (363.5 ± 30-8 young vs. 240-8 ± 19-6 ml/min elderly, p < 0.01). This implies that conjugation is impaired with age.

References

Comparison between levels of gastrin radioimmunoactivity and gastrin-like bioactivity estimated by a cytochemical section bioassay

R. W. HOILE (introduced by A. G. Johnson) (Surgical Unit, Chartering Hospital, London) The technique, specificity, and preliminary use of a cytochemical bioassay for gastrin-like bioactivity has been described. The method is based on measurement of hormone-induced changes in carbonic anhydrase activity in the parietal cells of sections of guinea-pig fundus. Radioimmunoassay does not measure the biological activity of gastrin molecules.

We report here a comparison of these two techniques of measurement in 15 normal fasting subjects (seven males and eight females, age range 20-39 years).

Heparinised plasma was used for cytochemical bioassay and serum for radioimmunoassay; all samples contained aprotinin (Trasylol) and were stored at -70°C for transport and until measurement. Radioimmunoassay was performed using the carboxyl-terminal specific gastrin antibody 1296. The standard for both assays was natural human gastrin -17-I. (The radioimmunoassay was kindly performed at the University of Liverpool by Dr G. J. Dockray).

Mean plasma gastrin-like bioactivity, 5.1 ± 1.8 (± SD), was significantly lower than mean serum gastrin radioimmunoactivity, 7.2 ± 2.0 (± SD), p < 0.01. There was however, little correlation between immunoreactivity and bioactivity (r = 0.392).

The molecular structures of the biologically active substances detected by cytochemical bioassay has not yet been characterised. However, it is suggested that, in the fasting state, radioimmunoassay will tend to overestimate the level of biologically active gastrin present.

References

Pneumatosis coli

S. HOLT, J. GILLON, R. C. HEADING, AND W. SIRCUS (University Department of Therapeutics and Clinical Pharmacology, and the Gastrointestinal Unit, Western General Hospital, Edinburgh) A review of 33 adult patients with pneumatosis cystoides intestinalis attending hospitals in the Edinburgh district from 1960-79 has provided new information on the clinical, radiological, endoscopic, and pathological aspects of this disease. In contrast with earlier reports only three out of 33 patients had pneumocystis within the small bowel, and there was a predilection for the disease to be restricted to the left hemicolon (pneumatosis coli). Although the disease usually runs a benign course, its natural history is unpredictable and complications requiring surgical intervention have resulted. Disabling bowel symptoms and a lack of awareness of this condition resulted in frequent misdiagnosis with occasional inappropriate treatment. Benefit has been achieved in symptomatic cases by high flow oxygen therapy and resolution, either spontaneous or in association with the administration of antibiotics, has been noted. Bacterial gas production is the most likely cause of the disease and factors which contribute to pneumocystis formation and resolution are discussed with reference to recent investigations into the pathogenesis of the disease. A wider recognition of the protein features of pneumatosis coli may result in improved diagnosis and more rational management of this condition.

References
Paracetamol absorption in coeliac disease and Crohn's disease

S. HOLT, R. C. HEADING, G. P. MCLoughlin, and L. F. PRESCOTT (University Department of Therapeutics and Clinical Pharmacology, and Department of Medical Physics, The Royal Infirmary, Edinburgh)

Simultaneous studies of gastric emptying and paracetamol absorption were undertaken in 13 control subjects, 12 patients with small bowel Crohn's disease and 16 with coeliac disease after ingestion of 400 ml paracetamol solution (20 mg/kg). Compared with controls, absorption was slower in the coeliac and Crohn's disease patients, as indicated by later and reduced peak plasma paracetamol concentrations, but total absorption, as indicated by 24 hour urinary recovery of paracetamol and metabolites, was no different. Paracetamol metabolism was similar in the coeliac patients and controls but was increased in Crohn's disease, as indicated by a shorter plasma paracetamol half-life and an increased urinary recovery of paracetamol glucuronide. Enhanced conjugation may be due to enzyme induction by other drugs.

Gastric emptying was slower in the coeliac and Crohn's disease patients than controls and correlation of the paracetamol absorption and gastric emptying data suggested that the slower absorption in these patients was largely attributable to slower gastric emptying. Thus, despite the impression given by the plasma concentration-time curves, malabsorption of the drug did not occur. In coeliac disease and Crohn's disease, as in normal subjects, gastric emptying appears to be the rate-limiting factor determining paracetamol absorption.

Reference


Measurements of sugar absorption by intestinal perfusion: the use of urea to elimate experimental variation

JOHN BULL AND I. S. MENZIES (introduced by Brian Creame) (Gastroenterological Laboratory and Department of Chemical Pathology, St. Thomas' Hospital, London)

The absorption of various pentose and hexose sugars has been studied in man using a jejunal perfusion with proximal occlusive balloon technique.

Simultaneous perfusion of several sugars enables direct assessment of their relative absorption rates. Comparisons between different perfusion experiments needed to evaluate individual variation and competitive interactions between different sugars are more difficult to interpret. This is due to uncontrollable variables affecting the experimental model. Though perfusion of the intestinal segment can be controlled by the infusion rate, peristaltic movement, which affects both area and time of mucosal exposure, is unpredictable. Dilution and concentration of the perfusate are monitored by the use of a non-absorbable marker. This, however, does not correct for the effect on absorption of the resulting variation in diffusion gradient and transit rate.

To overcome these difficulties the disappearance of urea added to the perfusate at a concentration 10 times the normal plasma level has been used as a correcting factor for the variables listed above. When the absorption of different sugars is related to that of urea the wide apparent variations between experiments are considerably reduced and the relative rates of absorption clearly demonstrated.

Therapy

Late results of the Royal Free Hospital prospective controlled trial of prednisolone therapy in chronic active hepatitis

A. P. KIRK, S. JAIN, S. POOCK, H. C. THOMAS, AND SHEILA SHERLOCK (Departments of Medicine and Clinical Epidemiology, The Royal Free Hospital, London)

A long-term follow-up of a controlled prospective trial of prednisolone therapy in chronic active hepatitis, initially reported in 1971, has been performed. Forty-four patients presenting with untreated active hepatitis in the period 1963-67 were randomly allocated into treatment and control groups and have now been followed up for 10-15 years.

Ten-year life table curves showed a significantly improved survival in the treatment group where 62-5% of the patients were alive at 10 years compared with 27% in the control group (log rank test $p = 0.03$). The majority of control patients died within five years of presentation, with the median survival being 3-3 years compared with 12-2 years in the treatment group. The mean duration of treatment was 4-5 years. Age, presence of antinuclear factor, cirrhosis, or level of transaminases at presentation were not prognostic factors. Male patients untreated had a poorer prognosis than female (log rank test—adjusting for treatment $p = 0.09$).

The natural history in untreated patients with chronic active hepatitis monitored by liver function tests and biopsy was from active hepatitis or cirrhosis to inactive macronodular cirrhosis. Hepatocellular failure was a frequent cause of early death.

In conclusion, prednisolone therapy significantly improved survival in chronic active hepatitis by reducing mortality in the early active phase of the disease. The only prognostic factor at presentation was the sex of the patient.

Reference


Treatment of alcoholic liver disorders with nafldifuroyl

S. K. MAUMDAR, G. L. SHAW, AND A. D. THOMSON (Elmene Alcohol Treatment Unit, Bexley Hospital, Kent and Gastroenterology and Liver Unit, Greenwich Hospital, London)

The need for an effective drug to improve hepatic function in alcoholic liver disease (ALD) has recently been stressed. A prospective, double-blind trial of nafldifuroyl, known to improve membrane transport, was carried out on 32 male chronic alcoholics (average age 43-2 years) with a five to 15 years' history of drinking above a level of 100 g alcohol/day. Alcoholic liver damage was assessed by the history, physical examination, conventional liver function tests—indocyanine green (ICG) clearance and liver biopsy. Seventeen patients received the drug (40 mg/5 ml intramuscularly t.i.d. for six days) which was well tolerated, and 15 patients received placebo (5 ml normal saline intramuscularly t.d.s. for six days).

There was a significant improvement in the rate of ICG clearance in the treated group. A substantial three-fold improvement occurred in 10/17 (60%) patients, moderate improvement in 6/17 patients.
and deterioration in 1/17 patients. In seven (41%) patients rates of clearance returned to the normal range (t = 2.61; p < 0.02). In contrast, in the placebo group there was only modest improvement in 11/15 patients and deterioration in 4/15 patients. In no case did the clearance rate revert to normal and the overall improvement was slight. Similar changes occurred in γ-glutamyl transferase. These studies suggest that nafcifuroyl increases hepatocytic membrane transport and thereby significantly improves liver function.

Reference


Primary biliary cirrhosis (PBC): improvement of clinical pathology, liver copper and organelle pathology on low-dose D-penicillamine

J. SCOTT, W. J. JENKINS, G. WELLS, C. SELDEN, AND T. J. PETERS (introduced by V. S. CHADWICK) (Royal Postgraduate Medical School, London) PBC is a chronic, fatal hepatic disorder associated with copper overload. The chelating agent D-penicillamine (600-1,000 mg/day) has been used with apparent therapeutic success, but serious side-effects are common1. We have therefore studied the clinical chemistry, hepatic organelle pathology2 and liver copper in seven patients with early PBC before and after three to six months on low-dose D-penicillamine (250 mg/day).

Significant improvement was shown in serum alkaline phosphatase (309 ± 42 (SEM) to 199 ± 39, normal 30-130 IU/l, p < 0.02) and IgM (54 ± 13 to 23 ± 6, normal 5-18 g/l, p < 0.05). Liver copper decreased (429 ± 158 to 248 ± 88, normal 75 μgCu/g protein), but this was not significant. Pretreatment liver biopsies showed increased activities of liver cell plasma membrane (alkaline phosphatase and γ-gammaglutamyl transferase) and lysosomal enzymes, and increased lysosomal fragility. Endoplasmic reticulum, peroxisomal, mitochondrial, and cytoplasmic marker enzymes were normal. After three to six months' treatment plasma membrane and lysosomal enzymes (p < 0.05) and lysosomal fragility (p < 0.05) returned towards normal. Skin rashes (two patients) were the only complications on low-dose D-penicillamine.

Thus: (1) PBC is associated with liver cell plasma membrane and lysosomal enzyme abnormalities. (2) Lysosomal damage may contribute to the lesion in PBC,(3)low-dose D-penicillamine therapy improves clinical chemistry and organelle pathology in PBC, and side-effects may be less common.

References


Elemental diets, pancreaticobiliary secretions and gastrointestinal hormones

T. PANAYIOTIDES, N. CHRISTOFIDES, O. G. BJORNSSON, S. R. BLOOM, AND V. S. CHADWICK (Department of Medicine, Royal Postgraduate Medical School, London) Elemental diets (ED) require no digestion, are rapidly absorbed from proximal intestine and have been recommended to reduce pancreaticobiliary secretion in acute pancreatitis. For adequate nitrogen-calorie intake ED must be sipped frequently or administered by gavage. We compared the integrated pancreaticobiliary responses to ED sipped over three hours and an isocaloric isonitrogenous standard breakfast in five normal volunteers using a duodenal perfusion technique. The ED produced a reduction of 26% in trypsin (p < 0.001), 12% in bile acid (p < 0.04), and 12% in duodenal fluid output (p < 0.001) compared with the normal meal. ED are also recommended after intestinal resection where adaptive hyperplasia in residual intestine requires maintenance of oral nutrition which triggers gastrointestinal hormone release and pancreaticobiliary secretion both of which may be trophic to intestinal mucosa. Since pancreaticobiliary secretion was reduced by ED we measured the integrated gastrointestinal hormone responses in the above protocol. Plasma gastrin, insulin and GIP responses were increased (p < 0.01), whereas pancreatic glucagon (p < 0.01), pancreatic polypeptide (p < 0.01), motilin (p < 0.03), VIP (p < 0.02), and the two ileal hormones enteroglucagon (p < 0.01) and neurotensin (p < 0.02) were reduced.

We conclude that ED reduces both pancreaticobiliary secretion and most gastrointestinal hormone responses, which may be useful in pancreatitis but cause suboptimal trophic stimulation to residual gut after intestinal resection.

Improved control of pancreatic steatorrhoea with position-related enzyme supplement capsules

RODNEY H. TAYLOR, D. E. BARNARDO, N. POLANSKA, AND J. J. MISIEWICZ (Departments of Gastroenterology and Chemical Pathology, Central Middlesex Hospital, London, and Queen Mary’s Hospital, Roehampton, London) A preliminary uncontrolled study on seven patients with steatorrhoea due to pancreatic exocrine insufficiency suggested that pancreatic enzyme supplements delivered in position-related capsules (Duocaps-Biorex Laboratories Ltd.) reduced faecal fat output more than other preparations. To test this observation further, a single-blind crossover comparison of pancreatic enzyme extract BPC in Duocaps with the extract in gelatin capsules of the same appearance was done.

Ten selected patients with pancreatic steatorrhoea stopped their normal enzyme supplement and took one preparation three times daily for two weeks followed by the other preparation for two weeks in random order. Faecal fat measurements were made in the last three days of each fortnight. A record of capsule consumption, meal times, diet, and stools was kept on a weekly record sheet.

Mean daily faecal fat fell from 137±4 mmol on gelatine capsules to 92 mmol on Duocaps, a fall of 33%. The falls were most substantial (mean fall of 82.3 mmol/day), in the patients with fat outputs greater than 30 mmol/day. Stool frequency decreased slightly and patient well-being improved with the positioned release capsules. It appears that position-related enzyme delivery may be beneficial in pancreatic steatorrhoea particularly in those with high fat loss.

New H2-receptor antagonist inhibits human gastric acid secretion more strongly than cimetidine

W. DOMSCHKE, G. LUX, S. DOMSCHKE, AND L. DEMLING (Department of Medicine, University of Erlangen-Nuremberg, Erlangen, Germany) Like histamine, conventional H2-receptor antagonists in-
cluding cimetidine bear an imidazole ring regarded as an essential structural feature. Recently, however, a furan derivative, AH 19065, has been shown to be also a specific competitive H₂-blocker in vitro.

The inhibitory actions of AH 19065 and cimetidine on gastric acid response to pentagastrin (1·5 μg kg⁻¹ hr⁻¹ intravenously) were compared intradividually. On separate days, in each of seven healthy volunteers, AH 19065 (0·125, 0·25, 0·5, 1·0 mg kg⁻¹) and cimetidine (0·41 and 0·82 mg kg⁻¹ hr⁻¹ equimolar to the two highest AH 19065 doses) were intravenously infused in random order in the mid-hour of a three-hour pentagastrin period. Normal saline served as control.

The maximum inhibitory effect of AH 19065 was reached and maintained 60 to 75 minutes after beginning of AH 19065 infusion. Reduction of acid output was almost linearly related to the log dose of AH 19065 (about 67, 80, 90 and 99%) and was significant (p < 0·05) except for the lowest dosage. Cimetidine led to an average acid depression of 58 and 80% respectively. On a molar basis, AH 19065 was thus several times more active than cimetidine. No untoward side-effects were observed with either compound. Routine laboratory parameters, including serum prolactin, did not change. Clinical studies using AH 19065 in peptic ulceration seem justified.

Cimetidine and duodenal ulcer: efficacy of low-dosage maintenance treatment

J. WALTERS, P. CREAN, D. KELLY, P. CAHILL, D. COLE, M. WHELTON, D. WEIR, and C. MCCARTHY (University College Galway, St. Finbarr’s Hospital, Cork, Trinity College, Dublin, and The Research Institute, Smith Kline & French Research Limited, Welwyn Garden City) In a three-centre study, 118 patients with endoscopically-proven duodenal ulcers were treated with cimetidine 1 g daily. In 88 patients (74·6%) the ulcers had healed endoscopically in one month, and another 16 patients (13·6%) had healed after two months’ full treatment. The speed of healing was unrelated to duration or severity of symptoms. Eighty-six per cent of females examined had healed at one month and 70% of males.

The 104 patients with healed ulcers were then given maintenance cimetidine 400 mg or placebo at night, on a double-blind basis, and review endoscopy was carried out at five and 11 months if symptoms recurred. The distribution of the patients in the centres was: Cork 17, Dublin 41, and Galway 46. Of the 114 patients, 28 (26·9%) dropped out for reasons other than relapse, 12 received cimetidine, and 16 placebo. On maintenance cimetidine, 23 of 39 patients (59%) who completed 11 months maintenance treatment remained healed throughout, and 10 of 37 (27%) patients on placebo remained healed. Most cimetidine relapses were symptomatic. Evidence of clinical toxicity was not observed, but some minor biochemical abnormalities were recorded. These occurred in both treatment groups and did not lead to withdrawal of treatment.

Effect of one year treatment with cimetidine on gastric acid secretion, serum gastrin, blood concentration of cimetidine, and inhibition of gastric acid secretion by cimetidine in duodenal and gastric ulcer patients

H. FESTEN, C. LAMERS, A. TANGERMAN, and J. VAN TONGEREN (introduced by R. Hunt, Gosport) (Division of Gastroenterology, Department of Medicine, St. Radboud Hospital, Nijmegen, The Netherlands and Department of Medicine St. Joseph Hospital, Eindhoven, The Netherlands) Twenty-one duodenal and sixteen gastric ulcer patients were treated with 2 × 400 mg cimetidine daily for one year, after their ulcers were healed during placebo-controlled double-blind or subsequent open treatment with cimetidine. Before double-blind treatment and one year later after stopping cimetidine (concomitant blood cimetidine concentrations being nil) the following tests were performed (number of patients within parentheses): basal and pentagastrin-stimulated gastric acid secretion (20 DU, 13 GU); idem after 200 mg cimetidine (11 DU, 6 GU), cimetidine blood concentrations 60, 90, 105, 135 minutes after 200 mg cimetidine (9 DU, 4 GU); fasting and meal stimulated serum gastrin levels (8 DU, 5 GU).

Results were that no change was observed in the parameters studied either in duodenal or in gastric ulcer patients, except for a slight but significant rise in fasting serum gastrin levels (42 ± 4 to 52 ± 6 pg/ml p < 0·05). During treatment four DU and three GU patients relapsed. Mean pretreatment blood cimetidine concentrations after 200 mg cimetidine were significantly lower in five relapses than in 13 non-relapse patients (55 ± 10 vs 87 ± 7 μg/ml; p < 0·05), however without significantly lower inhibition of gastric acid secretion.

We conclude that inhibition of gastric acid secretion remains effective during one year’s treatment with cimetidine. There is no lasting effect on acid secretion and meal-stimulated serum gastrin levels after stopping cimetidine. In this respect duodenal and gastric ulcer patients react similarly. Relapse ulcers might be due to lower blood cimetidine levels.

Cimetidine in anastomotic ulceration after partial gastrectomy

H. FESTEN, C. LAMERS, W. DRIESSEN, and J. VAN TONGEREN (introduced by R. Hunt, Gosport) (Division of Gastroenterology, Department of Medicine, St. Radboud Hospital, Nijmegen, The Netherlands and Department of Medicine St. Joseph Hospital, Eindhoven, The Netherlands) Twenty-one patients with anastomotic ulcer after partial gastrectomy entered a double-blind prospective clinical trial to compare cimetidine with a placebo. Four patients had Billroth I and 17 Billroth II anastomoses and in three patients vagotomy was also performed. Patient groups were comparable for age, duration of disease and present relapse, type of anastomosis and vagotomy, gastric acid secretion and fasting serum gastrin levels. Only patients with ulcers measuring 5 mm or more in diameter at endoscopy within three days before entering the trial were admitted. Patients were treated as outpatients and were randomly allocated to cimetidine, 1 g daily, or matching placebo.

Results showed that at endoscopy after four weeks, eight of 12 patients treated with cimetidine compared with one of nine patients who received a placebo had healed ulcers (p < 0·05). Evaluation of symptom relief supported the efficacy of cimetidine compared with placebo. Healing rate after one month’s treatment was 67% and increased to 86% after two months’ treatment with cimetidine. During one year maintenance therapy with cimetidine, 2 × 400 mg daily, three of 19 patients relapsed. No side-effects were observed.

We conclude that cimetidine is beneficial in the treatment of anastomotic ulcers. A treatment course longer than four weeks may be indicated in this disorder. Maintenance treatment with cimetidine is as effective in this condition as reported for duodenal ulcer.
Oral glucose electrolyte therapy after massive intestinal resection

G. Griffin, H. J. Hodgson, and V. S. Chadwick (Department of Medicine, Royal Postgraduate Medical School, London) After massive small bowel resection the extent of associated colonic resection largely determines whether or not fluid and electrolyte homeostasis is eventually achieved. Life-long parenteral feeding or regular fluid and electrolyte supplementation may be necessary when most of the colon is resected. This study describes an alternative approach in a patient with 25 cm of jejunum anastomosed to mid-descending colon. Initially he had diarrhoea (> 13 l/day) on oral feeding but, with dietary management and intestinal adaptation, this dropped to 3-5 l. Although adequate calorie nutrition was achieved, with maintenance of lean body mass, persistent diarrhoea caused negative sodium (640 mEq weekly), potassium (80 mEq weekly), and water (4-6 l weekly) balance, requiring biweekly intravenous fluid and electrolytes. We tested oral glucose-electrolyte therapy, of established benefit in cholera. Isotonic glucose-electrolyte solution (NaCl 116 mM, glucose 35 mM, KCl 4mM, Ca gluconate 5 mM) 750 ml given first thing in the morning and again last thing at night resulted in positive sodium and potassium balances. Intravenous infusions were no longer required, plasma electrolytes became normal and faecal weights were unchanged. Efficiencies of sodium and water absorption from the glucose-electrolyte solution were 53% and 48% respectively. Potassium losses fell by 38% probably due to reduced secondary hyperaldosteronism with the improved sodium balance. Thus oral glucose-electrolyte therapy may avoid the need for parenteral supplementation.

Oral whole bowel irrigation: a rapid acceptable method of mechanical bowel preparation

S. Minervini, I. A. Donovan, J. Alexander-Williams, and M. R. B. Keighley (The General Hospital, Birmingham) Conventional mechanical bowel preparation with enemas and purgatives is not always effective and takes three to five days. Whole bowel irrigation (WBI) with normal saline delivered through a nasogastric tube is rapid and efficient, but unpleasant for the patient and associated with sodium and water retention. Oral mannitol may reduce the electrolyte disturbances of whole bowel irrigation.

We have developed a method of oral preparation with mannitol and water (group A) which avoids a nasogastric tube. Results have been compared with patients having WBI with mannitol (group B) or WBI alone (group C). In group A (n = 12) preparation was successful in all except two patients with a small lumen diameter (< 8 mm). In group B (n = 16) preparation was successful in all but had to be stopped because of vomiting in two patients. In group C (n = 20) six patients had inadequate bowel preparation. The mean duration of preparation was 3-6 h for group A, 3-1 h for group B, and 4-5 h for group C. The mean fluid gain was 761 ml for group A, 800 ml for group B, and 2700 ml for group C. The mean sodium gain was −220 mmol for group A, 290 mmol for group B, and 570 mmol in group C. These results indicate that oral mannitol is effective and is more acceptable to patients than WBI and avoids the problems of fluid and sodium retention.

References

Controlled trial of bulk forming evacuants in the treatment of patients with haemorrhoids

G. E. Foster, J. S. Bolwell, J. Wright, and J. D. Hardcastle (Department of Surgery, The General Hospital, Nottingham) Anal canal pressures are raised in patients with haemorrhoids compared with normal controls and are reduced by anal dilatation. Associated symptoms may improve after treatment with bulk forming evacuants, but it is not known if this is associated with a change of anal canal pressure. Forty-one patients with haemorrhoids, age and sex matched, were randomly allocated into two groups. One group (n = 20) took one month's supply of ispaghula (Fybogel) and the other (n = 21), a matching placebo. Preparations were supplied double blind. Symptoms were assessed and anal canal and rectal pressures measured before sigmoidoscopy using a 5 mm diameter probe with 1 mm diameter perfused orifices. The internal sphincter EMG was recorded by a bipolar Ag/AgCl needle electrode. After one month, the procedure was repeated.

There were no significant differences between groups (p > 0.99) in symptomatic improvement with either preparation, 15 of the ispagula group (75%) and 13 (62%) of the placebo being improved. There were no significant differences in anal canal ultra-slow waves, rectal pressures, or EMG. We noted not only a symptomatic placebo response but also a significant fall in anal canal pressure after placebo. This finding suggests caution in using anal pressure as an objective assessment of methods of treating haemorrhoids.

The British Society of Gastroenterology

Which is the best drug for chronic diarrhoea?

R. E. Pounder and C. D. Shee (Gastrointestinal Laboratory, St. Thomas' Hospital, London) There is no controlled trial that compares the three drugs (loperamide, diphenoxylate, and codeine phosphate) that are available for the oral treatment of chronic diarrhoea.

In a double-blind crossover trial lasting eight weeks, 11 outpatients with chronic diarrhoea randomly received four courses of treatment lasting two weeks. They were advised to take as many capsules as necessary to control their diarrhoea (0-6 capsules/day, in divided doses). The capsules contained either 2 mg loperamide (two separate courses), 5 mg diphenoxylate, or 30 mg codeine phosphate. The patients consumed a mean of 3-5 capsules/day and opened their bowels 3-9 times/day. No difference was detected between the two periods of treatment with loperamide, nor among the three drugs. The number of capsules consumed was significantly related to the number of bowel actions.

This study shows that for the treatment of chronic diarrhoea 30 mg codeine phosphate is equivalent to either one capsule of Imodium (2 mg loperamide) or two tablets of Lomotil (5 mg diphenoxylate). When equivalent doses are taken the three drugs are similarly effective.
although the most expensive, loperamide, may be the best drug for chronic diarrhoea, for it has no narcotic effect.

Retrograde spread of a 10% hydrocortisone foam through the colon in ulcerative colitis

M. J. G. FARTHING, M. D. RUTLAND, AND M. L. CLARK (Departments of Gastroenterology and Nuclear Medicine, St. Bartholomew's Hospital, London) A 10% hydrocortisone acetate foam (Colifoam) has been introduced as an alternative topical treatment for distal ulcerative colitis. Retrograde spread of this foam through the colon has not been studied and its place in the management of more extensive colitis is therefore not established.

We describe a method whereby 5 ml of the 10% hydrocortisone foam was labelled with 0-5 mCi 99mTc-colloid before introduction into the rectum. Posterior and posterior oblique gamma camera pictures were then taken at 0, one, two, four and six hours from which retrograde spread through the colon could be estimated. The labelled foam spread from the rectum into the sigmoid colon in all but one of the 14 patients investigated. In all of the nine patients with active disease the foam reached the mid-sigmoid colon and in seven (78%) the foam reached the proximal sigmoid colon. Retrograde spread of the foam tended to be more marked in patients with more extensive disease. Increasing the volume of labelled foam to 50 ml in several patients has enhanced its retrograde spread.

This study suggests that the 10% hydrocortisone foam may be useful in the treatment of patients with distal ulcerative colitis that is not necessarily confined to the rectum.

Which is the best route of antibiotic prophylaxis in elective colorectal surgery: oral or parenteral?

M. R. B. KEIGHLEY, Y. ARABI, AND J. ALEXANDER-WILLIAMS (The General Hospital, Birmingham) A prospective randomised trial compared oral (n = 47) with parenteral prophylaxis (n = 46) in elective colonic resection for malignant disease. Patients in both groups received metronidazole and kanamycin. Oral therapy was designed to reduce the bacterial flora of the colon without achieving therapeutic serum concentrations and systemic prophylaxis to provide adequate serum levels without altering the colonic microflora. Serum and colonic contents were sampled at operation for antibiotic assay and for counts of pathogenic bacteria in the colon. Patients with post-operative diarrhoea were investigated for evidence of pseudomembranous colitis by detection of toxins and Clostridium difficile in the stool.

Oral preparation significantly reduced the counts of Escherichia coli (106 to 109) and Bacteroides fragilis (109 to 1012) in the colon without achieving therapeutic serum levels. Nevertheless, kanamycin resistant bacteria were observed in 23 (50%) of the orally prepared patients. Intravenous prophylaxis provided therapeutic serum levels but had no influence on colonic microflora. The overall rate of sepsis was 36% in patients prepared orally compared with 7% in patients receiving parenteral prophylaxis (p < 0-02). Pseudomembranous colitis occurred in six patients receiving oral preparations but in none receiving systemic antimicrobials.

Parenteral antibiotic prophylaxis is therefore more effective at reducing sepsis and less likely to be complicated by antibiotic resistance and pseudomembranous colitis than oral antimicrobial bowel preparation.

References


Treatment of rectal prolapse and incontinence: a clinical and manometric study

D. MATHESON, G. A. G. MOOG, Y. ARABI, P. BUCHMANN, J. ALEXANDER-WILLIAMS, AND M. R. B. KEIGHLEY (The General Hospital, Birmingham) Anal incontinence frequently accompanies rectal prolapse but may occur spontaneously. Cure of the prolapse by abdominal rectopexy is said to cure the incontinence in only 50 per cent of patients suffering both.

Fifty-nine patients with rectal prolapse and/or incontinence have been studied before and four months after treatment. Anal pressures were recorded with a closed water-filled balloon probe under resting conditions (basal pressure: BP) and after contraction (squeeze pressure: SP).

In patients with rectal prolapse without incontinence (n = 10) the BP and SP did not differ from age and sex matched controls. In those with rectal prolapse with incontinence (n = 24) and those with idiopathic anorectal incontinence (n = 25) the BP was normal but the SP was significantly lower than controls (p < 0-01).

Pelvic floor exercises and faradism were used in all patients but there was no improvement in pressures and little clinical benefit apart from some male patients with incontinence alone. A modified Ripstein rectopexy cured all patients with prolapse, improved continence in 70% and was associated with an increase in SP (p < 0-05).

Correction of rectal prolapse by rectopexy usually restores continence and increases the power of voluntary contraction. Idiopathic anorectal incontinence or persistent incontinence after rectopexy can usually be treated successfully by post-anal repair.

References


Adhesion of enterobacteriaceae to baccal epithelial cells (BEC)

D. C. A. CANDY, T. S. M. LEUNG, A. PHILLIPS, W. G. MARSHALL, AND J. J. HARRELS (Institute of Child Health, Guildford Street and Queen Elizabeth Hospital for Children, Hackney, London) The pathophysiology of infantile diarrhoea is currently under intense investigation particularly in relation to adhesion of bacteria to the alimentary tract, which we have studied using human BEC.

A pathogenic strain of E. coli (026: K60) known to adhere to human fetal intestine adhered to adult BEC, while a non-pathogenic, non-adhesive strain (01: K1) did not. Adhesion was temperature-
dependent, correlated with fimbriae production, and was inhibited by breast milk. Serotypable E. coli from stools of seven infants with acute diarrhoea; and E. coli, Enterobacter sp., Proteus sp. (and C. albicans) from the small intestine of three infants with protracted diarrhoea, adhered to BEC from 6/7 and 3/3 of the infants’ BEC respectively. The non-adhesive E. coli (01:K1) adhered to BEC from the latter group. Adhesion of all Enterobacteriaceae was inhibited by D-mannose.

Our results indicate that BEC provide a simple model for studying intestinal adhesion of bacteria in man, and suggest that adhesion may be mediated by mannose-like receptors. Moreover, the test system has the important advantage that bacteria can be studied with cells from affected cases, and thus may provide a means of assessing the ‘enteropathogenicity’ of bacteria in individual patients.

References

Decay of 75Se-methionine labelled proteins in duodenal juice: evidence for a recirculation of digestive enzymes in man

G. LAKE-BAKAAR, G. E. RUBIO, J. A. SUMMERFIELD, AND S. MCKAVANAGH (Introduced by Sheila Sherlock) (Department of Medicine, Royal Free Hospital, London)

An enteropancreatic recirculation of digestive proteins has been demonstrated in rabbits1. 111In-trypsin introduced into the systemic circulation in man can be cleared via both biliary and pancreatic secretions into duodenal juice2. Further evidence for this recirculation in man has been obtained by comparing the decay of intrinsically labelled digestive proteins in two groups of patients.

Six patients have been studied three to four hours after a bolus injection of 75Se-methionine (3 μCi/Kg) for routine pancreatic scanning, against a background intravenous infusion of cholecystokinin-pyrogen (1 unit/kg/h) and secretin (1 unit/kg/h). In one group of three patients, duodenal juice was continuously aspirated via a Lundh tube and pooled into 30 minute aliquots for up to four hours. In the second group, 5-10 ml of juice was removed at 15 minute intervals over a similar period. Specific activity was calculated from the trichloroacetic acid precipitable radioactivity and protein concentration per unit volume of sample. In the first group (continuous drainage) specific activity decayed more rapidly (T½ after 120 minutes, 86, 90 and 93 minutes) than for the second (sampling) group (T½ after 120 minutes 135, 173 and 251 minutes). Non-acid-precipitable 75Se-selenium activity in serum did not increase in either group during the study. This difference in decay characteristics is therefore unlikely to be due to recycling of aminoacid or small peptides and suggests a recirculation of intact duodenal juice proteins in man.

Intestinal gastrin—ontogeny and tumour distribution

A. M. J. BUCHAN, M. G. BRYANT, C. M. TIMSON, J. M. POLAK, AND S. R. BLOOM (Departments of Histology and Medicine, R.P.M.S., Hammersmith Hospital, London) The existence of a distinct cell type containing intestinal gastrin has previously been reported. Of the two major forms of gastrin, G17 occurs mainly in antral tissue and G34 in the intestine. As it is possible that the different antral and intestinal endocrine cells containing gastrin produce mainly G17 and G34 respectively, further studies have been undertaken. Fetal intestine contains very large quantities of G34, therefore 14 fetal duodenums were investigated by the semithin/technique using region specific antisera. In 20 clearly identified gastrin-containing cells (6 cells at eight weeks, 4 cells at 13 weeks, 5 cells at 18 weeks, and 5 cells at 28 weeks) the diameter of the secretory granules was measured and was found to have a mean value of 200 ± 26 nm (n = 860), which is similar to that of the adult intestinal cells containing gastrin. In addition, five gastrinomas were investigated. The results showed that gastrinomas with large electron-lucent granules produced mostly G17, those with a mixture of granules produced both G17 and G34, and those with small, electron-dense granules produced mostly G34. Thus it seems that the storage granules containing G34 are morphologically distinguishable from those containing G17.

Effect of haemorrhagic hypotension on liver blood flow and oxygen consumption in the dog

A. SMITH, R. T. MATHE, R. L. HUGHES, A. M. HARPER, AND L. H. BLUMGART (University Department of Surgery, Glasgow Royal Infirmary, and Wellcome Surgical Research Institute, University of Glasgow, Glasgow) The influence of reductions in mean arterial blood pressure (MAPB) on total liver blood flow, portal venous blood flow (PVBF), hepatic arterial blood flow (HABF), and hepatic oxygen consumption was investigated in seven anaesthetised greyhounds. MAPB was decreased in equal steps to 40% of baseline by controlled haemorrhage.

Portal venous and hepatic arterial blood flows were measured by electromagnetic flowmeters. Hepatic tissue perfusion was measured by the 133Xenon clearance method1. Hepatic oxygen consumption and cardiac output were also measured.

At the levels of hypotension measured there were significant reductions in cardiac output and portal venous blood flow. Hepatic arterial blood flow, however, remained at or near control levels, indicating the presence of autoregulation in this vascular bed. Total liver blood flow (PVBF + HABF) and hepatic tissue perfusion were significantly reduced by equal amounts implying an absence of intrahepatic arteriovenous shunting of blood.

The portal vein component of total hepatic oxygen consumption decreased during shock, whereas there was a significant increase in the hepatic arterial component. The net oxygen consumption did not differ from control at any level of hypotension.

Reference

Vitamin D absorption in primary biliary cirrhosis and alcoholic liver disease

Normal subjects appear to have three phases of disappearance of radioactivity from plasma—4–12 hours, 12–72 hours, and 72 hours—21 days after injection. The corrected half lives were 1.9 ± 1.5 hours, 11.4 ± 11.1 hours, and 34.8 ± 108.5 hours respectively (± SD), showing no correlation with prevailing plasma 25-OHD.

Corresponding half-lives in alcoholic cirrhosis were 3.5 ± 3.07 hours, 8.2 ± 4 hours and 313 ± 54 hours, similar to those of normal subjects, and again showing no correlation with plasma 25-OHD.

The first half-life in PBC (37.5 ± 72.3 hours) showed a positive correlation with serum bilirubin (p < 0.001) but subsequent half-lives (11.3 ± 12.2, 348.4 ± 153) did not, and were similar to normal subjects.

Urinary tritium excretion within the first 24 hours was minimal and did not correlate with serum bilirubin. These results suggest that injected 3H-25-OHD is (1) rapidly distributed into pools other than plasma; (2) handled similarly by normal subjects and alcoholic cirrhotics; (3) initially removed more slowly from the plasma in the presence of biliary obstruction, but does not appear in the urine, suggesting that little 25-OHD is excreted in the bile.

**Prolactin: a new intestinal hormone**

FIONA M. STEVENS AND C. SHAW (Department of Medicine, Regional Hospital, Galway, and Queen’s University of Belfast, Northern Ireland) Raised levels of serum prolactin (> 2000 mU/l) have been found in several coeliac patients1. None of these patients had signs or symptoms suggestive of hypotalamic or pituitary disease. Cells containing immunoreactive vasoactive intestinal polypeptide and somatostatin have been found in both the brain and the intestine2.

Prolactin-like immunoreactive cells have been sought and identified in small intestinal biopsies from coeliac and non-coeliac patients using a recently described simple technique for the demonstration of polypeptide-secreting endocrine cells3. The 'enteroprolactin' cells were situated in the epithelium, mainly in the crypts and transitional zones. There was no cross-reactivity with any previously described gastrointestinal or pancreatic hormone or with ACTH or growth hormone.

As yet, no function can be attributed to this 'enteroprolactin'. High circulating blood levels of prolactin are found in coeliac patients with a favourable clinical and biopsy response to treatment; however, significantly lower values were found in a group of patients responding poorly to gluten withdrawal. Preliminary data show a marked increase in 'enteroprolactin' cells in the atrophic intestinal mucosa of the latter treated group. These results suggest that the poor response to dietary therapy in these patients may be due to a failure of release of enteroprolactin.

**Gut hormones in acute diarrhoea**

H. S. BESTERMAN, P. D. WELSBY, N. D. CHRISTOFIDES, D. L. SARSON, AND S. R. BLOOM (Department of Medicine, Royal Postgraduate Medical School, London, and Royal Free Hospital, London) Gross disturbance of normal gut motility occurs during an acute attack of diarrhoea and at least two gut hormones, motilin and enteroglucagon, are thought to have important influences on gut motility.

We have investigated the response of gut hormones to our standard test breakfast in 12 patients recovering from a severe attack of acute infective diarrhoea and compared it with the pattern in 13 normal subjects. The patients, all of whom were previously free of gastrointestinal symptoms, required acute admission to hospital and subsequently made a complete recovery.

Sixteen patients with diarrhoea had raised fasting plasma motilin and enteroglucagon levels on admission to hospital of 191 ± 28 (normal 40 ± 9, p < 0.001) and 83 ± 12 (normal 20 ± 3, p < 0.001) pmol/l respectively. The breakfast was ingested at an early stage during recovery when diarrhoea was still present. The three hour total integrated response of motilin (27.9 ± 5.5 nmol/l) and of enteroglucagon (45 ± 5 ± 30 nmol/l) were both significantly greater than normal (7.9 ± 1.7 and 5.2 ± 0.5 nmol/l respectively, p < 0.005 for both). In contrast the responses of gastrin, pancreatic polypeptide, gastric inhibitory polypeptide,
and vasoactive intestinal polypeptide were all similar to normal. The strikingly increased responses of motilin and enteroglucagon may thus in part explain the altered gut motility in diarrhoea.

Small intestinal bacterial overgrowth in systemic sclerosis

I. COBDEN, A. T. R. AXON, J. MCGOLDRICK, A. T. GHONEIM, AND N. R. ROWELL (Gastroenterology Unit, Department of Microbiology and Skin Department, The General Infirmary, Leeds) Small bowel contamination is a recognised complication of systemic sclerosis, and presumably results from the impaired intestinal motility which may exist in the condition. Most reports have related to individual symptomatic cases, and, apart from occasional studies referring to raised urinary indican values, little is known of the prevalence of this complication.

In 20 unselected patients with proven systemic sclerosis, jejunal aspirates were cultured and glucose/hydrogen breath tests4 for small bowel contamination performed. In three patients, cultures were sterile and 10 had counts ranging from 1.5 x 10⁴ to 1.4 x 10⁶ organisms/ml; similar counts were found in 14 control subjects. Seven patients (35%) had higher counts, ranging from 10 to > 10⁶ organisms/ml, regarded as pathological. The most frequent isolates were alpha-haemolytic streptococci, faecal streptococci, and coliforms. Four patients had a positive breath test: all were in the high-count group.

Six of the seven patients with high counts had biochemical steatorrhoea and three had lost weight, but only four were ever troubled by diarrhoea. These results suggest that small bowel bacterial overgrowth is surprisingly common in systemic sclerosis, and not always associated with florid symptoms.

References

Intestinal permeability and screening tests for coeliac disease

I. COBDEN, J. ROTHWELL, AND A. T. R. AXON (Gastroenterology Unit, The General Infirmary, Leeds) Standard screening tests for coeliac disease may be unreliable, giving both false positive and negative results in a relatively high proportion of patients tested.5 We have compared four standard tests with a recently developed test of intestinal permeability, which is based on the five hour urinary recoveries of two simultaneously-administered probe molecules.

Fifty-five patients with normal jejunal biopsies and without significant gastrointestinal pathology, had a mean cellobiose/mannitol ratio of 0.043 ± 0.023, with an absolute range from 0.005 to 0.10. In 24 untreated patients with villous atrophy, 23 had ratios which were clearly abnormal (the lowest of these being 0.15). Comparable false-negative rates were 5/15 for the xylose test, 8/21 for serum folate, 8/15 for red-cell folate, and 10/18 for reticulin antibodies.

When all patients with normal biopsies were considered—that is, the 55 controls described above, plus patients with pancreatic insufficiency, blind-loop syndrome or post-gastrectomy diarrhoea—the false-negative rate for the test ratio was 1/74, for the xylose test 8/24, serum folate 10/47, red-cell folate 2/38, and reticulin antibody 1/45.

The cellobiose/mannitol ratio appears to be more sensitive, and at least as specific as other screening tests for coeliac disease.

References

Oxalate loading test—a screening test for steatorrhoea

D. S. RAMPTON, G. P. KASIDAS, G. ALAN ROSE, AND M. SARNER (Gastroenterology Unit, University College Hospital, London, St. Peter’s Hospitals and Institute of Urology, London) Steatorrhoea is associated with hyperoxaluria, and it has been suggested that the 24 hour urinary oxalate output can be used as a screening test for steatorrhoea if the diet is supplemented with spinach. Unfortunately, the oxalate content of spinach is variable and its availability for absorption uncertain. We have estimated faecal fat and 24 hour urinary oxalate output in 32 patients suspected of malabsorption, while they were eating a diet containing 0.33 mM (30 mg) oxalate, 180 mM (50 g) fat, and 25 mM (1 g) calcium daily, for one week, during the last three days of which they took an oral supplement of sodium oxalate, 600 mg (oxalate 4.44 mM) daily.

Nineteen of 32 patients proved to have steatorrhoea (mean faecal fat 62 mM/24 h; range 19-186 mM), their diagnoses were: Crohn's disease (five), pancreatic insufficiency (six), coeliac disease (five), and miscellaneous (four). On the unsupplemented diet, 24 hour urinary oxalate, measured by a specific oxalate decarboxylase method, was raised in only nine of these patients (mean 0.25 mM/24 h, range 0.08 - 0.59, normal <0.20). During sodium oxalate loading, all 19 with steatorrhoea had hyperoxaluria (mean 0.91 mM/24 h, range 0.46 - 1.44, normal <0.44), and there was a significant positive linear correlation between urinary oxalate and faecal fat in all 32 patients on the oxalate load (r = 0.73, p < 0.001).

We conclude that measurement of the urinary oxalate during oral sodium oxalate loading is a reliable, simple and convenient test for steatorrhoea.

Studies on the therapeutic effect of Diodoquin in acrodermatitis enteropathica (AE)

P. J. AGGETT, H. T. DELVES, F. T. HARRIES, AND A. D. BANGHAM (Institute of Child Health, London, and A.R.C. Institute of Animal Physiology, Babraham, Cambridge) AE was an invariably fatal disease until it was discovered that Diodoquin induced a complete remission. Subsequently it was established that all the manifestations of AE were secondary to zinc (Zn++) deficiency. We have demonstrated that the intestine is in a net secretory state with respect to Zn++ and that this can be reversed by Diodoquin. In this paper we have studied the mecha-
nisms by which Diodoquin enhances Zn++ absorption, utilising liposomes.

Diodoquin enhanced membrane permeability to the divalent cations Zn++ and calcium but had no effect on sucrose translocation, and this phenomenon was independent of membrane incorporated cholesterol. Partition studies demonstrated pH dependence: at a physiological pH 90% of Zn++ translocated into an organic-Diodoquin medium, whereas corresponding values for iron, calcium and sodium were 0%, 15% and 4% respectively.

These results suggest that the therapeutic effect of Diodoquin in AE is due to a pH-dependent ionophore-like activity. Moreover, the experimental mode provides a basis for further studies concerned with cell membrane translocation events.

References

Total colectomy and ileoanostomy in the rat—intestinal adaptation and its relation to food intake

J. A. LYTTLE AND W. J. OWEN (introduced by I. McColl) (Department of Surgery, Guy’s Hospital, London) The adaptive response of small bowel after small bowel resection is well established. Less is known about the similar response which follows subtotal colonic resection. Total colectomy and ileoanostomy (IA) is attractive, in principle, in, for example, ulcerative colitis and familial polyposis coli, but has failed because of the severe perineal excoriation and incontinence which frequently follow.

Methods were as follows: Experiment 1: Using Wistar rat, ileorectostomy with a 3 cm rectal stump was compared with IA.

Over a four week period, food and water intake and weight were measured. After the animals were killed visceral measurements were made, including small intestinal mucosal weights and histological villous and crypt length.

Experiment 2: Two groups of IA rats were either fed ad libitum (IAAL) or pair-fed against laparotomy controls for four weeks (IAIF) with similar measurements made.

Results
Experiment 1: IA animals consumed 18% and IRA 11% more food, 93-6% and 61-2% more water than laparotomy controls, and showed significant splenic and renal hypertrophy. Mucosal weight increased significantly in both groups but histological changes were significant only in IA.

Experiment 2: Most, but not all, of the previously noted adaptive changes were reduced or abolished in the IAPF group, suggesting that much of this response is secondary to hyperphagia.

References

Suppression of contractility in human colonic muscle by endogenous prostaglandin

T. J. CROFTS, H. L. STOCKLEY, AND A. G. JOHNSON (Departments of Surgery and Pharmacology, Charing Cross Hospital, London) The relaxant effect of prostaglandin (PGE) on human colonic circular muscle is well known. More recently, PG-like activity (mainly PGE-like) has been identified in extracts of human colonic muscle. The possible role of this endogenous prostaglandin has now been studied using indomethacin to inhibit its synthesis.

Macroscopically normal colonic muscle was obtained at operation and circular muscle strips (approx. 15 mm x 1 mm) were suspended in an isolated organ bath at 37°C in Krebs' solution gassed with 5% CO₂ in O₂. Submaximal isotonic contractions to acetylcholine (dose range 0-05-50 μg/ml) were recorded to monitor muscle responsiveness, initially in Krebs solution alone (controls), then in the presence of indomethacin (10 μg/ml) and finally in the presence of indomethacin and PGE₂ (10 ng/ml).

In each of the nine muscle strips indomethacin caused a sustained, submaximal contraction, an increase in amplitude of spontaneous activity and enhancement of contractions to acetylcholine (to 136% of control levels; range 105-206%, p < 0.05). Conversely, PGE₂ reduced the tone and spontaneous activity to approximately pre-indomethacin levels and reduced acetylcholine-stimulated contractions to 92% of control levels (range 24-108%, p < 0.05).

These results indicate that PGE₂-like activity generated in these preparations continuously suppresses contractility and it is suggested that colonic prostaglandin synthesis in vivo might contribute to diarrhoea by inhibiting circular muscle activity.

References

Effect of dietary fibre on faecal bacterial mass

ALISON M. STEPHEN AND J. H. CUMMINGS (MRC Dunn Clinical Nutrition Centre, Addenbrooke's Hospital, Cambridge) The faecal bulking effect of dietary fibre is probably not due to its capacity to hold water, since very little fibre survives digestion in the colon. Also water holding by fibre in vitro has been found to be inversely related to in vivo faecal bulking.

A large proportion of the faecal mass is bacterial. We have isolated this component using a modified rumen fractionation technique. The success of separation of the microbial fraction from other debris was assessed using microscopic counts, gram and plant stains, and scanning electron microscopy. Faecal composition was measured in six subjects who took for three-week periods, a control diet, and the same diet with 18-3 g/day added cabbage fibre.

Cabbage caused a significant increase in faecal weight, control 87-7 ± 9.4 (SEM), cabbage 142-8 ± 16.3 g/day, p < 0.01: excretion of solids, control 26-1 ± 1.2, cabbage 34-6 ± 1.3 g/day, p < 0.01, and in faecal neutral detergent fibre, control 4-1 ± 0.2, cabbage 5-7 ± 0.4 g/day, p < 0.01. Faecal bacterial solids output was control 14-9 ± 1.0, cabbage 19-8 ± 0.7 g/day, and accounted for 57% of the increase in solids excreted.

Since bacteria are 80% water, this component is a major contributor to the increase in faecal wet weight for these subjects. By providing substrate in the colon, dietary fibre increases faecal weight by promoting microbial growth.
References

Clinical Surgery and Gallstones

Treatment of benign oesophageal strictures by intubation

J. B. BRISTOL, N. J. MORTENSEN, H. T. JOHN, AND M. G. WILSON (Royal United Hospital, Bath, Southmead Hospital, Bristol) In patients with benign oesophageal strictures the mortality and morbidity of reconstructive procedures has provoked consideration of alternatives. We describe the results of open intubation with a Celestin tube in 33 patients.

The patients’ mean age was 71 years. All had proven benign strictures and marked dysphagia. The tube was introduced at open operation via a gastroscopy. Forty had simultaneous repair of a hiatus hernia.

There were five deaths, all in patients over 70 years, two chest and two wound infections. One oesophageal perforation was successfully treated. Twenty-six patients were followed up for a mean of 32 months, there being a satisfactory outcome in 18 (70%). Eighteen had had the tube removed at a mean of 9-5 months post-intubation. Complications such as tube blockage or displacement occurred in 10 but the outcome was unaffected. Three patients were reintubated for recurrent dysphagia at a mean of 30 months post-intubation.

In patients with dysphagia and benign oesophageal strictures, this technique offers a simpler approach to management than traditional operations and may be all that is required in the elderly.

Does abnormal gastric mucosal permeability contribute to poor results after peptic ulcer surgery?

M. J. GOUGH, LINDA WOODHOUSE, C. S. HUMPHREY, AND G. R. GILES (University Department of Surgery, St. James’s University Hospital, Leeds) Some patients do badly after peptic ulcer surgery, possibly due to bile reflux, abnormal gastric emptying, or gastric mucosal damage. Gastric mucosal permeability assessed by back diffusion of lithium chloride may reflect mucosal damage. This study measured lithium fluxes in 18 patients with peptic ulcer, 12 patients with recurrent ulcer, post-vagotomy, and 12 patients with dumping, bile vomiting, or non-specific pain after peptic ulcer surgery. Simultaneously bile reflux under basal conditions, peak acid output to pentagastrin, and liquid test meal emptying times were measured.

Preoperative lithium fluxes were significantly lower (0-121 mmol Li + 0-017/15 min) than in patients with recurrent ulcer (0-177 mmol Li ± 0-022) and patients with a poor surgical result (0-194 mmol Li ± 0-023) (< 0-05). Bile reflux was absent in preoperative patients but present in patients with recurrent ulcer (0-22 mmol/h ± 0-16) and symptomatic patients (0-36 mmol/h ± 0-13). However, there was no significant correlation between the degree of bile reflux and back diffusion of lithium in any group.

Test meal emptying times in recurrent ulcer patients and symptomatic patients were significantly faster than in preoperative patients (> 0-025). These results did not correlate with lithium fluxes, though postoperative bile reflux was associated with more rapid gastric emptying.

Gastric mucosal permeability measured by lithium back diffusion is increased in patients with poor surgical results. These differences are not directly related to the degree of bile reflux, nor changes in gastric emptying or acid secretion.

Comparison of the effect of differing surgical policies on mortality in patients with bleeding peptic ulcers

M. W. DRONFIELD, M. ATKINSON, AND M. J. S. LANGHAM (City and General Hospitals, Nottingham) The role of surgery in patients with bleeding peptic ulcers has never been subjected to a controlled clinical trial, despite the fact that a large proportion of the potentially avoidable mortality in these patients occurs postoperatively.

In this city medical emergencies are admitted from general practitioners randomly on a rota system to one of two hospitals. During 1976-77 206 patients with bleeding peptic ulcers were admitted to Hospital A and 96 to Hospital B, and these two groups of patients were similar in age, sex, and the severity of bleeding as judged by haemoglobin levels and blood transfusion requirements.

In Hospital B a more aggressive surgical approach was used, 46% of patients...
receiving surgical treatment compared with 32% in Hospital A. The postoperative mortality rate in both hospitals was 20%, and as a result a larger proportion of the total number of patients in Hospital B died postoperatively (6% in A, 9% in B). The mortality rate from bleeding in unoperated patients was similar in the hospitals (5% in A, 4% in B).

Thus a more aggressive surgical approach does not reduce overall mortality, and may increase it. Postoperative mortality in our patients was common in the elderly, and in these patients particularly less frequent surgery might reduce mortality.

Reference
1 Allan, R., and Dykes, P. (1976). Quarterly Journal of Medicine, 45, 533.

Effect of highly selective vagotomy on pancreatic exocrine function and cholecystokinin release

N. I. RAMUS, R. C. N. WILLIAMSON, JANE M. OLIVER AND D. JOHNSTON (University Department of Surgery, Bristol Royal Infirmary, Bristol) Reduced pancreatic exocrine secretion after truncal vagotomy has been ascribed successively to parasympathetic denervation, suppressed release of intestinal hormones, altered gastric emptying and, most recently, interference with enteropancreatic reflexes. To determine the effect of highly selective vagotomy (HSV) on the exocrine pancreas, eight patients with endoscopically-proven duodenal ulcer were given a Lundh test meal before and two to three months after operation. Samples of duodenal aspirate and venous blood were collected at intervals for one hour before and two hours after the endogenous (food) stimulus. Basal and stimulated values were obtained for duodenal amylase and trypsin content and, by radioimmunoassay, for serum gastrin concentration and cholecystokinin-like activity (CCK). Completeness of vagotomy was confirmed by gastric acid measurements before and seven days after operation.

HSV affected neither the basal nor the stimulated levels of trypsin and amylase. Operation increased basal serum gastrin from 26 ± 10 (SEM) to 91 ± 47 pg/ml (p < 0.05), but the stimulated response, as assessed by integrated gastrin values, was unchanged. Basal CCK was also increased from 612 ± 317 to 2780 ± 1213 pg/ml (p < 0.01), and, in addition, the stimulated CCK response was greater postoperatively (p < 0.005).

Unlike truncal vagotomy, HSV does not impair the function of the exocrine pancreas. The postoperative increase in CCK after HSV probably reflects altered pancreatic sensitivity and may be related to decreased gastric acid secretion.

References

Impairment of the enteric insulin response after jejunoleal bypass surgery

D. L. SARSON, P. KOPELMAN, AND S. R. BLOOM (Department of Medicine, Royal Postgraduate Medical School and St. George’s Hospital, London) Gastric inhibitory polypeptide (GIP) has been postulated as a major component of the enteroinsular axis. We have previously reported a strikingly reduced release of GIP one year after bypass surgery, concomitant with greatly reduced plasma glucose and insulin release. After several years the plasma glucose returns to normal but insulin release remains impaired. Thus the alteration of bowel anatomy may permanently interfere with the enteroinsular axis. We investigated nine patients who had undergone bypass surgery four or more years earlier and 10 normal controls. Oral and intravenous glucose tolerance tests were performed, the latter being adjusted to mimic the glucose levels seen in each subject after the oral glucose. The total integrated release of insulin to the OGTT was significantly lower in the bypass group compared with normal subjects (23-7 ± 3-0 to 66-6 ± 11-4 nmol/l/120 min, p < 0.005), which was accompanied by a reduction of GIP (2-8 ± 0-3 to 4-3 ± 0-4 nmol/l/120 min) respectively (p < 0.05). The insulin response in the bypass group was greater after OGTT than IVGTT (23-7 ± 3-0 and 10-6 ± 1-0 nmol/l/120 min respectively, p < 0.001). Thus, in long-term bypass patients the enteroinsular axis is retained, though much reduced. The parallel reduction of GIP and insulin release provides further evidence of their causal relationship.

Postoperative sepsis in inflammatory bowel disease

CLARE HIGGENS, R. N. ALLAN, PHYL TILLOTSON, J. ALEXANDER-WILLIAMS, AND M. R. B. KEIGHLEY (The General Hospital, Birmingham) Infection is a common postoperative complication of surgery for inflammatory bowel disease. The reasons cited for the high sepsis rate include pre-existing fistulae, poor nutritional state, obstructed bowel and use of corticosteroids.

We have investigated the factors associated with postoperative sepsis among a consecutive group of 107 patients undergoing elective surgery for inflammatory bowel disease between 1973-77 (Crohn's disease, 93; ulcerative colitis, 14). The infection rates were—wound sepsis, 18%; perianal sepsis, 39%; intra-abdominal abscess, 13%; and septicemia, 4%. There were no deaths. The factors which significantly increased the rate of sepsis were: pre-existing fistula or abscess, low serum albumin (<30 g/dl), and high serum somatomedins (>400 mg). The rate of sepsis was also related to the number of significant risk factors present. The age of the patients, type of resection, antibiotic or steroid cover did not influence the incidence of postoperative sepsis.

This analysis suggests that postoperative sepsis in inflammatory bowel disease is related to disease activity and pre-existing sepsis and may explain why prophylactic perioperative antibiotic cover is not always effective.

Reference

Epidemiological study of antibiotic associated colitis

G. A. MOGG, D. W. BURDON, J. ALEXANDER-WILLIAMS, DENISE YOUNGS, MARGARET JOHNSON, R. H. GEORGE, AND M. R. B. KEIGHLEY (The General Hospital, Birmingham) Antibiotic associated colitis (AAC) has recently been attributed to a faecal toxin produced by Clostridium difficile. The presence of large numbers of this organism in the colon may represent either bacterial overgrowth or a true infection. Epidemics of AAC have been reported which may be due to cross-infection. 

A459
We have looked for Cl. difficile in faecal samples of all new admissions to a single surgical ward, the staff, and the ward environment. Patients developing diarrhoea were also investigated, their clinical course and contact with infected patients was monitored. The influence of ward closure, effective sterilisation methods, and early treatment were assessed.

There were no carriers of Cl. difficile among the staff or new patients admitted to the ward. Cl. difficile was isolated only once from the ward environment. Three patients who had previously developed AAC still carried the organism on a subsequent admission and were a probable source of cross-infection. Twelve new cases occurred in the month before ward closure but only two in the first month after reopening.

These results do not elucidate the pathogenesis of AAC but eradication of Cl. difficile from carriers and sigmoidoscopes has eliminated cross-infection.

References

Longmire procedure to right lobe of liver for nonocclusive obstruction of the main intrahepatic bile ducts

R. M. KIRK (Department of Surgery, Royal Free Hospital, London) Left hepatic duct drainage by intubation1 or intrahepatic cholangiojejunostomy4 fails to relieve obstructive jaundice unless the junction between the right and left ducts is patent. Drainage of the right ducts to the periphery4 relieves jaundice even when the carina is blocked.

Preoperative percutaneous cholangiography is valuable. At operation the right hepatic lobe is mobilised forwards, the tip is excised, and the largest duct is joined, mucosa-to-mucosa to a loop of jejunum, or duodenum. The bowel seromuscularis is sutured around the cut Glisson’s capsule to seal the raw surface. A tube passes through the anastomosis, then through the bowel to the surface, for postoperative cholangiography. It is withdrawn later.

The procedure has been used in eight patients. Of seven with bile-duct carcinoma, the main ducts could not be intubated in three, access was difficult in two because of previous operations, drainage of the left duct had proved ineffective in one, and in one jaundice recurred one year after right duct intubation. One patient had obstruction from secondary gastric carcinoma. There were no operative deaths. Jaundice resolved in all but one patient, who succumbed to progressive liver failure after 46 days. The longest palliation was 19 months. Theoretically, peripheral drainage should provide more sustained drainage than central intubation.

Arterial embolisation of primary hepatic tumours

P. WHEELER, W. MELIA, B. JONES, P. JOHNSON, P. DUBBING, H. NONNERLEY, AND R. WILLIAMS (Liver Unit and Department of Diagnostic Radiology of King’s College Hospital and Medical School, London) Tumour devascularisation by hepatic artery ligation may be useful as a short-term measure for reducing tumour mass, followed by chemotherapy where indicated, but requires technically difficult surgery and collaterals appear rapidly. The use of arterial embolisation to impair tumour blood supply has advantages and we have performed this in three patients with histologically-proven hepatocellular carcinoma, one in association with cirrhosis, and two with a normal underlying liver, in whom hepatic arteriography showed an independent arterial supply to their tumours which could be selectively catheterised and gelatin foam injected. In all patients there was a precipitous fall in serum α-fetoprotein concentration associated with clinical evidence of a reduction in liver size. Serial greyscale ultrasonography showed changes compatible with tumour necrosis. Subsequent treatment of intravenous doxorubicin was given when serum α-fetoprotein concentration had plateaued at a low level. Each patient remains well and symptom free at 11, nine, and two months after embolisation.

Calcium solubility in bile and gallstone formation

B. W. A. WILLIAMSON AND I. W. PERCY-ROBB (University Departments of Clinical Surgery and Clinical Chemistry, Royal Infirmary, Glasgow and Edinburgh) The occurrence of calcium in gallstones has prompted an investigation into the solubility of this ion in human bile.

The British Society of Gastroenterology

Two other patients with highly vascular and enlarging hepatic tumours associated with contraceptive pill also underwent embolisation, resulting in reduced tumour size based on serial scanning. Eventual tumour obliteration occurred in one and marked relief of biliary obstruction in the other.

Prolonged survival in patients with hepatocellular carcinoma (HCC) presenting with α-fetoprotein levels

W. M. MELIA, P. J. JOHNSON, AND ROGER WILLIAMS (Liver Unit of King’s College Hospital and Medical School, London) Serum α-fetoprotein (αFP) estimation is of proven value in diagnosis of HCC but the absolute serum level has not previously been considered to have prognostic significance. Of 58 European patients with proven HCC, survival was significantly better in 16 with normal αFP levels at presentation (78% at one year) compared with 41 with raised levels (12% at one year); (p < 0.001). Treatment protocol was similar for all: resection in non-cirrhotic patients with tumour confined to one lobe (four); orthotopic transplantation in patients without extrahepatic spread (six) and systemic chemotherapy in others (3).

Only 50% of patients with normal αFP levels had underlying cirrhosis compared with 95% of those with raised levels, so their improved survival may be due to resectability and better hepatic reserve. However, two-year survival was greater in non-cirrhotic patients with normal αFP levels (47%) than in non-cirrhotic patients with raised levels (18%). Patients with normal levels form a separate peak, not simply a normal skew in distribution of presentation αFP levels. Levels in these patients remain normal throughout the course of the disease, excluding the possibility that these are patients presenting earlier. Thus, HCC patients with normal αFP may represent a specific type of tumour behaviour.

Calcium solubility in bile and gallstone formation

B. W. A. WILLIAMSON AND I. W. PERCY-ROBB (University Departments of Clinical Surgery and Clinical Chemistry, Royal Infirmary, Glasgow and Edinburgh) The occurrence of calcium in gallstones has prompted an investigation into the solubility of this ion in human bile.
Total calcium concentrations in hepatic (n = 10) and gallbladder bile (n = 36) were 1.7 ± SEM 0.1 mmol/l and 5.0 ± 0.4 mmol/l respectively. Forty per cent of the calcium in hepatic bile and 13% of the calcium in gallbladder bile was ultrafilterable indicating that a major fraction of biliary calcium was bound.

Two types of calcium binding were defined. Soluble: in gallbladder bile calcium was reversibly bound to bile salt—lecithin micelles (40% of total calcium), protein (20%), acidic polysaccharide (20%), and molecules with mol wt. less than 1000 (10%), leaving 10% ionised. In hepatic bile micellar binding accounted for 75% of the ionised calcium. Insoluble: such complexes of calcium with bile salt and biliary polysaccharide were demonstrated in vitro.

Further, hepatic bile was supersaturated with calcium carbonate and gallbladder bile was saturated with calcium phosphate.

At low calcium concentrations, the calcium-binding system in bile acts as a damping mechanism, compensating for changes in total calcium concentration by maintaining constant the ionised fraction. It is thus protective against precipitation. However, at high calcium concentrations, the calcium-binding species are themselves capable of precipitation and are often found with calcium in gallstones. This may be relevant to both the nucleation and growth phases of gallstone development.

Incidence of gallstones after clofibrate therapy

M. C. BATESON AND I. A D. BOUCHIER (Department of Medicine, University of Dundee, Dundee) Gallstones and cholecystectomy are commoner in patients treated with clofibrate, but this might reflect confusion between symptoms of biliary and ischaemic heart disease before treatment, or be related to causes of hyperlipidaemia. All adult patients referred to a lipid clinic had an oral cholecystogram if they had not had cholecystectomy. Those patients with normal gallbladders who were subsequently treated with clofibrate 2 g daily for at least a year (but no other hypolipidaemic drug) were asked to volunteer for a repeat oral cholecystogram. Twenty consecutive patients agreed to participate after treatment with clofibrate for one to four (mean 2.2) years. There were eight men and 12 women aged 37-71 (mean 52-6) years. Four women and three men aged 38-71 (mean 58-6) years with various patterns of hyperlipidaemia and on various diets developed radiolucent gall stones after one to three (mean 1.9) years. Two of these patients subsequently developed biliary colic. These data suggest an annual incidence rate of 16% of new gallstones after clofibrate therapy, compared with a spontaneous incidence rate of well under 1%.

We conclude that clofibrate is a potent cause of gallstone disease.

Medical treatment of gallstones with chenodeoxycholic acid (CDCA): a follow-up at four years

M. PONZ DE LEON, N. CARULLI, R. IORI, P. LORIA, F. ZIRONI, AND G. ROMANO (Istituto de Clinica Medica, Universita di Modena, Modena, Italy) Since 1972 CDCA has been used in treating patients with gallstones. We report our experience with CDCA in 117 patients with radiolucent gallstones studied over the last four years. Emphasis has been given to: (a) efficacy, (b) resistance, (c) side-effects, (d) recurrence of stones. Of the 117 patients who entered the study 77 were treated for more than one year, whereas 30 interrupted for different reasons. Of the 77 treated for more than one year, gallstones disappeared in 29 (38%) and were reduced in 26 (33%). The percentage of success rose to 85% (49 out of 57) when only non-obese subjects with small stones (<10 mm) were considered. Of the 22 patients in whom CDCA had no effect, 17 had large stones (>15 mm) and five were obese. Mild diarrhoea appeared in 40%; mild and transient hypertransaminasemia in 13 (15%), marked but transient hypertransaminasemia in four. In four patients the treatment had to be interrupted owing to untreated diarrhoea.

Liver biopsies, before and during treatment, showed only minor histological abnormalities. Recurrence of gallstones was observed in one case. Finally, five patients with gallstones and chronic liver disease were treated; CDCA was well tolerated and stones disappeared in one.

In conclusion: (1) CDCA seems to be effective and safe, even in patients with liver disease; (2) small stones are more likely to dissolve than large stones; (3) recurrence of gallstones does not seem to be a frequent event.

Reduction in minimum effective dose of chenic acid with bedtime administration plus low cholesterol diet

D. P. MAUDGAL, R. BIRD, AND T. C. NORTHEFIELD (Norman Tanner Gastroenterology Unit, St. James’ Hospital, and Department of Medicine, St. George’s Hospital Medical School, London) We have previously demonstrated that bedtime administration1 and low cholesterol diet2 both enhance the effect of chenic acid (15 mg/kg/day) on cholesterol saturation index (SI). To determine the minimum effective dose of chenic acid (to give mean SI of 0.8), we carried out three randomised dose/response studies in 10 gallstone patients: (A) low cholesterol (100 mg/day) diet with bedtime chenic acid (250, 500, 750 mg/day); (B) normal cholesterol diet with bedtime doses as in (A); (C) normal cholesterol diet with mealtime doses (375, 750, 1125 mg/day). Fasting gallbladder bile samples were analysed for SI (Hegardt and Dam). Pretreatment SI was 1.28 ± 0.06 (mean ± SEM), and fell on A and B respectively to 0.94 ± 0.05 and 1.02 ± 0.06 on 250 mg/day (p < 0.01), to 0.83 ± 0.04 and 0.92 ± 0.06 on 500 mg/day (p < 0.05), and to 0.75 ± 0.04 and 0.86 ± 0.06 on 750 mg/day (p < 0.01). When regression lines were plotted of SI against dose, mean SI of 0.8 was obtained with 8 mg/kg/day on A, with 11.5 mg/kg/day on B, and 15 mg/kg/day on C. We conclude that the minimum effective dose of chenic acid is reduced by approximately half with bedtime administration plus low cholesterol diet.

This reduction is similar to that reported for the more expensive bile acid, ursodeoxycholic acid3.

References


Acceleration of gallstone dissolution with bedtime chenic acid plus low cholesterol diet

D. P. MAUDGAL AND T. C. NORTHEFIELD (Norman Tanner Gastroenterology Unit, St. James’ Hospital, and Department of Medicine, St. George’s Hospital Medical

A461
School, London) We have previously demonstrated that a low cholesterol diet and bedtime administration both enhance the effect of chenic acid on cholesterol saturation index (SI) of fasting gallbladder bile. Gallstone dissolution rate may depend on the degree of cholesterol unsaturation, but this relationship has never been demonstrated in vivo in man. We have therefore studied 24 gallstone patients receiving chenic acid (15 mg/kg/day). They were matched in pairs according to gallstone size, and randomly allocated to (A) mealtime chenic acid with unrestricted diet (conventional regimen); or (B) bedtime chenic acid with low (100 mg/day) cholesterol diet. Fasting gallbladder bile samples were analysed for biliary lipid composition and calculation of SI (Hegardt and Dam). Gallstone size was assessed by carefully standardised oral cholecystogram. At six months, mean (±SEM) reduction in gallstone size on regimen (A) was 22.2 ± 13.0%, and on regimen (B) it was 59.9 ± 18.5% (p < 0.02). SI on (A) fell from 1.14 ± 0.07 to 0.89 ± 0.10 (p < 0.05) and on (B) it fell from 1.19 ± 0.06 to 0.70 ± 0.05 (p < 0.001). We conclude that gallstone dissolution rate in man is related to the degree of cholesterol unsaturation of bile and that it is accelerated by bedtime administration of chenic acid plus low cholesterol diet.

References

Experience with various methods of management for residual stones in common bile duct

C. W. VENABLES, M. SLOOFF, R. BAKER, M. I. LAVELLE, AND R. M. R. TAYLOR (University Department of Surgery, Royal Victoria Infirmary, Newcastle upon Tyne) Various methods are available for the management of stones in the common bile duct after cholecystectomy. While there are enthusiasts for each technique, there is no consensus as to which is best and what the indications are for each. Since 1972 we have used all these techniques at various times and it is the purpose of this paper to examine the results obtained and the problems encountered. Sixty-seven patients have been treated for retained common bile duct stones using one or more of the following techniques: (1) cholic acid infusion through T tube; 11 cases, success = 45%; (2) Burhenne's catheter extraction: five cases, success = 60%; (3) oral chenodeoxycholic acid: six cases, success = 33%; (4) endoscopic sphincterotony: 37 cases, success = 70%; (5) surgical therapy: (a) removal calculus alone, four cases, success = 75%; (b) removal calculus and drainage procedure: 15 cases, success = 100%.

Success has been judged upon disappearance of all stones on repeat radiology in the first four groups. Surgical success has been judged on symptoms and biochemistry as repeat radiology was not always possible (mean FU = 4.2 yr).

Only one death was directly related to the procedure in this series: acute pancreatitis after endoscopic sphincterotomy.

The various problems encountered with each technique will be discussed and a comparison between surgery and endoscopic sphincterotomy will be presented.