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The Spring meeting was held at the University of Cambridge on 1 and 2 April 1977. On Friday morning a symposium on gastritis and duodenitis took place with Dr. S. Truelove in the Chair. The Spring Banquet was held in St. John's College, on Friday evening. On Friday afternoon and Saturday morning sessions were devoted to scientific papers on liver (Chairmen: Professor S. Sherlock and Dr. Roger Williams), oesophagus, stomach, and duodenum (Chairmen: Professor M. Hobsley and Dr. J. H. Baron), coeliac disorders (Chairman: Dr. A. Ferguson), small and large bowel (Chairman: Professor H. L. Duthie), clinical surgical topics (Chairman: Professor L. Blumgart), pancreas and clinical diagnostic topics (Chairmen: Dr. K. Wormsley and Dr. G. Watkinson), clinical medical topics (Chairmen: Dr. K. F. R. Schiller and Dr. D. E. Barnardo), inflammatory bowel disease and absorption and malabsorption (Chairmen: Dr. A. P. Dick and Professor C. C. Booth). Abstracts of the papers presented to the Society follow.

ENDOSCOPY

Delay in recovery from IV diazepam

A. R. W. HATFIELD, R. F. LONG, B. M. WRIGHT, AND A. J. LEVI (Academic Unit of Gastroenterology, The London Hospital; Roche Research Laboratories; Northwick Park Hospital and Clinical Research Centre) Although the sedative effects of IV diazepam appear to be short lived, previous data suggest that plasma diazepam concentrations remain raised for 24 to 48 hours and a second peak of activity occurs at six to 10 hours1.

Sequential plasma diazepam estimations were performed on 10 patients undergoing upper GI endoscopy. The patient's balance was assessed using a simple but sensitive sway meter and psychomotor function was assessed using a peg-board and digit-symbol testing.

The mean results from the sway meter, peg-board and digit-symbol tests demonstrated a progressive return to normal over 24 hours and correlated well with the fall in diazepam concentrations except at 24 hours, when the mean plasma level (0-14 μg/ml) was still raised to a quarter of the one hour value.

In four of the patients there was a secondary rise in diazepam concentration at six hours. This was accompanied by a deterioration in sway meter readings. In the remaining six patients, diazepam concentrations and the other parameters progressively returned to normal.

With increasing emphasis on day procedures, the delayed recovery from IV diazepam and the secondary peak at six hours needs to be stressed, and the use of synergistic agents recommended in some situations to reduce the initial dose of diazepam required.

Reference


Endoscopic dye-scattering in coeliac disease

FIONA M. STEVENS AND C. F. MCCARTHY (Department of Medicine, Regional Hospital, Galway, Ireland) Upper gastrointestinal endoscopy is part of the routine investigation of dyspepsia and anaemia, which may be presenting features in untreated coeliac disease. A method of endoscopically examining the duodenal cap has been used to determine the proximal extent of the villous atrophy of coeliac disease and the value of endoscopy in excluding a diagnosis of coeliac disease.

Using the dye-scattering technique of Kohli1, the proximal duodenum of 12 untreated adult coeliac patients has been studied at endoscopy. The dye, indigocarmine, outlines the mucosal contours and a severe villous atrophy with a mosaic pattern can be easily demonstrated throughout the duodenal cap. Endoscopic mucosal biopsies from the duodenal bulb in untreated coeliac disease show the characteristic histological abnormalities found in the distal duodenum.

In none of the untreated coeliac patients studied were villi present in the proximal duodenum. The demonstration of villi in the duodenal cap at endoscopic examination precludes a diagnosis of coeliac disease.

Reference


A prospective randomised trial to compare brush cytology before or after punch biopsy for endoscopic diagnosis of gastric cancer

H. THOMPSON, A. M. HOARE, P. W. DYKES, R. N. ALLAN, AND M. R. B. KEIGHLEY (The General Hospital, Birmingham) It has been suggested that brush cytology increases the diagnostic yield of gastric cancer1. However, it may be argued that if gastric lesions are brushed, the accuracy of subsequent histological diagnosis may be reduced. In order to investigate this hypothesis, we have undertaken a prospective trial among patients with solitary gastric lesions attending for their first endoscopy. All patients had a previous barium meal. Brush cytology and multiple punch biopsies were obtained from each patient. The order of obtaining histological or cytological material was defined by instructions on numbered randomisation cards.

Two hundred and eleven patients have so far entered the trial and have been followed up for at least two months, 10 have been withdrawn because of previous endoscopy. The final diagnosis included: 59 patients with adenocarcinoma, 109 patients with benign gastric ulcer, the remainder (33 cases) had polyps or areas of gastritis. Among the patients with malignant disease, the accuracy of diagnosis was as follows: histology alone 76%, cytology alone 90%, both 98%, and one patient where both cytology and histology failed to make a diagnosis of cancer. There were two patients where cytology or biopsy provided false positive findings. The best results were obtained when brush cytology was performed before punch biopsy (98 cases). However, the difference between the two test groups was not
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statistically significant.

These results indicate that both cytological and histological material should be obtained in all patients requiring gastroscopy and that brushing does not appear to impair the accuracy of interpreting subsequent gastric biopsies.

Reference


Is duodenitis a dyspeptic myth?

S. N. JOFFE, W. O. THOMSON, A. ROBERTSON, F. LEE, AND L. H. BLUMGART (University Department of Surgery, Royal Infirmary, Glasgow) Patients with endoscopically diagnosed duodenitis have been investigated to determine if 'duodenitis' is a separate disease or part of the duodenal ulcer diathesis. In a total of 502 fibreoptic oesophagogastroduodenoscopies carried out over 30 months, only 14 (2.8%) cases of symptomatic duodenitis without an associated duodenal ulcer were diagnosed. Clinical follow-up (one to 3.5 years) including repeat endoscopy, duodenal mucosal biopsy, and double contrast barium meal showed that six patients developed proven duodenal ulcers, with haemorrhage in two, and all have undergone surgery (43%). A further two patients continued to complain of dyspepsia and repeat endoscopy showed duodenitis, which was confirmed by histology. Six patients are at present asymptomatic. Repeat endoscopy in four showed a normal macroscopic duodenal mucosa, confirmed histologically in three, with mild duodenitis in one. One patient was considered to have mild duodenitis on endoscopy but this was not confirmed histologically. One patient declined further investigation.

In a randomised study, the duodenitis by histological criteria could not be distinguished from biopsies taken from areas adjacent to duodenal ulcers. The natural history and histological findings in these patients lend support to the concept that duodenitis is part of the pathophysiological spectrum of the duodenal ulcer diathesis rather than a separate disease. It may represent both the early production and later healing phases of duodenal ulceration.

Reference


Clinical impact of pancreatography, EMI scanning, and ultrasonography

P. B. COTTON, M. E. DENYER, J. HUSBAND, H. B. MEIRE, AND L. KREEL (Gastrointestinal Unit, The Middlesex Hospital and Division of Radiology, Clinical Research Centre and Northwick Park Hospital, London) Grey-scale ultrasonography (US), endoscopic pancreatography (ERP), and computed tomography (CT) using the EMI whole body scanner have been performed on 41 patients with known or suspected pancreatic disease. Reports were given in the full knowledge of previous clinical history and radiology. Their value in the 34 patients with a satisfactory final diagnosis was assessed by the whole panel, according to their impact on clinical management in three contexts: pain? pancreatic disease (eight patients), known pancreatic lesion? cancer or pancreatitis (nine), and known recurrent pancreatitis? local lesion (17).

Each report was scored on the scale: ++ correct and helpful; + correct but not helpful; 0 technical failure; — wrong but not hazardous; —— wrong and hazardous.

There were nine technical failures with US (poor pancreatic visualisation usually due to colonic gas), six with ERP (failed pancreatography), but none with CT. No test scored ——. Remaining scores were:

US: 15 ++ 5 + 5 − total 30
ERP: 24 ++ 4 + 0 − total 52
CT: 25 ++ 5 + 4 − total 51

Numbers in each clinical group were small and the scatter of results within them was similar. At the start of the study ERP was established, but experience in interpreting US and CT images was limited. Many of the incorrect reports can be explained on this basis. Two patients were diagnosed as having pseudocysts on CT scans when the appearances simply reflected previous surgery and inflammation. The pancreatic tail may be difficult to see on US scans, and to differentiate from the jejunum on CT scans, but techniques are improving. The low score for US reflects the nine technical failures; when the pancreas was seen, results were almost as good as those with other more complex techniques. CT gave more helpful information than the other two tests combined in only three patients.

Endoscopic sphincterotomy of the papilla of Vater

M. CLASSEN, D. WURBS, AND F. HAGENMÜLLER (I. Medizinische Abteilung, Allgemeines Krankenhaus Barnbek, Rübenkamp 148, D-2000 Hamburg 60, West-Germany) The technique of endoscopic sphincterotomy (EPT) as described by Classen and Demling1 was performed in 160 patients who suffered from chronic cholecystolithiasis (139), papillary stenosis without gall stones (16), or obstructive tumour of the papilla of Vater (five).

In 111 patients with cholecystolithiasis EPT led to spontaneous passage of the stones into the duodenum or the stones were extracted endoscopically with a Dormia basket. Benign papillary stenosis was removed in all cases by EPT as well as tumorous obstruction of the papilla of Vater. Complications occurred in 14 cases—namely, cholangitis (six), haemorrhage (three), stone impaction (four), and pancreatitis (one). One patient died of haemorrhage and another one of pulmonary embolism after pancreatitis had developed.

In Germany more than 900 patients have been treated successfully by EPT up to September 1976. EPT has proved to be an effective method for the treatment of papillary stenosis and cholecystolithiasis. Its risk seems to be lower than that of transduodenal papillotomy by means of surgery2.

References


Histological correlations with pancreato- graphy in necropsy specimens

M. KIZU, J. NEWMAN, P. B. COTTON, AND T. KASUGAI (Gastrointestinal Unit, The Middlesex Hospital, London, and Aichi Cancer Center, Nagoya, Japan) At endoscopic pancreatography the significance of minor calibre variations in the branch ducts is often obscure. We have studied the correlation between pancreatic histology and duct radiology in a total of 135 Japanese and British necropsy specimens, where both techniques gave good data.

There were 62 cases where histology showed no evidence of pancreatitis—that is, no focal necrosis, fibrosis, or cellular infiltrate. Minor calibre variations were seen radiologically in the branch ducts in 25 cases (40%), commoner over the age of 60 years (64% against 24%). The main
changes were mild dilatation with irregular stenoses, complete branch obstruction, and small cystic dilatations.

The data were then studied from the radiological standpoint. A total of 44 specimens showed minor calibre variations of the branch ducts on necropsy pancreaticography. The histological findings in these specimens were: normal 57%, pancreatic fibrosis 25%, pancreatitis 18%.

Significant correlations between radiological appearances and histology were: radiological duct narrowing with periductal fibrosis and epithelial metaplasia; obstruction with periductal fibrosis, metaplasia, protein plugs, and fat replacement; cystic dilatation with small cyst formation.

Minor branch duct changes should be interpreted with caution at endoscopic pancreaticography, and may have no diagnostic significance in older patients.

Malfunction of dorsal and ventral pancreas; a cause of pancreatitis?

P. B. COTTON AND M. KIZU (Gastrointestinal Unit, The Middlesex Hospital, London) The pancreas develops embryologically from dorsal and ventral buds which normally fuse. Failure of fusion results in a small ventral element draining through the main papilla, and a large dorsal element including the body and tail draining via Santorini's duct through the accessory papilla. This anomaly has been found in 24 patients investigated by endoscopic pancreaticography. In four patients the finding was clinically irrelevant; in six other patients presenting with abdominal pain, the relevance remains obscure. Fourteen patients were having definite episodes of pancreatitis, of varying severity. Five of these enjoyed alcohol, but no aetiological factors were apparent in the remaining nine, and we postulate that inadequate drainage via Santorini's duct may be important. It is certainly relevant to surgical management as four patients had had poor results from previous anatomically inappropriate procedures. Endoscopic cannulation of the accessory papilla is technically difficult. However, we have recently demonstrated an abnormal and dilated dorsal pancreatic system in three of these patients, and one has obtained good short-term results after endoscopic sphincterotomy at the accessory papilla.

LIVER

Enterohelpeatic circulation of silicon in man

J. W. DOBBIE, M. J. B. GRAY, AND C. W. IMRIE (INTRODUCED BY L. H. BLUMGART) (University Department of Renal Medicine and Surgery, Glasgow Royal Infirmary) Although there are several studies which show that silica (SiO₂) is absorbed from the mammalian alimentary tract, it is assumed that absorption in man is minimal. This has encouraged the widespread use of silicates as food additives. Recent studies in man have shown that silicates are absorbed and excreted in significant amounts in urine.

Si concentration in bile was measured by atomic absorption spectroscopy in 13 patients (11 female and two male) after biliary tract surgery. Eight three hourly collections of bile (over 24 hours) were obtained from T-tubes in CBD. Magnesium trisilicate (5 g) was given by mouth after the first three-hour basal collection of bile.

The mean base line concentration of bile Si, as measured in the first three hour period, was 0.66 ug/ml (SD ± 0.43). Three to nine hours after oral administration of magnesium trisilicate, the mean concentration of bile Si rose to a maximum concentration of 1.29 ug/ml (SD ± 0.57), a twofold increase. In one patient (excluded from the series) almost complete bile collection via a tube across Roux loop to common bile duct anastomosis revealed a tenfold increase in Si bile concentration after oral ingestion of silicate.

Oral administration of silicates thus causes a rise in the concentration of bile Si. The urinary concentration of silicon has been causally linked with the initiation of urolithiasis. This study suggests that the role of silicon in gallstone formation merits further investigation.

References


Clinical study of liver blood flow in man measured by 133Xe clearance after portal vein injection

I. TAYLOR, S. B. SHERIFF, AND R. C. SMART (INTRODUCTION BY PROFESSOR R. SHIELDS) (Departments of Surgery, Royal Hospital Sheffield and Liverpool, Department of Medical Physics, Sheffield Royal Infirmary) During the course of a clinical trial to assess the value of adjuvant liver perfusion of 5-fluourouracil after surgery for colorectal cancer, liver blood flow was measured in 14 patients. Access to the portal circulation was through the 'obliterated' umbilical vein.

The rate of clearance of a bolus of 133Xe was monitored using a gamma camera so that blood flow from different areas of the liver could be calculated using an on-line computer system (Nukab), to collect the integrated counts over the field of view.

The initial distribution of 133Xe reflected the distribution of contrast media in the portogram rather than the sulphur colloid image of functioning liver tissue.

The clearance curve of 133Xe was a double exponential of which the initial fast component accounted for a consistently high proportion of the total clearance. The perfusion studies have shown wide differences in blood flow to the various areas of the liver (40-110 ml/min/100 g liver), in addition to a wide variation in perfusion rate between the patients (range 52-8-122-6 ml/min/100 g liver).

This technique of quantitative estimations of liver blood flow to different areas of the liver may have importance in the planning of operative procedures and in understanding the haemodynamic mechanisms involved in liver disease.

Haemodynamic studies in vinyl chloride monomer workers with portal hypertension

L. M. BLENDIS, P. M. SMITH, B. W. LAWRIE, M. R. STEPHENS, AND W. D. EVANS (Welsh National School of Medicine, Cardiff, and Department of Gastroenterology, Central Middlesex Hospital, London) Haemodynamic studies were performed in five asymptomatic vinyl chloride monomer workers in whom splenomegaly (five) or thrombocytopenia (two) were detected during a screening programme at a major chemical plant. In addition to pressure measurements, splenic blood flow was measured by externally monitoring the washout curves of radio-xenon after splenic arterial injections, and cardiac output by using Indocyanine Green.

Three patients had portal hypertension, with intrasplenic pressures between 18 and 29 mm Hg (all pressures less inferior vena caval pressure), associated with normal wedged hepatic venous pressures of 8-11 mm Hg and free hepatic vein pressures of 1-6 mm Hg. Two patients had normal pressures. Splenic blood flow was increased at 68-123 ml/min 100 g, giving total splenic blood flows of 332-843 ml/min (upper limit of normal 250 ml/min). Cardiac indices were increased at 4-4-5-5 l/min/M². All three patients with portal hypertension had collateral veins in intrasplenic veno-
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The British splenorenal graphy, one patient having a massive spontaneous splenorenal shunt. Liver histology was either normal or showed slight non-cirrhotic portal fibrosis.

In conclusion, significant rises in portal pressure with collaterals occurring in asymptomatic vinyl chloride workers with normal or only slightly abnormal liver histology appears to be due to pre-sinusoidal haodynamic portal hypertension and increased splenic blood flow.

Kupffer cell uptake of microaggregated albumin: (a) in relation to liver blood flow; (b) in inflammatory bowel disease

A. J. ANDERSON, OLIVER JAMES, AND E. N. WARDLE (Departments of Medicine and Medical (Geriatrics), University of New-castle-upon-Tyne) The use of microaggregated albumin in a reticulo-endothelial saturation test based on determination of the half-life in plasma of successive doses of 2.5/5/0/10 mg/kg of microaggregated albumin has already been described. This study was to determine how far liver blood flow (estimated by Indocyanine Green and BSP clearance) might influence the microaggregated albumin clearance. Patients with inflammatory bowel disease were studied because of the possibility of circulating immune complexes in these conditions.

Ten normal subjects and 30 subjects with a variety of liver diseases were studied. Overall BSP clearance correlated extremely well with the albumin clearance at a dose of 2.5 mg/kg. Albumin clearance fell off at larger doses, especially when there was impaired phagocytosis. Thus, the overall effectiveness of the liver in clearing the microaggregated albumin could be seen to depend (1) on the extraction efficiency of the Kupffer cells, and (2) on liver blood flow.

Twelve patients with ulcerative colitis, 12 with Crohn's disease were studied. All but three had normal RES saturation tests; these three were the only subjects receiving large doses of prednisone. Prednisone has been shown to reduce phagocytosis of Kupffer cells. It is concluded that inflammatory bowel disease does not itself alter Kupffer cell function.

Abnormal vitamin D metabolism in cirrhosis

R. T. JUNG, M. DAVIE, J. O. HUNTER, AND T. M. CHALMERS (Addenbrooke's Hospital, Cambridge) Vitamin D deficiency may be associated with cirrhosis and superimposed liver disease increases the requirement of vitamin D needed to heal rickets in experimental animals. Low plasma 25-hydroxycholecalciferol (25-OHCC) levels have been reported in cirrhosis, but the reason is not clear.

We investigated vitamin D metabolism in 10 biopsy proven cirrhotic patients (eight ethanolic, two cryptogenic). Mean plasma 25-OHCC levels in alcoholic patients was lower than in controls investigated in the same season (winter), but the difference was not significant. In three patients re-studied after the summer, plasma 25-OHCC had risen. The half life of intravenously administered red 3H-cholecalciferol was short and showed no correlation with plasma 25-OHCC in contrast with normal subjects, nor did half life change in those patients where plasma 25-OHCC rose after the summer. Appearance of 3H-25-OHCC from 3H-cholecalciferol was apparently deficient compared with the control group four hours after injection.

Serum calcium and phosphate levels and Ca absorption were within normal limits and serum parathyroid hormone level was raised in only one patient. Bone biopsy showed no evidence of osteomalacia or hyperparathyroidism.

These results suggest that cirrhotic patients can respond to ultra-violet light and that deficient production of 25-OHCC and an increased rate of metabolism of cholecalciferol contribute to vitamin D deficiencies in liver disease.

Intestinal absorption of 25-hydroxyvitamin D and osteomalacia in primary biliary cirrhosis

JULIET COMPTON AND R. P. H. THOMPSON (Gastrointestinal Research Unit, Rayne Institute, St. Thomas' Hospital, London) The prevalence of histologically proven osteomalacia and its relationship to the intestinal absorption of 25-hydroxyvitamin D (25-OHcc) have been investigated in 11 patients with primary biliary cirrhosis (PBC). Full thickness iliac crest bone biopsies were assessed quantitatively. Plasma 25-hydroxyvitamin D and D (25-OHcc) was measured by competitive protein-binding assay before four, eight and 24 hours after the oral administration of 25-OHcc, 10 μg/kg/bw.

Four patients (one anicteric) had severe osteomalacia; all had received cholestyramine for longer than 18 months, in contrast with none of the seven patients without osteomalacia. Mean plasma 25-OHcc levels were at all times significantly lower (p < 0.001) in the patients compared with controls, and patients with osteomalacia had lower levels than those with normal bone histology. There was no correlation between the 25-OHcc absorption and serum bilirubin or albumin levels. Mean serum calcium and urinary calcium were significantly lower (2.32 v. 2.54 mmol/l, p < 0.05; 0.64 v. 3.79 mmol/l/24 h, p < 0.01) and serum alkaline phosphatase significantly higher (134.8 v. 53.4 KA units/dl, p < 0.01) in patients with osteomalacia compared with those without.

It is concluded that intestinal absorption of 25-OHcc is reduced in patients with PBC, and that this is further decreased by cholestyramine, thus increasing the risk of developing osteomalacia.

References


Osteomalacia, osteoporosis, and parathryroid function in chronic liver disease

R. G. LONG, E. MEINHARD, Z. VARGHESE, M. R. WILLIS, AND S. SHERLOCK (Departments of Medicine and Chemical Pathology, Royal Free Hospital and the Department of Histopathology, The London Hospital) Thirty-two patients with chronic liver disease have had quantitative examination of bone histology using a computerised technique with measurement of osteoid and total bone volume proportion and osteoblastic and osteoclastic surface extent. Parathyroid hormone (iPTH) was measured by a radioimmunoassay technique; other biochemical measurements were performed by standard laboratory methods.

Eighteen of 25 patients with cholestatic disease and four of seven with hepatocellular disease had an increase in osteoid tissue. An increase in the amount of osteoid correlated with total bone (p < 0.05) but there was no correlation with
Plasma bile acid disappearance rate as a test of liver function—a critical reassessment

I. T. GILMORE and R. P. H. THOMPSON (G. I. Laboratory, Rayne Institute, St. Thomas' Hospital) We have recently reported that in normal subjects the plasma clearance of $^{13}$C-cholylglycine is rapid (415 ± 25 ml/min/m², mean ± SEM, n = 15), equivalent to an extraction of 85% during a single passage through the liver. Thus its clearance should be sensitive to changes in liver function—a prediction at variance with reports that the disappearance rate of cholylglycine from blood may detect patients with mild liver disease.

We have studied the plasma clearance of intravenously administered $^{13}$C-cholylglycine (5 µCi) in 70 patients with liver disease. Clearance was impaired only in those with advanced alcoholic or primary biliary cirrhosis (133 ± 26 ml/min/m², n = 14, p < 0.01), and was within normal limits in seven patients with acute viral or alcoholic hepatitis (367 ± 17 ml/min/m²) and in 18 with anicteric chronic liver disease (ACLD) (400 ± 32 ml/min/m²). Similarly, the clearance of Indocyanine Green (ICG), 0.25 mg/kg IV, was normal in patients with acute hepatitis (normals 248 ± 22, n = 14, patients 212 ± 12 ml/min/m², n = 7) and with ACLD (256 ± 20 ml/min/m², n = 18). The mean volume of distribution for cholylglycine and ICG was larger in patients with ACLD than in normal controls (cholylglycine—patients 9.34 ± 0.84, controls 8.40 ± 0.00 1.m⁻², n.s.; ICG—patients 1.48 ± 0.08, controls 1.22 ± 0.06 1.m⁻², p < 0.01). This interesting finding may help to explain reports that a greater percentage of cholylglycine is retained at 60 minutes in patients with ACLD, because of differences in distribution rather than in hepatic bile acid extraction.

References


Plasma amino-acids: their role as an indicator of hepatocellular dysfunction

MARSHA Y. MORGAN, JUDITH P. MILSOM, AND SHEILA SHERLOCK (Department of Medicine, Royal Free Hospital, Hampstead, London) Specific plasma amino acid patterns have been described in patients with hepatic insufficiency and encephalopathy. The most consistent abnormalities are an increase in phenylalanine, tyrosine, tryptophan, and methionine and a reduction in valine, leucine and isoleucine. We have determined the molar ratio of valine + isoleucine + leucine : phenylalanine + tyrosine in a group of patients with liver disease of varying aetiology and severity. In the control population this ratio was 2.3 ± 0.5 (± ISD). A significant lowering of this ratio has been reported in patients with chronic portal systemic encephalopathy. In addition to confirming this finding we have shown a significant lowering of the ratio in patients with parenchymal liver disease even when the degree of liver damage was minimal and hepatic encephalopathy was absent. Patients with uncomplicated cholestasis had a normal ratio. Although the ratio varied throughout the day, it always remained within the normal range. Correlation studies with routine liver function tests, bile acids, and liver histology suggest the ratio to be a sensitive index of hepatocellular dysfunction. Serial estimations may be used as a prognostic indicator.

Reference


T lymphocyte mediated cytotoxicity in HBsAg positive liver disease: development of a new assay

N. E. SHELIEKH, C. G. OSMAN, H. CULLENS, A. L. W. F. EDDELSTON, AND ROGER WILLIAMS (Liver Unit, King’s College Hospital and Medical School, London) It has been assumed, but never demonstrated, that T lymphocytes are responsible for the destruction of virus-infected hepatocytes in acute and chronic type B hepatitis. Since virus-infected hepatocytes have not as yet been cultured in vitro, we have investigated this further by developing an assay of lymphocyte-mediated cytotoxicity for HBsAg-coated, chromium-labelled red cells. Significant cytotoxicity was observed in all of 13 patients recovering from acute type B hepatitis and HBsAg negative at the time of testing. Fractionation of the patients’ lymphocytes clearly showed that T cells were the principal effector in the assay system.
In six patients investigated within two weeks of the onset of acute type B hepatitis, all of whom were HBsAg positive at the time of testing, cytotoxicity could not be demonstrated. Similarly, positive results were obtained in only 10% of cases with HBsAg positive chronic liver disease. However, when the lymphocytes were washed 10 times, cytotoxicity was then demonstrable in all of those with acute hepatitis and in 70% of those with chronic liver disease. Blocking of cytotoxic T cells could be induced in vitro by incubating them with highly purified HBsAg and it is possible, in vivo, that the antigen or antigen/antibody complexes are responsible for suppressing T cell activity. Such an inhibition of specific T cell cytotoxicity could be of importance in the maintenance of virus infection in patients with chronic liver disease.

Drinking history and objective criteria for alcohol-induced liver disease

A. N. HAMLYN, MILENA LESNA, AND A. J. WATSON (Departments of Medicine and Histopathology, Royal Victoria Infirmary, University of Newcastle upon Tyne) Recent attempts at correlating alcoholism with liver histology have been based on the traditional clinical interview as a means of assessing problem drinking. This study aimed at eliciting a reproducible, scored drinking history by means of an embedded questionnaire technique and correlating it with simultaneous casual blood ethanol determination and needle liver biopsy histology, interpreted double-blind by two independent observers.

The subjects were 46 patients consecutively investigated for clinical features suggestive of chronic liver disease. Low scores for alcoholism were seen in 17 of these and in this group no blood ethanol was detected. High scores for alcoholism were seen in 29 patients and in 11 the blood ethanol test was positive. There was no difference between high and low score groups for abnormality of liver function tests, incidence of biopsy fat, fibrosis, Mallory's hyaline, or frequency of cirrhosis. The incidence of alcoholic hepatitis (18% and 48% respectively) did, however, reach statistical significance.

It is concluded (1) that casual blood ethanol was the most reliable evidence of problem drinking in this study, (2) that the variable relationship of elicited drinking history to liver histology may render suspect some estimates of the relative frequency of alcoholic liver disease.

References


Effect of iglycamide (Billigram) on bile flow and biliary lipid secretion in man

G. D. BELL, J. DORAN, M. FAYADH, G. MURPHY, AND R. H. DOWLING (University Department of Therapeutics, City Hospital, Nottingham, and Gastroenterology Department of Guy's Hospital, London) The hepatic secretion of both phospholipid (PL) and cholesterol (C) into bile is closely related to bile salt secretion (BS) but we are totally ignorant as to (1) the mechanism involved or (2) the exact anatomical site or origin of biliary PL and C. Any compound found to affect the mechanism coupling BS to the biliary secretion of PL and C would thus be of interest; particularly if, like chenodeoxycholic acid, it could be shown to 'uncouple' biliary C output and enhance cholesterol solubility.

While studying the cholangiographic agent iglycamide (Io) in the rhesus monkey we unexpectedly found that it significantly (p < 0.001) enhanced biliary cholesterol solubility. We have measured BS, PL, and C output in 21 postoperative patients with a t-tube in situ. Eleven patients were given an IV infusion of Io, while the other 10 subjects acted as controls. Io effected the bile salt independent fraction of bile flow and acted as a potent choleretic. It also caused a significant (p < 0.001) decrease in PL and C output and increased the cholesterol solubility of bile (p < 0.01).

It was concluded that iglycamide could prove a useful model for studying the mechanisms controlling biliary lipid secretion.

References


OESOPHAGUS, STOMACH AND DUODENUM

Effects of betanechol chloride and cigarette smoking on lower oesophageal sphincter pressure in normal subjects

D. K. CHATTOPADHYAY, M. G. GREANEY, AND T. T. IRVIN (The University Surgical Unit, Royal Infirmary, Sheffield) It has been reported that lower oesophageal sphincter pressure (LOS P) is reduced by cigarette smoking1 and increased by ingestion of the cholinergic drug betanechol chloride. However, these reports were based on station pull-through techniques of oesophageal manometry and it has been shown that these methods are less accurate than a rapid pull-through (RPT) method of manometry2.
The RPT technique of oesophageal manometry was used in a study of the effects of cigarette smoking and bethanechol chloride on LOSP in healthy volunteers without symptoms of gastrooesophageal reflux.

In 13 subjects, measurements were made for a basal period and for 60 minutes after the oral administration of 25 mg bethanechol chloride. No significant changes in LOSP were found. In 10 subjects, LOSP was measured for a basal period and for 15 minutes during cigarette smoking. There was a significant reduction in LOSP from a basal value (mean ± SEM) of 3.52 ± 0.2 kPa to 2.84 ± 0.12 kPa during smoking (r = 0.21, P < 0.01).

We have confirmed that cigarette smoking causes a reduction in LOSP but it appears that bethanechol chloride has no significant effect on LOSP.

References

Assessment of lower oesophageal sphincter pressures measured by the rapid pull-through method

M. G. GREANEY, D. K. CHATTOPADHYAY, AND T. T. IRVIN (The University Surgical Unit, Royal Infirmary, Sheffield) Recent studies have suggested that highly reproducible measurements of lower oesophageal sphincter pressure (LOSP) are achieved with a rapid pull-through (RPT) technique of oesophageal manometry.

We have studied the reproducibility of the RPT technique in the measurement of LOSP in eight student volunteers without symptoms of gastrooesophageal reflux. A hydraulic perfusion system was used and its suitability was confirmed by bench occlusion tests. LOSP was measured with a tube assembly of four catheters with distal orifices radially orientated in the oesophageal lumen at the same axial level. Using needle valves, the catheters were perfused at a constant rate of 5 ml per minute.

There was a significant correlation between the highest and lowest LOSP measurements obtained in subjects during a recording session (r = 0.77, t = 4.47, P < 0.001), but no significant correlation between LOSP values in individuals at separate sessions (r = 0.43, t = 2.21, P > 0.05). However, the mean values (+ SEM) for the LOSP of the group were similar in the two recording sessions (3.13 ± 0.21 kPa and 3.14 ± 1.92 kPa).

RPT measurements of LOSP in individual subjects are suitable for analysis only within the period of a single recording session.

References

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IV. Variations in the chloride content of gastric juice and their significance. Journal of Biological Chemistry, 97, 585-604.

Cimetidine and prostaglandins: evidence for different modes of action on the gastric mucosa

H. A. CARMICHAEL, L. M. NELSON, AND R. I. RUSSELL (Gastroenterology Unit, Royal Infirmary, Glasgow) We recently reported that the prostaglandin analogue 15 (R) 15-methyl-PGF2α methyl ester significantly inhibits the production of gastric mucosal erosions in rats by aspirin. We have also looked at the effect of cimetidine in similar circumstances. The incidence of erosions induced by aspirin (128 mg/kg) was significantly reduced from 70% in 20 rats to 9.5% in 21 rats by cimetidine 50 mg/kg (P < 0.01).

The mode of action of both these types of compounds in protecting the gastric mucosa has been assumed to be secondary to acid inhibition. We therefore set out to test this assumption by investigating the effect of cimetidine and the prostaglandin analogue on the incidence of aspirin-induced erosions in the presence of HCl. Male Sprague-Dawley rats, after an overnight fast, were fed a solution containing aspirin 392 mg/kg in 160 mM HCl alone or with either cimetidine (50 mg/kg) or prostaglandin (50 μg/kg). Thereafter the rats were fed similar volumes of 160 mM HCl at hourly intervals for three hours and then killed one hour later. The incidence of bleeding produced by aspirin and HCl was 100% in 20 rats. This was not significantly reduced by cimetidine (90% in 20 rats). However, the incidence of erosions produced in the presence of prostaglandin was 13% in 23 rats. This was significantly less than the incidence produced by aspirin and HCl alone or with cimetidine (P < 0.01 in each case). Therefore the prostaglandin analogue inhibits aspirin-induced erosions in the presence of HCl, whereas cimetidine does not. This suggests that the mode of action of prostaglandin is not entirely or even largely due to acid inhibition.

Cimetidine and salbutamol combined inhibition of gastric acid

R. F. MCCLOY, S. C. PARMENTER, AND J. H. BARON (Department of Surgery, Royal
Postgraduate Medical School, Hammer smith Hospital, London) A combination of antisecretory drugs may have an important role in the treatment of patients unable to tolerate, or resistant to, high doses of a single inhibitory agent. Salbutamol, a beta-2 adrenergic agonist, is a powerful inhibitor of gastric acid. We have combined salbutamol with the potent H2 receptor antagonist cimetidine against pentagastrin-stimulated gastric acid secretion in five conscious dogs with gastric fistulae.

A dose response curve was established to six doses of pentagastrin (0.5, 1, 2, 4, 8, 16 μg/kg-h) infused intravenously for three hours. The antagonists were infused for one hour before and throughout the pentagastrin infusion: (1) cimetidine 4 μmol/kg min, (2) cimetidine 8 μmol/kg min, (3) salbutamol 0.4 mmol/kg min, (4) cimetidine 4 μmol/kg min + salbutamol 0.4 mmol/kg min. Each antagonist was tested against each of the six doses of pentagastrin in each dog.

Cimetidine and salbutamol, individually, produced depression and flattening of the pentagastrin dose-response curve characteristic of non-competitive inhibition. Inhibitions of up to 70% (salbutamol), 60% (cimetidine 4 μmol/kg min) and 83% (cimetidine 8 μmol/kg min) were achieved. The combination of salbutamol and cimetidine caused additive inhibition, up to 93%, of the pentagastrin dose-response curve. This summation of inhibition is comparable with the summation of an anti-cholinergic, atropine, with an earlier H2 antagonist, metiamide.

References


In vivo effects of bile salts on acid secretion by the rat stomach

S. H. Elmasri, M. R. Lewin, and C. G. Clark (Surgical Unit, University College Hospital Medical School, London) The effects of conjugated bile salts on basal and stimulated (histamine or pentagastrin) acid secretion have been examined in the perfused rat stomach preparation. Dextrose (5.4%) alone or with bile salts added in concentrations varying from 1 to 10 mM was perfused in random order for 30 minutes each period while recording pH continually. This technique allows the calculation of acid output expressed as nanomoles per hour.

The results in 22 rats showed that increasing concentrations of bile salts reduced acid output in both basal and stimulated stomachs. At a bile salt concentration of 1 mM, acid was reduced from 76.7 to 23.2 n mol/h in the basal state and from 13.1 X 103 to 422.0 n mol/h in the stimulated state. In the basal stomach, the reduction in acid secretion, after perfusion with all bile salt concentrations, was restored to normal within five minutes. In the stimulated stomach this recovery was often prolonged for an hour or more.

These results cannot be accounted for by the precipitation of bile salts, as the pH of all perfusing solutions was well above the pKa of the bile salts used. Further experiments were performed to study the bile salt effects on sodium and potassium changes in stimulated stomachs. There were no significant changes in the electrolyte concentrations. This suggests that the mechanism of reduction of acid secretion by bile salts is not by back
diffusion of hydrogen ions but may be due to a direct effect on the parietal cells.

Liability to recurrent ulceration after vagotomy: a fresh comparison of insulin and histamine-stimulated secretion

P. B. BOULOS, N. K. MAYBURY, P. K. JENA, and M. HOBESLEY (Department of Surgical Studies, The Middlesex Hospital and Medical School) It has been asserted that 'histamine-stimulated secretion provides the best criterion by which recurrent ulceration (RU) can be predicted'. However, the prognostic value of the insulin test has recently been improved. A fresh comparison was therefore undertaken. As histamine immediately followed the insulin test, it was necessary to show that previous insulin does not affect the histamine response. The regressions of histamine secretion versus height in 52 tests where histamine followed basal secretion and 52 where histamine followed insulin did not differ significantly.

Seventy-one postvagotomy patients (including 19 RU) underwent both insulin and histamine stimulation. The results were compared with their respective ranges before vagotomy, established in 48 patients with duodenal ulceration (DU).

Values above the lower 95% tolerance limit of the preoperative range were designated positive and those below negative. Histamine-stimulated secretion (60% false positives) was a less satisfactory criterion than insulin (35% false positives, p < 0.005).

Thirty-three DU (including seven RU) were tested before and after operation with both secretogogues. Those with a reduction of secretion less than 60% were arbitrarily designated positive. The false positives were greater for histamine (72%) than for insulin (50%, p < 0.01). Thus the new insulin test is better than histamine at predicting RU after vagotomy.

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After an overnight fast 15 duodenal ulcer and 16 normal subjects each drank 25 mmol HCl (250 ml of a 100 mM solution) to which had been added 1 M. Indium 113. Gastric emptying was monitored by the loss of radioactivity from the stomach. Plasma immunoreactive secretin (IRS) levels were measured by radioimmunoassay for three hours after acid.

Gastric emptying was significantly faster in the duodenal ulcer subjects when assessed by T 50% (p < 0.025) or by the loss of the middle 10 mmol HCl (T 30-70%, p < 0.0125).

No significant rise in mean plasma IRS was found in normal subjects at any point although a significant rise was noted in ulcer subjects five minutes after acid (p < 0.01).

Mean rise in plasma IRS during T 30-70% was correlated with rate of acid loss from the stomach, the closest correlation being observed with the logarithm of the latter: DU r = 0.816, p < 0.0025; controls r = 0.673, p < 0.01. The threshold for IRS release, however, appears to be higher in the DU subjects.

These studies suggest that secretin plays a role in acid neutralisation only under conditions of high acidity, but in such circumstances, its release may be impaired in duodenal ulcer subjects.

References


Use of synthetic fragments for specific immunostaining of CCK cells

A. M. I. BUCHAN, J. M. POLAK, P. FACER, S. R. BLOOM, M. SZELKE, D. HUDSON, and A. G. E. PEARSE (Royal Postgraduate Medical School, Hammersmith Hospital, London) Gastrin-like immunoreactivity has been described in the intestine and substances with gastrin-like biological activity have been extracted. CCK can be extracted from the same areas of the intestine but, unlike gastrin, insignificant amounts are found in the antrum. The CCK and gastrin molecules share a C-terminal sequence and thus antibodies to that portion of either molecule will react to both. It is obviously important for specific immunocytochemistry to use antisera free from any cross-reaction, even by minor subpopulations of antibodies not normally detected by radioimmunoassay procedures. Antibodies were produced in rabbits to synthetic human gastrin I and to a synthetic fragment of the middle portion of the CCK molecule, prepared by the solid phase method (H-Met-Ile-Lys-Asn-Leu-Gln-Ser-Leu-Asp-Pro-Ser-His-OH). The high specificity of the CCK antibodies produced was shown by their lack of cross-reactivity with antral G cells.

Serial 3 μm paraffin or 1 μm resin embedded sections were obtained from human jejunal biopsies and stained with both antibodies (gastrin and CCK). Two distinctive and separate populations of cells, about equal in number, were seen. Thus for the first time the separate identity of these two cell types has been proved. The use of high specific antibodies is essential when there is a possibility of immunocytochemical cross-reactions with homologous hormones and can often be obtained only with complete reliability by immunising with selected hormone sequences prepared synthetically.

Gastric emptying and plasma secretin levels after oral administration of hydrochloric acid in normal and duodenal ulcer subjects

J. C. MCLoughlin, R. GREEN, and K. D. BUCHANAN (Departments of Medicine and Surgery, Queen's University, Belfast, Northern Ireland) Most authorities accept that abnormalities in production or handling of acid play a role in the pathogenesis of duodenal ulceration. Secretin is a potent pancreatic exocrine stimulant and is stimulated by intraduodenal acid infusion, although the physiological relevance of this has been questioned. Defective release of secretin in response to acid has been described in duodenal ulcer (DU) subjects.

However, 113.

N. D. CHRISTOFIDES AND S. R. BLOOM (Department of Medicine, Hammersmith Hospital, London) We previously demonstrated that motilin may be regarded as one of the main factors regulating gastric emptying in man and thus the rate of duodenal acidification. The possible role of motilin in duodenal ulcer (DU) was therefore of considerable interest. Plasma motilin was measured in six controls, 16 DU patients, and eight patients after a successful vagotomy (Hollander –ve). The mean basal motilin levels in the three groups studied (controls 41 ± 6 (SEM) pmol/l, DU 61 ± 12 pmol/l,
postvagotomy 93 ± 36 pmol/l) were not significantly different. After insulin-induced hypoglycaemia motilin levels fell reaching a nadir at 35 minutes (controls 58 ± 8% fall, DU 42 ± 3%) which coincided with the lowest blood glucose levels (mean in both groups 2-1 ± 0-1 mmol/l). Plasma motilin rose thereafter, coinciding with the recovery of blood glucose. The motilin fall also occurred in the eight postvagotomy patients, but levels remained significantly depressed for longer, probably related to the slower recovery of glucose. The correlation coefficient between motilin and glucose levels in all 30 subjects was highly significant (r = 0.95, p < 0.001).

These results show that motilin release is not under vagal control and fails to demonstrate any significant abnormalities in duodenal ulcer. The close connection with blood glucose suggests that this new hormone may have an unexpected role in carbohydrate metabolism.

References


Duodenoscopy and sphincter of Oddi

B. F. RIBEIRO, P. B. COTTON, J. B. DILAWARI, M. ROBERTS, AND B. LAURENCE (Gastrointestinal Unit and Department of Surgical Studies, The Middlesex Hospital and Medical School, London) Duodenoscopy allows the passage of pressure sensitive probes through the sphincter of Oddi and into the bile duct. Catheter tip transducers, balloon catheters, double and single lumen perfused systems have been tried. These studies employed a single lumen Teflon catheter with a side hole 5 mm from the tip, constantly perfused with water at 0-2 ml/min; pressures were measured by external transducers, and recorded. Patients were sedated with diazepam (previously shown to have no short-term effect on sphincter activity), but were given no anticholinergic or antispasmodic drugs. Using standard ERCP technique, the catheter was passed deep into the bile duct. Pressures were measured during withdrawal through the papilla where a high pressure zone (HPZ) was identifiable—except after sphincterotomy. In five patients with unexplained pain after cholecystectomy, there was no evidence of excess sphincter activity (mean peak pressure 17 mmHg, range 12-22). Adequate controls were not available, but these figures were significantly lower than those found in patients with chronic pancreatitis (mean peak 23 mmHg, range 17-31). HPZ was manometrically short (<2 mm), and consistent recording was difficult. It proved simpler to record the pressure gradient between the bile duct and duodenum as a measure of sphincter activity. In no patient did this gradient exceed 8 mmHg. Mean value for seven patients with chronic pancreatitis was 2-8 mmHg (SD ± 2-2), and for 11 patients after cholecystectomy was 4-4 mmHg (SD ± 2-1). In 11 patients examined within weeks of endoscopic sphincterotomy, the pressure gradient had fallen to zero in eight, 2 mm in two, and 1 mm in one. We also examined six patients who had previously undergone surgical sphincterotomy; only one had a zero gradient.

Endoscopic manometry provides a new tool for research into biliary and sphincter dynamics. However, the techniques are not straightforward, and deep cannulation may fail, especially as antispasmodic agents are not used. Endoscopic manometry allows long-term sequential documentation of the evolution of endoscopic sphincterotomies, but cannot so far claim other clinical indications.

Duodenal bombesin cell pathology

M. V. MCCROSSAN, J. M. POLAK, S. R. BLOOM, S. HOBBS, AND A. G. E. PEARSE (Royal Postgraduate Medical School, Hammersmith Hospital, London) A counterpart of the bombesin group of hormonal peptides produced in the amphibian skin has been recently found in the mammalian gastrointestinal tract. In man a bombesin-like material was found, by immunocytochemistry, in gut endocrine cells especially numerous in the duodenal mucosa. Fresh duodenal biopsies were taken from (1) patients with duodenal ulceration (DU), (2) patients with pernicious anaemia (PA), and (3) control subjects.

Immunocytochemical studies were carried out using highly specific antibodies raised to synthetic amphibian bombesin and quantification of the findings was done using an Automatic Image Analyser Computer (Quantimet 720). Quantitative immunocytochemical results showed a 70% increase in the number of bombesin cells (28-62 cells/mm²) in DU cases and a 50% decrease in PA cases (9-95 cells/mm²) as compared with normal control subjects (19-76 cells/mm²).

These results fit well with the established effect of bombesin on gastrin release and indicate a possible physiological role for bombesin as an important modulator of acid secretion. Its disturbance in disease states requires urgent further investigation.

Reference


COELIAC DISORDERS

Enterobacterial colonisation of ileum with vitamin B₁₂ malabsorption measured by whole body counting techniques in tropical malabsorption (TM)

A. M. TOMKINS, S. G. WRIGHT, T. SMITH, AND B. S. DRASAR (Department of Human Nutrition and Microbiology, London School of Hygiene and Tropical Medicine; Radioisotopes Division, Clinical Research Centre, Northwick Park, Harrow) Malabsorption of vitamin B₁₂ occurred in nine of 11 patients, without parasitic disease, who developed diarrhoea and weight loss in India persisting for months after return to the UK. Morphological abnormalities of the ileal mucosa were present in six of eight patients. Anaerobic and aerobic culture of luminal fluid and mucosal samples from the ileum revealed high numbers (up to 10⁶/ml) of bacteria in six of eight patients. Enterobacteria identified were Klebsiella pneumoniae, Alcaligenes faecalis, and Enterobacter Hafniae. Total numbers (log₁₀ enterobacteria/ml luminal fluid) were higher in TM (3-9 ± 0-4) than in control subjects (1-4 ± 0-6) (p < 0.02). Gram -ve anaerobes were present in similar numbers in TM and controls (2-2 ± 0-4, 1-8 ± 0-7 respectively, NS).

Changes in vitamin B₁₂ absorption occurring within 48 hours of starting tetracycline therapy were studied in seven patients, given sequentially administered doses of Co⁵⁷ and Co⁵⁸ labelled vitamin B₁₂, measured using whole body counting, (normal absorption > 40%). Rapid improvement from pretreatment (mean 16-9%, range 2-1-32-3%) to intreatment (mean 35-0% range 4-5-65-0%) levels occurred too early to be attributable to morphological recovery, suggesting that the vitamin B₁₂ malabsorption may be due to interaction of bacterial metabolism and the ileal epithelial cell.
Folate deficiency and DNA synthesis of jejunal mucosa in tropical malabsorption (TM)

A. M. Tomkins, M. McNurlan, and S. Wright (Department of Human Nutrition, London School of Hygiene and Tropical Medicine and Hospital for Tropical Diseases, London) Folate deficiency occurs in patients with TM and its inhibitory role on DNA synthesis may contribute to the mucosal lesion. Previous studies on bone marrow have shown that thymidylate synthesis (methyltransferase-thymidylate) is the essential folate-mediated step in DNA synthesis. Incorporation rates of thymidine into DNA (Tdr/DNA), via the salvage pathway, increase if folate dependent de novo synthesis of thymidylate is impaired. Human jejunal mucosal specimens were incubated in organ culture to determine if such alterations occur in human gut.

Tdr/DNA (dpm/μg DNA) was greater in seven patients with TM and systemic folate deficiency (962 ± 216) than in six patients with similar mucosal lesions with normal folate status (505 ± 124) (p < 0.05). Both were higher than controls 234 ± 76 (p < 0.02). Addition of folic acid (100 μg/ml) produced 28 ± 8% decrease in Tdr/DNA in those with systemic folate deficiency without effect in mucosa with normal folate.

Healthy mucosa incubated in solutions containing 2 × 10⁻⁴ M deoxyuridine which dilutes the thymidylate pool suppressed Tdr/DNA below 16%. Mucosa from five of seven patients with TM and folate deficiency failed to suppress below 20% (range 10-80%).

These abnormalities indicate a functional deficiency of folate in intestinal mucosa which may contribute to the mucosal lesion of TM.

Isolating the component of gluten which causes the mucosal damage in coeliac disease

B. S. Anand, R. E. Offord, J. Piris, and S. C. Truelove (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, Gibson Laboratories, Radcliffe Infirmary, Oxford, and Laboratory of Molecular Biophysics, Department of Zoology, University of Oxford) In a previous study, Frazer's fraction III of wheat gluten was separated by ultrafiltration into three further fractions, named A, B, and C in order of ascending molecular size. By feeding experiments in treated coeliac subjects, A was found to be harmless, whereas both B and C caused mucosal damage.

Fraction B has now been separated by passage through a large Sephadex column into three subfractions, named B1, B2, and B3 in order of ascending molecular size. Feeding experiments in coeliac subjects have shown that B1 is harmless but B2 and B3 can cause damage. B2 has been found to stimulate the lymphocytes of coeliac subjects but not those of controls. Various fractions of gluten give an Arthus-type skin reaction in coeliac subjects and B2 is the most active in this respect.

Examination of B2 by high voltage paper electrophoresis and by paper chromatography shows that it is a heterogeneous mixture of polypeptides. It has been further separated into a number of subfractions, some of which show immunological activity while others do not.

References


Specific immunofluorescence and immunoperoxidase reactions in the jejunal mucosa of coeliac subjects after challenge with a fraction of gluten

B. S. Anand, R. E. Offord, J. Piris, and S. C. Truelove (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, Gibson Laboratories, Radcliffe Infirmary, Oxford, and Laboratory of Molecular Biophysics, Department of Zoology, University of Oxford) Two coeliac subjects on a gluten-free diet volunteered to undergo serial jejunal biopsy after intraduodenal instillation of a fraction of gluten (fraction B) which is known to be damaging to coeliac subjects. A control subject with no organic disease was studied similarly. Both coeliac subjects showed marked histological abnormalities in the jejunal biopsy specimens a few hours after the challenge, whereas the control subject was unaffected. These changes occurred at the same time as coeliac subjects develop Arthus-type reactions in the skin after the intradermal injection of various gluten fractions, suggesting that the mucosal lesion in coeliac disease is itself the result of an Arthus-type reaction, a suggestion which has also been made by previous workers.

In one of the coeliac subjects, serial biopsy specimens were used to study the development of specific immunofluorescence. This occurred at the same time as the histological damage. The pattern of staining was similar for IgA and IgM and was seen chiefly in the epithelial cells, especially in the brush border. For IgG, the pattern was completely different with diffuse staining of the lamina propria and sparing of the epithelial cells. Immunoperoxidase preparations showed marked increases in IgA- and IgM-containing plasma cells in the jejunal mucosa of the coeliac subjects.

Peripheral blood lymphocyte subpopulations in adult coeliac disease (CD)

A. W. Bullen and M. S. Losowski (Department of Medicine, St. James's Hospital, Leeds) In untreated CD there is T cell depletion in the peripheral blood, perhaps due to increased enteric loss of lymphocytes. However, total lymphocyte counts are not significantly different from controls. In some patients there is also splenic dysfunction, which has not hitherto been implicated in the understanding of changes in lymphocyte subpopulations.

We have studied 40 patients with CD. In untreated patients, T cell numbers were significantly lower than in controls, but because of a significant increase in null cells, total lymphocyte counts were not significantly different.

Seven patients with CD and the peripheral blood film of splenic atrophy had significantly lower T cell percentages and significantly higher null cell percentages than seven other patients matched for age and stage of treatment. Absolute null cell numbers and total lymphocyte counts were significantly higher in those with splenic atrophy, but absolute T cell numbers were not significantly different.

The results are consistent with the
B-cell antigens in coeliac disease (gluten-sensitive enteropathy)


The association of coeliac disease and the histocompatibility antigen HLC-B8 is well established. Recently two other cell surface markers have been found to be associated with this disease: (1) GSE-associated B-cell antigen\(^1\) and (2) HLA-D locus antigen DW3\(^2\).

We have studied the relationship between GSE-associated B-cell antigens and HLA-DW3 in 17 control individuals, 20 patients with coeliac disease, and 37 members of seven unrelated families of patients with coeliac disease. The method used was that of microcytotoxicity testing of purified peripheral B-cells. To type for HLA-DW3 locus antigen, an antisera that has previously been shown to react only with cells which do not respond in MLC reaction to homozygous DW3 typing cells was used. To type for GSE-associated B-cell antigens three different sera from mothers or wives of coeliac patients were used.

The HLA-DW3 antigen was present in 75-0\% of the patients and in 35-2\% of the controls. There was a stronger correlation of DW3 antigen than with HLA-B8 antigen in the coeliac patients as previously found\(^1\). The GSE-associated B-cell antigen (B-I) was present in 70-0\% of the patients and in 5-9\% of the controls. From this study and the results obtained in the seven families it appears that DW3 antigen and GSE-associated B-cell anti-
gen are non-identical and under control of separate genes. One gene is controlled by the major histocompatibility locus (DW3) and appears to be dominant, the other is controlled by another locus in another chromosome and appears to be recessive.

These surface cell specificities associated with coeliac disease could form all or part of a genetically determined receptor site on the surface of lymphoid cells which result in cell activation and immune responses upon exposure to gliadin.

References


Immunoblasts in coeliac disease

D. P. O’DONOGHUE, R. SEWELL, J. HALL, S. MCGEEHAN, K. L. CLARK, AND P. J. KUMAR

Evidence for mucosal immune complexes in untreated coeliac disease

BRIAN B. SCOTT, D. G. SCOTT, AND M. S. LOSOWSKY

Extracellular IgA, IgG, IgM, C3, and Clq were studied by direct immunofluorescence in the jejunal mucosa of seven untreated coeliac patients, and compared with the findings in 11 treated coeliac patients and 16 non-coeliac subjects.

There was a very significantly increased incidence of IgA together with C3 in the basement membrane region of untreated coelia (6/7) compared with patients on a gluten-free diet (2/11) and non-coelia (0/16). The findings were similar in the lamina propria. In addition IgG with Clq and C3 was demonstrated, particularly in untreated patients.

These findings suggest that a local antibody-antigen reaction involving IgA and complement may contribute to the ongoing mucosal damage in untreated coeliac disease. Furthermore, there may in addition be a secondary IgG antibody response contributing to the damage as postulated by Brandtzæg\(^9\).

References

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SMALL BOWEL AND LARGE BOWEL

Distribution of enkephalin in the gut and brain

S. N. SULLIVAN, S. R. BLOOM, AND J. M. POLAK (Departments of Medicine and Histochemistry, Hammersmith Hospital, London) The pentapeptide enkephalin belongs to a group of endogenous peptides (endorphins) which interact with specific opiate receptors in the brain and gut. Using two independent techniques, indirect immunofluorescence and radio-immunoassay, we have now been able to demonstrate the presence of this peptide not only in the brain but also in the gut. Within the brain the highest enkephalin concentrations are found in the cendate nucleus, being 100-fold greater than those of the cortex. In the gut highest concentrations of enkephalin are extractable from the gastric antral mucosa, where it is easily located in characteristic APUD cells. This demonstration of the presence of enkephalin both in the brain and the gut provides further support for the neuroectodermal origin of hormone-producing cells of the gut. In addition, it provides an explanation for the powerful effects of opiates on the gut and suggests that endogenous opiate peptides are important in the regulation of gastrointestinal function.

Possible precursor relationship between gut glucagon-like immunoreactivity (GLI) and glucagon

J. M. CONLON, R. F. MURPHY, AND K. D. BUCHANAN (Departments of Biochemistry and Medicine, Queen’s University, Belfast) Many polypeptide hormones are released from inactive precursors by specific proteolysis. The predominant GLI1 from porcine ileum and colon has molecular weight 10 000 to 12 000 (large GLI) but fails to bind glucagon receptors and activate adenylyl cyclase in liver plasma membranes. Large GLI reacts 50 times more strongly with antibodies which bind N-terminal fragments (residues 1 to 18) of glucagon than with antibodies binding C-terminal fragments (residues 19 to 29). Incubation of large GLI with trypsin (EC 3.4.21.4) or cathepsin D (EC 3.4.23.5) immobilised on agarose, leads to increased immunoreactivity measured with antibodies specific for the C-terminal region of glucagon concomitant with destruction of immunoreactivity with antibodies to the N-terminal region. When the GLI is hydrolysed using enzymes of broader substrate specificity pepsin (EC 3.4.23.1) or chymotrypsin (EC 3.4.21.1) increased immunoreactivity with antibodies to the C-terminal region of glucagon is not detected. These findings indicate that large GLI has homology both with N- and C-terminal regions of glucagon, exposed and masked, respectively, in the native conformation. This may be analogous to pancreatic GLI which contains glucagon with a C-terminal polypeptide extension. Gut GLI may thus function as precursor to a biologically active molecule structurally similar to glucagon.

Multiple hormonal apud cells

J. M. POLAK, S. R. BLOOM, A. M. J. BUCHAN, AND A. G. E. PEARSE (Royal Postgraduate Medical School, Hammersmith Hospital, London) The endocrine cells of the gut have long been recognised and classified by the ultrastructural characteristics of their granules. With the application of immuno-cytotoxicchemical and biochemical techniques it became possible to correlate the various gastrointestinal hormones with separate cell types in well-defined areas of the gut and the Wiesbaden/Bologna classification of endocrine cells became widely accepted. At that time it was universally assumed that each endocrine cell secreted a single product (amine or hormone). Since the discovery of motilin in small intestinal 5HT containing EC cells the ‘one cell, one hormone’ theory has been challenged. Recent findings with sophisticated immuno-cytotoxicchemical techniques for localising peptide hormones in gut sections at subcellular thickness have provided further evidence of multiple product cells: (1) substance P, a peptide neurotransmitter is present, together with 5HT in a population of EC cells separate from those producing motilin; (2) bombesin is a newly discovered amphibian kin peptide, and a bombesin-like immunoreactivity is present in VIP containing cells of the upper gastrointestinal tract; (3) a morphine-like brain peptide, enkephalin is found in the G cells of the human antral mucosa.

The present findings are of importance both to the cell biologists and to the gastroenterologists. New areas of intragranular ultrastructural cytochemistry have been opened up and the possibility of multiple functions of a single cell type has given a new insight into the endocrinology of the gut.

References


Influence of high and low fibre diet on induction of colorectal tumours in the rat using dimethylhydrazine HCI

R. CARACHI, A. BUSUTTIL, AND S. N. JOFFE (University Department of Surgery, Royal Infirmary, Glasgow and Department of Pathology, Western General Hospital, Edinburgh) The symmetrical dialkylhydrazine, 1:2 dimethylhydrazine dihydrochloride (DMH) was administered subcutaneously to a group of 80 male Sprague-Dawley rats. The drug was given in a dose of 15 mg/kg body weight at weekly intervals for a period of 16 weeks. Premalignant changes were seen histologically at four weeks and multiple adenocarcinomas of the colon were a constant feature in all the experimental animals from the 16th week onwards. At 20 weeks metastases were present and two rats developed multiple liver metastases after 28 weeks. Both histologically and morphologically the induced-tumours were similar to human colorectal adencarcinomas.

This model was used to study the influence of dietary fibre on the induction of these tumours. Forty rats were paired into a high fibre and a low fibre group. Rats on a high fibre diet developed plague-like lesions which were metastatic and simple adenomas. The ones that developed adenocarcinomas were fewer in number, better differentiated, and less invasive than those rats on a low fibre diet. Multiple hepatic metastases were discovered in rats on the low fibre diet, and these were anaplastic mucin-secreting signet ring adenocarcinomas.

The fibre content in the diet appears to
be one of many factors involved in the protection of colonic mucosa from the alkylating carcinogen used in this model.

The high organotropism for colonic mucosa by this carcinogen in the dose and duration of injection makes it a reliable, reproducible, and effective model of colorectal cancer to study its relationship to diet.

Duration of symptoms and prognosis of colorectal cancer

T. T. IRVIN AND M. G. GREANEY (University Department of Surgery, Royal Infirmary, Sheffield) It has been suggested that future progress in the treatment of cancer of the colon and rectum will depend on the earlier diagnosis of the disease. It appears that the prognosis is substantially improved by the detection of asymptomatic disease but the potential value of the earlier diagnosis of symptomatic patients seems less certain.

We have studied the relationship between the duration of the symptomatic illness and the prognosis in 335 patients undergoing surgical treatment of colorectal cancer. The crude five year survival rate was 30.2%. The duration of the illness was not significantly related to survival or tumour pathology (Dukes' stage) but patients presenting within five or nine months of the onset of symptoms had a significantly higher incidence of tumours of the upper rectum (p < 0.01), and multiple symptoms or abdominal pain at the onset of the illness (p < 0.0005).

The results suggest that the prognosis of colorectal cancer is largely determined by the biological behaviour of the primary tumour rather than by the length of the symptomatic illness, and it appears that the earlier diagnosis of symptomatic patients may result in comparatively small gains in survival.

References


Colonic compliance—an improved index of colonic muscular activity?

A. M. HAY AND C. J. VICKERY (R. B. WELBORN) (Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London, and Department of Engineering in Medicine, Imperial College, London) Theoretical considerations suggest that the measurement of pressure-volume relationships within the colon might provide a more precise index of its contractile status than other techniques. We have extended the scope of two earlier studies by measuring colonic distensibility in four unanaesthetised dogs.

Series of highly reproducible pressure-volume curves were generated by siting a 10 cm cylindrical balloon in the descending colon and filling it with water to a maximum volume of 100 ml: (1) in increments of 20 ml, equilibrium pressures being determined at each step (static response); (2) at varying rates up to 30 ml/s (dynamic response).

Compliance varied inversely with the filling rate. With rapid filling (15, 30 ml/s) successive distension cycles produced progressive, persistent increases in compliance. In any one experiment, however, a stable response was obtained after 5-8 cycles.

Morphine (0-015 mg/kg/min) decreased compliance at all filling rates. Hyoscine N-butylbromide (0-05 mg/kg/min) increased compliance at slow filling rates (0-57, 1-43 ml/s) but did not affect the static response or the response to rapid distension.

The rate-dependent nature of the response to hyoscine indicates that slow distension provokes contractile activity, whereas rapid distension inhibits it. More generally, the pressure-volume response at slow rates of distension may provide a sensitive index of contractile status and of any alteration induced in it by pharmacological agents, acting directly or indirectly. This technique is suitable for use in man and may prove valuable in the assessment of normal and abnormal colonic function.

References


Rectal goblet cell mucous glycoproteins in ulcerative colitis: studies using fluorescein-labelled lectins

R. J. MACHELL AND R. W. STODDART (INTRODUCED BY A. P. DICK) (Department of Medical Gastroenterology, Addenbrooke's Hospital, Cambridge, and the Strangeways Research Laboratory, Cambridge) Histological studies in ulcerative colitis have shown changes in the carbohydrate content of the goblet cells without precise biochemical definition, while chemical analysis of colonic mucus fails to localise the cellular dysfunction. This difficulty can be overcome by the use of lectins, plant proteins, having specific carbohydrate-binding properties.

The secretory activity of the mucosal goblet cells in 10 normal rectal biopsies and 17 biopsies from patients with active or quiescent ulcerative colitis has been examined using fluorescein-labelled lectins as previously described. The lectins used were concanavalin A, for α-D mannose, soybean agglutinin for α-D-galactosamine, Ricin agglutinin for β-D-galactose. Sialic acid was detected by fluorescein-labelled aprotinin. The stained sections were examined by fluorescence microscopy.

Sections from normal rectal biopsies showed intense, neuraminidase sensitive, staining of goblet cells by aprotinin, showing that sialic acid is a widespread terminal sugar in rectal mucus.

Rectal biopsies from 12 acute colitics showed varying degrees of goblet cell depletion and striking reduction in the aprotinin staining of the remaining goblet cells, demonstrating depletion of the sialic acid residues in the mucus. In five biopsies from quiescent colitics, sialic acid depletion was less marked and in four of these, the staining pattern indicated some increase in the mannose content of mucin, despite goblet cell recovery, showing a persistent biochemical defect. Possible implications will be discussed.

References


Effect of dietary protein with and without added dietary fibre on faecal ammonia concentrations and on colonic function

J. H. CUMMINGS, W. J. BRANCH, HELEN HOUSTON, AND D. J. A. JENKINS (MRC Dunn Nutrition Laboratory, Cambridge and MRC Gastroenterology Unit, London) Large bowel cancer is common in countries where animal protein intakes are high.
and is uncommon where dietary fibre intakes are high. Colonic microflora are thought to produce carcinogenic substances in the bowel lumen from dietary and other residues. On the basis of the epidemiological evidence high protein diets should increase the colonic concentration of carcinogenic substances, while high fibre diets should dilute them.

Four normal male subjects have been fed, under metabolic conditions, a low protein diet (LPD) 63 g protein/day; a high protein diet (HPD) 137 g/day; and the HPD with added wheat fibre (HPD + F) 27 g/day additional dietary fibre. The three diets were fed for three weeks each consecutively. Faecal weight, mean transit time, faecal marker concentration, and faecal ammonia using the dialysis bag technique of Wrong et al.¹ have been measured.

Results showed that in the third week of each diet period, the faecal weights in g/day averaged: LPD-80 (±SD 20); HPD 81 ± 23; HPD + F 210 ± 18. The mean transit times in hours were respectively 75 ± 23, 70 ± 11, and SD ± 70. The faecal marker concentrations in g/stool/unit of marker were 2.7 ± 0.7, 2.7 ± 0.8 and 7.0 ± 0.6. The faecal ammonia concentrations in mmol/kg were 14.8 ± 2.4, 30.3 ± 1.4 and 28.2 ± 1.4.

It was concluded that faecal ammonia concentration increased significantly with the high protein diet (t = 2.46 p < 0.025 but faecal weight and MTT did not change. Adding fibre to the HPD significantly increased faecal weight (t = 16.57 p < 0.001), shortened MTT (t = 7.89 p < 0.005), and diluted the inert marker (t = 16.89 p < 0.001) but did not alter ammonia concentration.

Reduction of animal protein intake may become more important in avoiding large bowel cancer than increasing fibre intake.

Reference


CLINICAL—SURGICAL

Closed-system plastic surgical isolator for sterility in abdominal surgery

S. N. JOFFE, W. O. THOMSON, J. MCGAVIGAN, AND P. C. TREXLER (University Departments of Surgery and Veterinary Gnotobiotics, Glasgow Royal Infirmary and Royal Veterinary College, London)

Wound sepsis is one of the major problems in abdominal surgery and has an incidence from 4.5% to 40%. In an attempt to reduce the exogenous pollution which exists in operating theatres a closed-system isolator—surgical isolator, has been designed, consisting of a portable and disposable plastic film barrier. This ‘surgical isolator’ is presterilised with gamma irradiation and inflated with sterile air through a bacterial filter. The surgical team operate on the patient from outside the surgical isolator through a series of sterile surgical gloves. Patients undergoing major elective upper gastro-intestinal operation were investigated in an open study.

Using the isolator, there was no increase in the operating time and visibility was unimpaired. Bacteriological examinations were made of the theatre, isolator, medical and nursing staff, and patient. Air sampling showed air from the isolator to be sterile, but there was a gross contamination of the operating theatre with mainly Gram-positive cocci, Staph. aureus (42%), and fungi, and all medical personnel had Staph. aureus on more than one occasion.

The wound edge, gloves, and fingers postoperatively were sterile after a conventional skin preparation. The wound infection rate in the clean and clean-contaminated control group of patients was 12.7% (n = 150). These were all major wound infections with the following organisms cultured: Staph. aureus (11), E. coli (six), Strep. faecalis (five), Cl. welchii (four), bacteroides (one), pseudomonas (one) and candida (one). Only one patient (5%) in whom the surgical isolator was used developed a minor wound infection (n = 20).

These results suggest that the surgical isolator has a place in abdominal operations and will be of value in the high risk, elderly cachectic patients, or leukaemic patients on cytotoxic therapy.

Reference


Prophylactic single dose cephalosporin therapy in major abdominal surgery

A. J. PAPACHRISTODOULOU AND S. J. KARRAN (Professorial Surgical Unit, Royal South Hants Hospital, University of Southampton) Prophylactic antibiotics in general surgery remain controversial.¹²³ We report the use of a wide-spectrum antibiotic of low toxicity given as a single dose.

Fifty-eight patients undergoing major abdominal surgery were given 2 g cephalozin IM with their premedication. Fifty-two matched patients acted as controls.

Blood and bile samples were cultured and assayed for antibiotic. Cultures were taken at operation from peritoneum, anastomoses, and wound edges and of the wound, sputum and urine at one, three, five, and seven days postoperatively.

One hour after induction average cephalozin levels were 69 mg/l in blood and 34 mg/l in bile. In the control group 6/30 patients undergoing biliary, 8/18 colorectal, and 3/10 gastric procedures developed wound sepsis requiring drainage of pus, compared with 0/30, 1/12, and 0/10 respectively in the cephalozin group.

Wound sepsis was reduced overall from 29.4% to 2% (χ² = 17.0, p < 0.001). Respiratory and urinary infections were reduced from 12/58 and 6/58 to 1/52 and 0/52 respectively (χ² = 17.0, p < 0.001).

No toxic reactions occurred with cephalozin. Discharge from hospital was delayed by an average of up to five days by sepsis. This technique appears to be simple, safe, and effective.

References


Pectin and postgastric surgery: prevention of postprandial hypoglycaemia

D. J. A. JENKINS, M. A. GASULL, A. R. LEEDS, G. METZ, J. B. DILAWARI, BRENDA SLAVIN, AND L. M. BLENDS (Medical Research Gastroenterology Unit and Chemical Pathology Department, Central Middlesex Hospital, London) Gel-forming types of dietary fibre to which class pectin belongs have recently been shown to modify carbohydrate absorption. Pectin is also a time-honoured constituent of anti-diarrhoeal medications—for example, Kaolin-pectate. As both abnormal carbohydrate absorption and diarrhoea may result after gastric surgery, we have looked at the effect of pectin on blood glucose,
Dismantling of the anastomosis for problems consequent upon truncal vagotomy and gastroenterostomy

M. J. McMahan, D. Johnston, and J. C. Goligher (University Department of Surgery, General Infirmary, Leeds) A drainage procedure is normally regarded as a necessary adjunct to truncal vagotomy in order to prevent postoperative gastric retention, but may be a major contributory factor to the side-effects which sometimes occur after this operation. It is unclear whether the drainage procedure is still necessary after the initial postoperative months have been passed.

Nine patients who suffered severe symptoms after truncal vagotomy and gastroenterostomy were submitted to dismantling of the gastroenterostomy. Radiology and endoscopy had shown no evidence of recurrent ulceration or pyloric stenosis. Patients were followed-up blindly in a gastric follow-up clinic for a mean of 15 months.

These were four female and five male patients whose average age was 41 years. The mean length of time between construction and dismantling of the gastroenterostomy was seven years.

The effect of the procedure was to reduce the incidence of pain from four cases to zero, bile vomiting from five to one, food vomiting from five to three, epigastric fullness from five to four, dumping from six to one, and severe diarrhoea from three to one. In many cases the severity of a symptom was reduced, even though it was not abolished. Preoperatively all nine patients were classified as Visick 4, but only one remained in this category after the procedure.

There was no evidence of gastric retention. It was felt that the improvement produced made an acceptable case for this very simple technical procedure.

Measurement of bile acids in the gastric juice as a test for bile reflux after gastric surgery

A. M. Hoare, M. R. B. Keighley, B. Starkey, J. Alexander-Williams, and Clifford Hawkins (Queen Elizabeth and General Hospitals, Birmingham) We have attempted to define the best method for assessing the presence and severity of bile reflux after gastric surgery. The study is divided into two sections.

1. Total bile acid concentrations have been measured in gastric aspirates, which were collected overnight, fasting, after a 'meal' and after pentagastrin. Seven patients with symptoms of dyspepsia and vomiting and seven without symptoms after partial gastrectomy were studied. Mean concentrations of bile acids were higher in samples from symptomatic patients, but the two groups overlapped except for fasting samples. Greatest separation was obtained when the amount of bile acids aspirated over half an hour from the fasting patient was measured. We have called this the fast rate of bile reflux (FBR) as expressed as mmol/h. The FBR was less than 100 mmol/h in all asymptomatic patients but greater in all the symptomatic. Measurement of FBR in each patient on three separate occasions showed that it was reproducible.

2. Measurement of FBR has been compared with reflux assessed radiologically (RR) and endoscopically (ER). Twenty asymptomatic patients have been studied; FBA was less than 100 mmol/h in all, but five had positive RR and 12 positive ER. Ten of 15 symptomatic patients had FBR greater than 100 mmol/h, 11 positive RR, and 13 positive ER.

Adaptation of the shortened gut: transfer of a humoral agent by cross-circulation

R. C. N. Williamson, T. W. Buckholtz, and R. A. Malt (Sponsored by Dr. Johnston) (Surgical Services, Massachusetts General Hospital and Department of Surgery, Harvard Medical School, Boston, Massachusetts 02114, USA) Potential involvement of humoral factors in the control of compensatory intestinal hyperplasia was tested 48 hours after jejunal transection or resection in individual rats and in rats maintained in free-running vascular parabiosis. In single animals, transection increased DNA content of mid small bowel mucosa by 31% (p < 0.001), but reduced DNA specific activity by 25% (p < 0.005), as compared with controls. Resection caused increments in RNA (38%), DNA (16%), and DNA specific activity (68%) over transection (p < 0.01). The response in the distal small bowel was similar but of lesser magnitude.

In parabiotic studies, one rat with transection (T) or resection (R) was cross-circulated with an intact partner (XT, XR); control pairs (C) had no abdominal operation. XT and XR showed increments of 59-128% over C in the ileal total radioactivity (p < 0.005) and specific activity of DNA (p < 0.05). Similar rises in specific activity in T and R were accompanied by raised RNA (48%) and DNA (27-43%) contents.

Jejunal transection causes transient distal hyperplasia, but the response to resection is more intense and prolonged. Both transection and resection transmit a humoral factor which stimulates cell proliferation in intact parabiosis. The transmitted response is weaker than the direct response. Both systemic and local factors must therefore be involved in adaptation of the shortened gut.

References


Internal sphincter a cause of symptoms in anal fissure

Y. Arabi, D. Gatehouse, J. Alexander-Williams, and M. R. B. Keighley (The General Hospital, Birmingham) Patients with anal fissure usually obtain remission of symptoms by procedures which reduce
the activity of the internal sphincter such as anal dilatation (MDA) or sphincterotomy (LSS).

To determine the importance of the internal sphincter in anal fissure, we measured anal pressure after proctoscopy in 30 consecutive patients with anal fissure and in 43 patients without anal disease (controls). Anal pressures were measured with a closed water filled balloon attached via a transducer to a recorder. Patients with anal fissure have entered a randomised prospective clinical trial to compare treatment by LSS (n = 24) and MDA (n = 26).

The mean maximum anal pressure in acute and chronic fissure was 170 cm H₂O and 120 H₂O respectively, which was significantly greater than in controls (85 cm H₂O). Anal pressures represent internal sphincter activity, as they were uninfluenced by scomine anaesthesia.

There was a 25% mean reduction in anal pressure one and three months after treatment. The mean maximum anal pressure one and three months after LSS was 93 cm H₂O and 80 cm H₂O respectively. After MDA there was a reduction to 87 cm H₂O and 82 cm H₂O at one and three months. The pressures recorded after both LSS and MDA did not differ from the controls and there was immediate relief of symptoms after both forms of treatment.

These results suggest that excessive internal sphincter activity is responsible for symptoms in acute and chronic anal fissure.

References


Denervation of the anal sphincter in idiopathic anorectal incontinence

A. G. PARKS AND M. SWASH (St. Mark's Hospital and the London Hospital) Idiopathic anorectal incontinence occurs predominantly in women. Surgical reconstruction of the pelvic floor muscles has proved an effective treatment. The operation is performed behind the anal canal; the viscus is lifted off the external anal sphincter and levator ani muscles, which are thereby exposed. Biopsies were taken of each group of muscles in 25 cases.

Twenty-five patients aged between 24 and 80 years (mean 58 years) were studied. The histological changes in the external anal sphincter, puborectalis, and levator ani muscles were investigated, as were similar specimens from five normal subjects, obtained at necropsy, as controls. The biopsies were examined in sections prepared from paraffin-embedded and fresh frozen muscle, using standard enzyme histochemical methods. Almost all of the 75 muscles examined from 25 patients were abnormal. The external sphincter was always the most grossly affected of the three muscles and the levator ani the least so. In most cases the external sphincter showed gross degenerative changes but in those with a lesser degree of abnormality there were groups of fibres, separated by bands of fibrous or adipose tissue, of uniform size and histochemical type. Fibres in the external sphincters were generally smaller than in the others. Fibres. A similar difference between the diameters of type I fibres and of type II fibres was found in the biopsies of the external sphincter muscles in the five control cases but in the latter the two fibre types were intermingled in a random mosaic pattern and fibre type grouping was absent. Sections of small nerve twigs supplying the external sphincter, obtained from three patients, were examined by electron microscopy and showed marked endoneurial fibrosis. These changes are suggested either of nerve entrapment or of stretch damage to the nerves during repeated defaecation straining.

Two new cells in the human pancreatic islets

J. M. POLAK, A. M. J. BUCHAN, C. M. TIMSON, S. B. BLOOM, AND A. G. E. PEARSE (Royal Postgraduate Medical School, Hammersmith Hospital, London) It is well known that the A, B, and D cells of the pancreatic islets produce glucagon, insulin, and somatostatin respectively. The application of more sophisticated immunocytochemical techniques, applied simultaneously at light and electron-microscopic levels, has revealed two additional cell types. These belong to a population of small-granulated cells, which can be subdivided into two groups. One has spherical granules, diameter 130-140 nm with a tightly fitting membrane, and is found mostly in fetal, neonatal, and young pancreata in the periphery of the islets and scattered throughout the exocrine pancreas. Immuno electron cytochemistry indicates that these cells contain the recently discovered gut hormone vasoactive intestinal peptide (VIP). The other small-granulated cells occur in equal number in fetus and adult, around
the periphery of the islets in the head of the pancreas and scattered singly in the exocrine area of the tail. This cell-type has slightly larger and more irregular granules (150–170 nm). Immunoelectronmicroscopy shows that it produces the newly discovered hormone "pancreatic polypeptide" (PP).

The actions and pathological involvements of VIP and PP are still being investigated; thus the precise identification of their cells of origin in the human pancreas could be extremely important in the interpretation of pancreatic pathology involving one or other of these two hormones.

Secretin: lack of response to oral feeding

F. A. O’CONNOR, K. D. BUCHANAN, W. HENRY, AND H. CALVERT (Departments of Medicine and Surgery, Queen’s University, Belfast, Northern Ireland) Secretin is generally accepted as the major stimulant for pancreatic bicarbonate secretion. Duodenal acidification (HCl 100 mmol/15 min) leads to raised peripheral venous levels of immunoreactive secretin (IRS). The physiological significance of this is doubtful, as the intraduodenal pH threshold for endogenous secretin release (4.5) is not achieved after protein feeding.

The purpose of this study was to measure peripheral venous IRS levels after separate meals of glucose (25 g), protein as mince beef (25 g) and as Bovril (20 g), fat (40 g) and mixed meal (CHO 90 g, protein 30 g, fat 40 g) in respectively six, 12, 14, and nine fasting normal human volunteers. IRS was measured using a sensitive (6 ng/l) and specific radioimmunoassay.

After glucose IRS levels were significantly lower (p < 0.05) than basal values throughout the test period (three hours) apart from the 15 minute sample. After protein in the form of mince no significant change in IRS levels occurred, but after Bovril significant suppression occurred at 40 and 50 minutes (p < 0.05). After fat no significant change in IRS levels occurred. After the mixed meal IRS levels were significantly lower than basal values (p < 0.05) throughout the test period.

These data show that feeding does not cause a rise in peripheral IRS levels and, indeed, after meals containing carbohydrate suppression occurs. Consequently, we conclude that secretin is unlikely to be the major stimulant for pancreatic bicarbonate secretion which occurs after feeding.

References

Pure pancreatic juice response to secretin in normal subjects and chronic pancreatitis

M. E. DENERY, S. TOUGH, J. TOWNSEND, AND P. B. COTTON (Gastrointestinal Unit and Courtauld Institute of Biochemistry, The Middlesex Hospital and Medical School, London) Using duodenoscopic cannulation of the main duct, pure pancreatic juice (PPJ) has been collected, and the response to secretin measured in 33 patients: 12 with no evidence of pancreatic disease, 11 with definite chronic pancreatitis (CP), and 10 with early pancreatitis (EP—recurrent acute pancreatitis or pain). Diazepam sedation was given to most patients, but no anticholinergic drugs. Bolus intravenous injections of G1H secretin (1, 4, and 70 CU) were given at 10 minute intervals, and PPJ collected minute by minute. Volume, mean bicarbonate and protein concentrations were measured for each 10 minute period, and outputs calculated.

In normal patients the respective mean 10 minute responses after 1, 4 and 70 CU were: total volume 16±3, 27±0, 41±4 ml; bicarbonate concentration 114, 127, 121 mmol/l; bicarbonate output 18, 34, 50 mmol/l. There was some overlap in individual patients, but after 1 and 70 CU (but not after 4 CU), mean volume and bicarbonate outputs of CP patients were significantly less than that of normal subjects. There was no significant difference in mean bicarbonate concentration in normal subjects and CP subjects after 1 CU (114 ± 12 mmol/l and 101 ± 16 respectively) or after 70 CU (121 ± 7 and 114 ± 19). The difference after 4 CU was statistically significant (127 ± 9 and 110 ± 12; p = < 0.01). All CP patients achieved peak PPJ concentrations in excess of 85 mmol/l. EP patients showed no significant difference in mean volume and bicarbonate responses compared with normal and CP patients.

PPJ protein concentrations correlate well with total enzymes. In all three groups of patients, protein concentration fell from high initial values as volumes increased. Mean concentrations after stimulation (around 2 g/l) did not differ significantly between the groups. Mean protein output was significantly less in CP patients compared with normal subjects only after the 70 CU stimulus.

These studies demonstrate considerable overlap in PPJ responses to secretin between normal subjects and those with pancreatitis. In pancreatitis the volume response may be impaired, with bicarbonate and protein concentrations maintained; there was no evidence of hypersecretion, or of protein hyperconcentration. Further analyses are being made.

Amylase thermolability: its application in the diagnosis of acute pancreatitis and pancreatic pseudocysts

M. J. BRODIE, L. A. DONALDSON, W. MCINTOSH, AND S. N. JOFFE (Department of Gastroenterology, Surgery, Biochemistry, Stobhill General Hospital and University Department of Surgery, Royal Infirmary, Glasgow) Salivary and pancreatic glands are the presumed sources for human serum amylase. It is controversial whether other tissues produce amylase and this in part has been due to difficulty in identifying the isoenzymes of amylase. A technique for identifying the isoenzyme of LDH and alkaline phosphatase—namely, thermolability—was used to investigate the amylase activity in pancreatic juice, saliva and serum. This confirmed the findings of Warshaw et al. that more than 99% of the amylase activity present in saliva (n = 6) and pancreatic juice (n = 8) was thermolabile (destroyed by heat) at 65°C. In contrast, the serum from normal patients (control) was only 44% thermolabile (SD ± 10%) the remainder being heat stable.

In acute pancreatitis (n = 20) or mumps (n = 12) more than 84% of the serum amylase was thermolabile in type, indicating that the hyperamylasaemia was due to an outpouring of the respective isoenzymes into the serum. On resolution of the pancreatitis or mumps the percentage of amylase which was thermolabile returned towards normal. In neonates (n = 14), who are known to have minimal exocrine pancreatic function, less than 25% of cord serum amylase was thermolabile.

In patients developing a pancreatic pseudocyst after acute pancreatitis (n = 9) when serum amylase may be normal, the thermolabile fraction remained raised.
(88% ± 6) similar to that in the acute phase of the disease.

This simple test for determining the isoenzymes of amylase by thermomobility may be of value in the diagnosis of acute pancreatitis and early recognition of pancreatic pseudocyst formation.

References


Peptide hormones as markers for gastrointestinal tumour pathology

J. M. Polak, A. Bishop, S. R. Bloom, and A. G. E. Pearse (Royal Postgraduate Medical School, Hammersmith Hospital, London) Many marker peptides, several of which are hormones, can be demonstrated in tumours and in the circulation. It is well established that VIP is a marker for tumours responsible for the Verner-Morrison syndrome1 and that PP (pancreatic polypeptide) is a specific marker for pancreatic apudomas2.

However, it is also known that apudomas can produce silent hormones. One of them, HCG, is a particularly important tumour marker as it normally circulates only in pregnant women. Its ectopic production therefore differs from that of an endogenous hormone—ACTH—which may be masked—for example, by the fall in normal production due to its feedback system. Detection of minute amounts of circulating HCG will thus indicate the presence of a tumour.

We have found specific HCG immuno-reactivity in blood and tumour tissue in six of 32 gastrointestinal (GI) apudomas and none in five nonapudomas (carcinomas) investigated. Five of the six positive cases were carcinoids (5 HT secreting) and one a glucagonoma.

Apudomas are potentially malignant so that, provided pregnancy or a trophoblastic tumour is excluded, HCG can be a very important marker for the early detection of a GI apudoma and for post-operative follow-up of a patient or monitoring during the course of drug treatment.

References


Comparison of double-contrast radiology, standard radiology, endoscopy, also of histology and cytology in the diagnosis of gastric cancer

J. F. Mackenzie, I. M. Rogers, B. Moule, J. A. Young, H. E. Hughes, F. D. Lee, R. I. Russell, and L. H. Blumgart (Gastroenterology Unit, Departments of Surgery, Radiology, Pathology and Cytology, Royal Infirmary, Glasgow) A prospective survey has been performed to compare endoscopy, radiology, histology, and cytology in the diagnosis of gastric cancer. Ninety patients entered the survey in whom a diagnosis of gastric cancer was suspected for one or more of the following reasons: clinical suspicion, gastric ulcer, radiological suspicion other than gastric ulcer, radiologically negative dyspepsia, and gastrointestinal bleeding. The ability of radiology and endoscopy to confirm or reject the diagnosis of cancer was compared by a graded scoring system. In 36 patients who had double contrast radiology, this technique was 80% accurate, compared with 83% for endoscopy in the same patients. Fifty patients had standard radiology and this was 68% accurate compared with 86% accuracy for endoscopy in the same patients.

Cytology and histology were assessed as being either positive or negative. Out of 33 cases of proven gastric cancer, histology missed six cases, two of them also being missed by cytology (probably due to sampling error). Histology gave two false positives but there was no false positive cytology.

We conclude that the double contrast technique significantly improves the accuracy of radiology, and that cytology improves the diagnostic accuracy of endoscopy in gastric cancer.

ERCP and fine needle percutaneous transhepatic cholangiography in the diagnosis of biliary tract disease

I. S. Benjamin, M. E. M. Allison, B. Moule, and L. H. Blumgart (University Department of Surgery and Department of Radiology, Royal Infirmary, Glasgow) Prompt accurate preoperative diagnosis is desirable in obstructive jaundice and both percutaneous transhepatic cholangiography (PTC)3 and ERCP4 are of proven value in management. We have studied the early use of PTC in the investigation of suspected obstructive jaundice and other complex biliary surgical problems.

PTC was performed in 35 patients including 19 with jaundice. The biliary tract was successfully outlined in all with dilated intrahepatic ducts (17 cases). Non-dilated intrahepatic ducts were shown in 14 cases. In the remaining four 'unsuscessful' cases a non-dilated biliary tract was subsequently shown (ERCP, three patients; necropsy, one patient). ERCP was also used in two patients with dilated ducts to define the limits of an obstructing lesion. A combination of PTC and ERCP yielded a radiological diagnosis in all but one case. Liver biopsy was reserved for cases shown to have non-surgical jaundice.

In three patients, PTC was followed by pyrexia, and one of these died of septic shock. In no case was immediate surgical intervention required. In 19 patients who underwent subsequent surgery, no evidence of significant biliary collection or haemorrhage was found.

An approach to investigation of jaundice is proposed involving use of PTC within 48 hours of admission and selective use of ERCP and liver biopsy.

References


Transjugular liver biopsy

I. T. Gilmore, R. D. Bradley, and R. P. H. Thompson (Gastrointestinal Laboratory, Rayne Institute, and Department of Clinical Physiology, St. Thomas' Hospital, London) Percutaneous needle biopsy of the liver is a safe and reliable method of obtaining liver tissue for histological examination. However, when there is an increased bleeding tendency the procedure is more hazardous, and, as impaired coagulation or thrombocytopenia is common in patients with severe liver disease, such patients are then often managed without obtaining a biopsy specimen. This risk of bleeding into the peritoneal cavity can be eliminated by taking the biopsy
specimen through a hepatic vein, entering from the right internal jugular vein, an approach described in two recent studies. We report here our experience of this still unorthodox approach to liver biopsy.

The procedure was performed in the Intensive Therapy Unit, and an x-ray image intensifier and electrocardiogram monitor used. Sixteen patients were studied, and adequate specimens for histological diagnosis were obtained in 10, while in five others sufficient tissue was obtained to confirm a clinical diagnosis of cirrhosis. There were no significant complications, and in 11 patients hepatic venography and/or hepatic vein wedged pressure measurements were simultaneously performed. While it should be attempted only by those experienced in catheter techniques and cannulation of the internal jugular vein, it is suggested that transjugular liver biopsy is valuable when routine percutaneous biopsy is hazardous or when pressure measurements are also required.

References


Computer display and analysis of liver gamma camera scans

G. S. RAI, J. W. HAGGOTH, J. FENWICK, AND OLIVER JAMES (Departments of Medical Physics and Medicine (Geriatrics), University of Newcastle upon Tyne) Computer display and analysis of liver scan images has recently become available. The present study was undertaken to assess the possible clinical value of this costly addition to scanning equipment.

The X and Y pulses of a gamma camera used for routine liver scanning were collected on a Nova 2 computer on a 32 k matrix and stored on magnetic tape. The information was subsequently transferred to Polaroid film. The data was displayed on eight isocount levels (between six and 100) to assess which presentations displayed information most clearly. An analysis of count rates obtained over the liver was also carried out and represented as a series of 'Kupffer cell function' curves.

Sixty-two patients in whom the clinical diagnosis was confirmed by liver biopsy, laparotomy, or necropsy were studied. Scans and computer display images were analysed by two independent observers.

Thirteen scans were reported as showing one or more definite SOLs. In one case a normal liver was subsequently found. Seventeen computer displays showed one or more definite SOLs. All 17 were correct. The 'Kupffer cell function' curves gave graphic evidence of the subjective reports regarding focal lesions. Comparison between liver and spleen count rates were helpful in the diagnosis of cirrhosis. Count rate levels 6, 10, and 25, when examined together, were found to be most helpful.

It is concluded that computer display may well improve ability to detect SOLs in the liver.

Value of whole body computerised axial tomography in the diagnosis of liver disease

A. I. MORRIS, R. A. FAWCITT, M. N. MARSH, AND I. ISHERWOOD (Department of Medicine, Hope Hospital (University of Manchester School of Medicine), Salford, and Department of Diagnostic Radiology, University of Manchester) The value of whole body computerised axial tomography (CAT) was assessed and compared with conventional techniques in the diagnosis of 54 patients with various liver diseases. Diagnostically useful information was obtained in 38.

In 10 of 11 patients with total extrahepatic obstructive jaundice, dilated intrahepatic ducts were demonstrated. The primary pathology was demonstrated as carcinoma of the pancreas (5/5), chronic pancreatitis (1/1) and radiolucent gall stones (3/5). In two patients with intrahepatic cholestasis the duct system was normal.

Although the CAT was abnormal in 21 of 22 patients with cirrhosis, the abnormalities were not always diagnostic. In two patients with untreated haemachromatosis a striking increase in hepatic density was noted.

Hepatic tumours were detected in four patients with secondary deposits but not in two patients with large primary hepatic carcinomata.

Hepatic density was abnormally reduced in three patients with fatty infiltration of the liver but in seven other patients with a variety of parenchymal liver diseases, including hepatitis, no abnormalities were detected.

We conclude that this non-invasive technique is of considerable value in the diagnosis of obstructive jaundice. It can differentiate extra from intrahepatic causes and can detect pancreatic carcinoma and common duct stones. It is of less value in the diagnosis of hepatic infiltrations with iron or fat and provides helpful information in cirrhosis and metastatic deposits. It is of less value in the diagnosis of non-fibrotic parenchymal liver diseases.

Diagnosis of extrahepatic portal obstruction by greyscale ultrasound

L. J. WEBB, L. A. BERGER, AND S. SHERLOCK (Department of Medicine, Royal Free Hospital, Hampstead, London) A greyscale ultrasound examination of the portal vein was made in 20 patients with extrahepatic portal obstruction, 17 patients with liver disease, and 20 age-matched controls. All the extrahepatic obstructions had been confirmed by splenic venography or superior mesenteric angiography. All examinations were performed without reference to the diagnosis.

A normal portal vein is easily seen by greyscale ultrasound, whereas an incompletely thrombosed or recanalising vein is seen as irregular and reduced in diameter. A thrombosed vein is not detected.

An obstruction of the extrahepatic portal system was correctly diagnosed in all 20 cases. Two of these cases had a localised splenic vein thrombosis. This was correctly diagnosed in one, and the other was diagnosed as a splenic and portal vein thrombosis. In summary, the presence or absence of a thrombosed portal vein was correctly assessed in 19 of the 20 extrahepatic portal obstructions, all the 17 patients with liver disease, and all the 20 controls.

We conclude that the greyscale ultrasonography is a rapid, reliable and non-invasive method of diagnosing obstruction of the extrahepatic portal system and is also of value in following the natural history of the thrombosis.

Comparison of hepatic scintiscanning and greyscale ultrasonography in the diagnosis of cholestatic jaundice

M. J. G. FARTHING, E. P. WRAIGHT, J. TUDOR, AND J. O. HUNTER (Departments of Medical Gastroenterology, Nuclear Medicine and Radiology, Addenbrooke's Hospital, Cambridge) The demonstration of a dilated biliary system is of great value in differentiating surgical causes of

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cholestatic jaundice from those due to hepatocellular disease. A comparison has been made of the diagnostic accuracy of hepatic scintiscanning and greyscale ultrasound in the detection of dilated bile ducts.

One hundred and twenty-five patients with cholestatic jaundice in whom the diagnosis was subsequently confirmed by laparotomy or liver biopsy were studied using 99mTc-sulphur colloid and 131I-Rose Bengal scintiscans, greyscale ultrasonography, or both. Eighty-three per cent of cases with surgical obstruction were correctly identified by scintiscans, and obstruction was excluded in 87% of those with hepatocellular disease. Obstruction caused by carcinoma of the pancreas or bile ducts was detected in 31 of 33 cases, but in only four of 11 cases due to gallstones.

Ultrasonography correctly excluded dilatation of bile ducts in all cases with hepatocellular disease, but in 24% of those subsequently shown to have an extrahepatic obstruction, dilated bile ducts were not detected. Metastases were better demonstrated by scintiscans, but cysts by ultrasonography. Difficulties were encountered in the diagnosis hepatoma by ultrasonography and of biliary atresia by both techniques.

Evaluation of ultrasonic scanning in pancreatic disease

J. G. B. RUSSELL, A. G. VALLON, JOAN M. BRAGANZA, H. B. TORRANCE, AND H. T. HOWAT (Department of Radiology and University Department of Gastroenterology, Manchester Royal Infirmary) The usefulness of ultrasonic scanning of the pancreas in the management of 50 patients with exocrine pancreatic disease has been evaluated. Patients were scanned using a Kretz 4100 Ultrasonic Scanner with biphasic presentation, and the results related both to clinical status and function tests.

In acute pancreatitis ultrasonic scanning established the presence, location, size, and progression of pseudocysts. Equally it proved a useful guide to treatment in acute necrosis, as serial scans gave early evidence not only of pseudocysts but also of complicating abscess and ascites. Ultrasonic scanning is particularly useful in the detection of dilated bile ducts, which can be confirmed by using a Kretz 4100 Ultrasonic Scanner with biphasic presentation.

In chronic pancreatitis in remission, ultrasonic examination of the pancreas was normal except that duct calculi produced randomly distributed punctate echoes. Within eight weeks of a relapse the pancreas was minimally enlarged, the main pancreatic duct was occasionally prominent but no pseudocysts were noted. In all five patients who suffered from relentless pain the head of the pancreas was swollen and contained cystic areas or emitted abnormal echoes. In four of these the pancreatic duct was prominent; in three major pancreatic surgery was indicated.

Enlargement due to cancer of the pancreas could not be differentiated from the enlargement of pancreatitis until the tumour was sufficiently large to indent contiguous structures. However, it could be readily distinguished from cystic enlargement by its indistinct outline and differing sonic reflectivity.

Preliminary assessment of computerised axial tomography in pancreatic disease

R. A. FAWCITT, I. ISHERWOOD, JOAN M. BRAGANZA, AND H. T. HOWAT (Departments of Diagnostic Radiology and Gastroenterology, The University of Manchester) Computerised axial tomography (CT scanning), a recently developed non-invasive radiological technique, can define intra-abdominal viscera particularly those surrounded by fat. We have used the EMI CT 3000 whole body scanner to study the pancreas and retroperitoneal structures in 40 patients with established pancreatic disease and correlated the results with the clinical findings.

The pancreas was adequately visualised in 90% of all patients. In chronic pancreatitis a feature was the patchy heterogeneous density of the gland which mirrored the characteristic pathology of patchy acinar destruction and fibrosis. Duct calculi associated with duct dilatation were observed in a third of patients. The outline of the pancreas was smooth or crenated and the gland remained mobile. The pancreas was uniformly enlarged by a retention pseudocyst in one patient, and reduced in size in patients with painless chronic pancreatitis. In three patients with constant epigastric pain CT scans demonstrated enlargement of the head of the pancreas in which calcified or cystic areas were identified. After acute pancreatitis the appearances of CT scans varied with the extent to which recovery had taken place. When resolution was complete the pancreas appeared normal. Incomplete resolution was associated with a swollen irregular pancreas, diffusely mottled by low density areas of presumed necrosis. The extent and precise location of pseudocysts in relation to adjacent viscera could be accurately delineated.

Role of VIP in diarrhoea

J. M. MODLIN, S. R. BLOOM, AND S. J. MITCHELL (Departments of Surgery and Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London) VIP (vasoactive intestinal peptide) has been found in many human tissues and may be the cause of the Verner-Morrison syndrome of watery diarrhoea, hypokalaemia, and achlorhydria (WDHA). These patients have diagnostically high levels of VIP in both tumour and plasma, but the role of VIP in diarrhoea production is not fully established.

Femoral arterial and jugular venous catheters were inserted in five pigs under general anaesthesia. Three days later pure natural porcine VIP was infused continuously at 5-10 pmol/kg/min for 12 hours into the ambulant and unseeded pig. Thirty minute arterial samples were analysed for VIP, sodium, potassium, glucose, and calcium. Plasma levels of VIP rose to between 90-120 pmol/l. Within eight hours the pigs developed copious watery diarrhoea (up to 25 ml/kg) with persistent cutaneous flushing. Plasma potassium levels fell significantly, but the other blood values did not alter. Bowel habit returned to normal immediately after stopping the VIP infusion. Thus VIP can cause watery diarrhoea.

This diarrhoea developed at blood levels of VIP similar to those we have found in patients with the Verner-Morrison syndrome, suggesting a causal role for this polypeptide in the pathogenesis of the clinical features of the human disease. These experimental studies provide a rational basis for the measurement of plasma VIP levels in patients with the features of the WDHA syndrome. The Verner-Morrison syndrome is frequently fatal and the VIP producing tumour often malignant; early diagnosis may be life saving.
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Chronic acid in gallstone patients: effect of low cholesterol and of high plant sterol diets

D. P. MAUDGAL, R. BIRD, V. O. ENYOBI, W. S. BLACKWOOD, AND T. C. NORTHFIELD (Department of Medicine, St. George's Hospital Medical School, and Norman Tanner Gastroenterology Unit, St. James' Hospital, London) Chronic acid therapy reduces biliary cholesterol secretion, probably by inhibiting endogenous hepatic cholesterol synthesis. We hypothesise that residual cholesterol secretion is due to absorption of exogenous dietary cholesterol, and that therefore (1) reduced intake of dietary cholesterol (or 2) reduced absorption due to addition of plant sterols should potentiate the effect of chronic acid. Cholesterol saturation index (SI) of fasting gallbladder bile of 14 gallstone patients receiving a bedtime dose of chenic acid (15 mg/kg) was 0.88 ± 0.04 (mean ± SEM) on an unrestricted diet, and fell to 0.75 ± 0.05 on 100 mg cholesterol daily (P < 0.005). To exclude an order effect, seven of these patients (SI 0.83 ± 0.04 on unrestricted diet) were allocated to four different monthly dietary regimes in random order: (1) 630 mg cholesterol daily (SI 0.75 ± 0.05); (2) 630 mg cholesterol + 3G β-sitosterol (SI 0.79 ± 0.05); (3) 100 mg cholesterol (SI 0.67 ± 0.05); (4) 100 mg cholesterol + 3G β-sitosterol (SI 0.77 ± 0.05). SI on 100 mg cholesterol was significantly lower than on an unrestricted diet (P < 0.001) and on the other three regimes (P < 0.05). Before chenic acid, SI was 1.23 ± 0.07, and this was unaffected by a low cholesterol diet alone (SI 1.19 ± 0.08). We conclude that a low cholesterol diet, but not a high plant sterol diet, potentiates the effect of chenic acid.

References


Effect of prolonged chenodeoxycholic acid feeding on bile in patients with and without gallstones

M. C. BATESON, P. E. ROSS, J. MURISON, AND L. A. D. BOUCHIER (Department of Medicine, Ninewells Hospital and Medical School, Dundee) Nineteen patients who received chenodeoxycholic acid 750 mg/day for six months had duodenal bile aspirated before and after treatment. In five patients with hypertriglyceridaemia but no gallstones cholesterol saturation was reversed in every case, the mean cholesterol saturation index (SI ± Standard Deviation) changing from 1.38 ± 0.31 to 0.68 ± 0.06 (P < 0.005). In 14 patients with gallstones there was also an improvement in bile cholesterol content, but this was not sufficient to produce mean unsaturation, SI changing from 1.55 ± 0.52 to 1.13 ± 0.43 (P < 0.05). Only seven out of 14 gallstone patients achieved cholesterol unsaturation.

In four patients with hypertriglyceridaemia and gallstones, mean unsaturation was produced and the SI changed from 1.70 ± 0.45 to 0.86 ± 0.47 (P < 0.05).

When all nine patients with hypertriglyceridaemia were grouped, the mean SI fell from 1.52 ± 0.40 to 0.76 ± 0.30 after therapy (P < 0.001). In contrast, the 10 patients without hypertriglyceridaemia showed no significant fall in SI, which was 1.50 ± 0.54 before and 1.24 ± 0.40 after therapy.

The ability of chenodeoxycholic acid feeding to improve bile saturation with cholesterol correlated with the presence of hypertriglyceridaemia whether or not gallstones were present. It did not correlate with gallstone dissolution or body weight.

Management of bile salt diarrhoea with aluminium hydroxide

A. SALI, G. WATKINSON, AND C. MACKAY (Departments of Surgery and Gastroenterology, Western Infirmary, Glasgow) The management of bile salt diarrhoea remains a problem. Bile salt binding agents such as cholestyramine are useful but have disadvantages. Aluminium hydroxide has bile salt binding properties in vitro and we have recently shown this in vivo.

Eight patients with severe diarrhoea of at least four years' duration were studied before and during treatment with aluminium hydroxide. Six of these patients had extensive ileal Crohn's disease and the other two had diarrhoea after truncal vagotomy.

Bowel habit and faecal bile salts were studied before and during treatment. The faecal bile salt outputs were significantly raised before treatment compared with controls (P < 0.01). Bowel habit changed from a mean of eight bowel actions per day before treatment to a mean of two bowel actions per day during treatment. Treatment has been continued for at least two months.

Bile salt induced diarrhoea can be alleviated with treatment with aluminium hydroxide. This finding can be explained by the bile salt binding property of aluminium hydroxide.

References


Experience with cimetidine in the treatment of gastric ulceration

P. J. CICLITIRA, R. J. MACHELL, M. J. FARTHING, A. P. DICK, AND J. O. HUNTER (Department of Medical Gastroenterology, Addenbrooke's Hospital, Cambridge) The H2-antagonist cimetidine is now known to be of great importance in the management of duodenal ulcer. As little is known of its value in gastric ulcer, we have started a double-blind trial of cimetidine in this condition.

Patients are admitted into the trial within four days of fibreoptic gastroscopy. Every ulcer is biopsied to exclude malignancy. The patients are divided into two groups. The first receive cimetidine 200 mg three times daily with 400 mg at night. The second group receive identical tablets containing lactose. Both are supplied with antacid tablets and diary cards on which to document symptoms and number of tablets taken. After four weeks the gastroscopy is repeated.

To date 35 patients have completed the study. The ulcer has healed in eight out of 16 patients receiving placebo, but in 15 out of 19 given cimetidine. Contrary to general experience with duodenal ulcer, symptoms were not invariably relieved by...
cimetidine even when the ulcer was shown to have healed.

While the difference between the two groups does not yet reach significance, the high rate of ulcer healing in patients receiving cimetidine suggests that this drug may prove to be of value in the treatment of gastric ulcer.

Reference


Double-blind trial comparing cimetidine with carbenoxolone in the treatment of benign gastric ulcer

R. H. TAYLOR, J. M. LAIDLOW, R. G. CHAPMAN, D. G. COLIN-JONES, P. L. GOLDING, R. H. HUNT, S. H. VINCENT, G. J. MILTON-THOMPSON, AND J. J. MISIEWICZ (Central Middlesex Hospital, London; Queen Alexandra Hospital, Portsmouth and Royal Naval Hospital, Haslar) Increase in the healing rate of gastric ulcer (GU) by carbenoxolone sodium is generally accepted. In a pilot trial1 cimetidine was associated with GU healing. These treatments are compared in a controlled trial.

Thirty-two outpatients with endoscopically proven benign gastric ulcers were randomly allocated to two groups. One group received a six week course of cimetidine 200 mg qds, the other had carbenoxolone 100 mg tds for one week followed by carbenoxolone 50 mg tds for five weeks. Both groups received antacid tablets ad libitum. The patients recorded symptoms on a diary card and were examined weekly when blood and urine specimens were taken. The ulcer was reassessed endoscopically after six weeks and scored healed or unhealed. The endoscopist was unaware of the patient’s treatment and not involved in his clinical care.

Of the 32 patients in the trial one on carbenoxolone defaulted. The GU healed in 11 of 15 patients treated with cimetidine and in eight of 16 on carbenoxolone. \( \chi^2 \) (Yates) = 0-929; NS. Symptomatic response was similar in the two groups. Seven patients on carbenoxolone developed hypokalaemia and nine had subjective side-effects compared with five on cimetidine. Side-effects were more severe and often multiple on carbenoxolone.

These results suggest that H2 histamine receptor blockade is at least as effective as carbenoxolone in the treatment of GU but produces fewer side-effects.

Reference


Prevention of relapse of duodenal ulcer by bedtime cimetidine2 a double-blind clinical trial

W. S. BLACKWOOD, D. P. MAUDGAL, AND T. C. NORTHELD (Department of Medicine, St. George’s Hospital Medical School, and Norman Tanner Gastroenterology Unit, St. James’ Hospital, London) Cimetidine promotes healing of duodenal ulcer.3 The purpose of the current study is to determine whether subsequent relapse can be prevented by long-term maintenance therapy.

A single dose of 800 mg of cimetidine, given at bedtime, was used because this regimen supresses nocturnal acid secretion4, and bedtime medication increases patient compliance. Before entering the maintenance trial, patients were treated with cimetidine 400 mg or placebo four times daily. Thirty-one patients, with endoscopically-confirmed healed ulcers, then entered a double-blind maintenance trial of either 800 mg cimetidine or placebo taken at bedtime. Clinic visits were monthly and symptoms and antacid consumption were recorded. Endoscopy was repeated routinely at six weeks, three months, and then at three monthly intervals; or when definite symptomatic relapse occurred.

At six weeks, one of 13 cimetidine and nine of 14 placebo patients had endoscopic relapse, with recurrence of active duodenal ulceration (p < 0-01). At three months, two of nine cimetidine and eight of nine placebo patients had relapsed (p < 0-02). At six months, two of seven cimetidine and all seven placebo patients had relapsed (p < 0-05).

No patient was withdrawn as a result of side-effects or of changes in routine haematological and biochemical screening.

The results suggest that a single bedtime dose of cimetidine will prove to be a safe and effective long-term prophylaxis against duodenal ulcer relapse.

References


Maintenance cimetidine in the control of duodenal ulcer symptoms

G. R. GRAY, I. S. SMITH, G. GILLESPIE, AND I. MACKENZIE (Division of Surgery, Victoria Infirmary, Glasgow) The ability of oral cimetidine (1 g/day) to relieve symptoms and heal ulcers in a group of patients with severe duodenal ulcer diathesis referred for surgery has already been reported.

The efficacy of a single bedtime dose of oral cimetidine (400 mg) in maintaining such patients’ remission has now been assessed by a double-blind controlled trial. Sixty patients whose ulcers had been observed to heal endoscopically on cimetidine (1 g/day), were randomised into the study. Follow-up clinical and laboratory assessments were made monthly with endoscopy only if symptoms recurred. Mean follow-up period is 19-5 weeks (±11-5 SD) with 45 patients being studied beyond 13 weeks. Three patients were lost to follow-up. Twenty-one of the remaining 57 patients have had symptomatic relapse with endoscopic ulcers. Seventeen of these had received placebo, whereas four had received cimetidine (p < 0-001).

Mean time from entry to relapse of symptoms was 7-2 weeks (±4-8 SD). Thirty-six patients continue in the trial; 23 cimetidine at 17-3 weeks (±12-4 SD), 13 placebo at 19-8 weeks (±14-4 SD) p NS.

Cimetidine 400 mg taken at night appears to be effective in maintaining the remission of duodenal ulcer symptoms obtained by our higher regime. Throughout the trial no patient has shown significant clinical or consistent laboratory abnormalities.

Reference


Effect of one year’s treatment with cimetidine on pariatal cell mass in duodenal ulcer patients

R. W. SPENCE, L. R. CELESTIN, AND D. A. MCCORMICK (Department of Gastro-
enterology, Frenchay Hospital, Bristol)

We have previously reported a 24\% reduction in histamine-stimulated PAO in duodenal ulcer patients after three months' treatment with cimetidine 1-6 g daily. Currently eight patients (one-third of this group) have completed one year's continuous treatment at this dosage and have undergone single repeat histamine infusion tests 56 hours after the last dose of cimetidine. In order to establish whether or not the fall in PAO observed at three months was due to a decrease in parietal cell mass or to a reduction in sensitivity of an unaltered mass we employed increasing doses of histamine 25, 50, and 100 \( \mu g/kg/h \) by means of a variable speed infusion pump. Gastric secretion was collected in 10 minute aliquots until steady state secretion was reached at each infusion rate.

BAO was measured from the basal secretion collected over one hour and PAO, peak volume, and \( H^+ \) concentration were calculated as means from the two aliquots yielding the highest consecutive output figures. Results before treatment and after three months and one year were compared by means of a paired \( t \) test and \( p \) values are shown where differences were significant. Pretreatment, three months, and one year means \( \pm SDs \) were respectively as follows: BAOs: 8-8 \( \pm \) 5-1, 4-5 \( \pm \) 2-4, 6-1 \( \pm \) 5-5 mmol/h; PAOs: 44-0 \( \pm \) 7-4, 37-2 \( \pm \) 12-3 (\( p < 0-05 \)), 37-8 \( \pm \) 13-9 mmol/h; peak volumes 86 \( \pm \) 12, 89 \( \pm \) 25, 79 \( \pm \) 20 ml; peak \( H^+ \) concentrations 127-1 \( \pm \) 6-3, 107-5 \( \pm \) 13-5 (\( p < 0-01 \)), 116-1 \( \pm \) 20-8 mmol/l. Mean PAOs at one year at histamine infusion rates 25, 50, 100 \( \mu g/kg/h \) were respectively: 33-4 \( \pm \) 9-9, 41-9 \( \pm \) 10-7, 39-2 \( \pm \) 18-8 mmol/h.

The results from this small number of patients need to be interpreted cautiously, but they suggest that no further reduction in acid output was achieved by prolonging treatment beyond three months. PAO was not increased by increasing the histamine infusion rate above 50 \( \mu g/kg/h \) and this implies that the reduction in PAO observed at one year was due to a reduction in actual parietal cell mass.

Reference


Cimetidine in the treatment of gastrointestinal bleeding

A. M. HOARE, J. Y. KANG, P. W. DYKES, C. F. HAWKINS, AND JANE MILLS (The General and Queen Elizabeth Hospitals, Birmingham)

A double-blind controlled study is reported on relating to the possible effects of cimetidine on the prevention of rebleeding in patients admitted to hospital with acute gastrointestinal haemorrhage. Forty-two patients have been entered into the trial, the majority suffering from peptic ulceration; patients with cancer, liver disease, or renal failure have been excluded, as have those with only minimal amounts of haemorrhage. Patients have been stratified according to age and severity of bleeding and the diagnosis established by endoscopy within 24 hours of admission. Rebleeding has not occurred in the presence solely of erosions or inflammation but only in association with definite ulceration. It was three times commoner in the placebo treated patients, and it seems probable that this difference is largely due to an effect on gastric rather than duodenal ulceration. It is also evident in older and more severely ill patients, and to date, the only two deaths that have occurred in the control group. No difference is currently seen in the time at which rebleeding occurred.

Hepatitis B and its subtypes in a study of viral hepatitis in West London

ISABEL M. SANDERSON, L. J. FARROW, S. G. LAMB, R. L. LINDON, N. F. COGHILL, R. E. CLIFFORD, A. J. ZUCKERMAN, AND J. S. STEWART (West Middlesex and South Middlesex Hospitals; Ealing, Hammersmith and Hounslow Area Health Authority; and London School of Hygiene and Tropical Medicine) During a three year total population survey in three West London boroughs 455 patients with viral hepatitis were seen and tested for the hepatitis B antigen (HBsAg) which was found in 93 (20\%). None of the children (under 15 years) was HBsAg positive.

Fifty-six per cent of the patients who had had a diagnostic venulecture in the previous six months were HBsAg positive, as were 15 of the 19 drug addicts. The finding of HBsAg was not associated with previous therapeutic interventions such as inoculations or local dental anaesthetics. Among patients with hepatitis B, the male to female ratio was 2:1 in those aged under 30 years and 5:1 in those aged 30 years and over. Significantly more of these men were single than in the local community or among HBsAg negative men. Many of the HBsAg positive single men were either known to be or strongly suspected of being homosexual.

Seventy-six of the HBsAg positive patients were tested for \( \text{ad/ay} \) subtype. The eight HBsAg positive drug addicts who were tested were found to have the \( \text{ay} \) subtype. All 11 HBsAg positive men who admitted to being homosexual and all but one of the 17 who were strongly suspected of being homosexual were of the \( \text{ad} \) subtype.

Optimal dose of sulphasalazine for the maintenance treatment of ulcerative colitis: interim results of a controlled therapeutic trial

A. K. AZAD KHAN, D. T. HOWES, J. PIRIS, AND S. C. TRUELOVE (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, and Gibson Laboratories, Radcliffe Infirmary, Oxford) Sulphasalazine in a dose of 2 g daily has been shown to reduce the relapse rate of ulcerative colitis sharply and this beneficial effect persists with long-term maintenance treatment. A further question is whether the dose of 2 g daily is the optimal for long-term maintenance therapy. On the one hand, some workers have suggested that a larger dose is likely to be more efficacious, while others have suggested a dose of 1-5 g daily to minimise the haematological side-effects of treatment.

In the present study, patients being maintained on sulphasalazine volunteered to take part in a study which implied that the dose would be 1, 2, or 4 g daily for a trial period of six months. In the 128 patients who have completed the study, the relapse rate was significantly higher in those receiving the 1 g daily dose. The relapse rate was similar in the patients receiving 2 g and those receiving 4 g. Side-effects in the form of nausea, headache, and malaise were common with the 4 g daily dose. Haematological side-effects were negligible at all three dosage levels.

We conclude that a daily dose of 1 g sulphasalazine is inadequate but that a daily dose of 2 g is suitable for general use as long-term maintenance treatment.

References


Laxatives and gastric mucosal damage—the danger of diocyl sodium sulphosuccinate

K. M. COCHRAN, L. NELSON, R. I. RUSSELL, AND E. GODDING (Gastroenterology Unit, Royal Infirmary, Glasgow) Diocyl sodium sulphosuccinate (DSS), an anionic detergent, is the active ingredient of a widely used series of laxatives, acting on the colon in a manner similar to dihydroxy bile acids1. Previous work has shown that bile acids and acetylsalicylic acid (ASA), in the stomach break the gastric mucosal barrier (GMB), and may be associated with gastric haemorrhage. We have studied the effect of DSS on the GMB in man and compared the effect with that after ASA, using the technique of transmucosal electrical potential difference measurement (EPD).

After oral administration of DSS the transmucosal EPD was significantly reduced (from -30.7 mV to -21.2 mV after DSS 40 mg, p < 0.025; from -37.0 mV to -18.0 mV after DSS 80 mg, p < 0.05; and from -32.0 mV to -16.0 mV after DSS 200 mg, p < 0.001). A significant reduction of the transmucosal EPD was observed with ASA in all doses used: (150 mg: 300 mg; 600 mg).

These results demonstrate that DSS significantly breaks the gastric mucosal barrier to a degree similar to ASA. The effect of DSS in breaking the gastric mucosal barrier may be of clinical importance in relation to ingestion of DSS alone or in combination with other agents known to damage the gastric mucosa.

References


Evaluation of metronidazole in the management of Crohn’s disease

ROBERT ALLAN and W. T. COOKE (Nutritional and Intestinal Unit, The General Hospital, Birmingham) We are evaluating metronidazole in two studies. The first is a double-blind controlled study with strict histological and radiological criteria for entry. All patients were symptomatic with at least three abnormal indices (low serum albumin, raised seromucoids, weight loss or anaemia). They were allocated at random to receive either metronidazole 20 mg per kg per day or placebo prepared in identical capsules for six months with clinical and laboratory evaluation at monthly intervals. Eleven patients have completed the study so far, one patient in each group has improved, and the remainder are unchanged or worse. Side-effects include headache, paraesthesiae, and auditory hallucinations.

The second study now in progress involves twelve patients with symptomatic Crohn’s disease who have not taken metronidazole. The criteria for the controlled trial have been evaluated in a second study. The principal indications for treatment have been patients with diarrhoea (12), flatulence (two), enterocutaneous fistulae (three), severe perianal disease (two), and longstanding erythema nodosum (one). Diarrhoea related to colonic lesions has improved in two patients with transient benefit in three others. Perianal lesions were strikingly improved. The erythema nodosum resolved rapidly and has not returned.

The controlled study has not so far confirmed the reported benefit of metronidazole in the treatment of Crohn’s disease3. The uncontrolled study suggests that it may be of value in symptomatic control if diarrhoea due to colonic lesions and in the management of perianal disease, probably because of its antibacterial activity.

Reference


Salicylate ingestion in patients attending a gastrointestinal clinic

J. A. H. FORREST, J. PARK, AND R. C. HEADING (Gastrointestinal and Liver Service and Department of Therapeutics, The Royal Infirmary, Edinburgh) Over an eight month period, all patients attending a gastrointestinal clinic were asked to provide a urine sample. Altogether 1,003 urines were obtained and examined for salicylate by the method of Trinder4. After control studies, concentrations greater than 50 mg/l were considered to be positive. Patients taking sulphasalazine gave positive results and 118 patients on this drug were excluded from further analysis.

One hundred and forty-three urine samples (16.2%) contained salicylate but only 33 patients (3.7%) admitted salicylate ingestion in the previous 24 hours. There was no difference in positive rates between new and follow-up patients but the rate was greater in females (18.7%) than males (13.5%) (p < 0.05). In males the highest positive rate was in those aged over 60 years (27.1%); in females in the range 30-44 years (25.9%). Compared with the group as a whole, the patients with inflammatory bowel disease had a higher positive rate (25.6%, p < 0.05), whereas duodenal ulcer patients had a lower rate (9.4%, p < 0.01). Rates in gastric ulcer, gastritis, diverticular disease, and irritable bowel syndrome were no different from the overall rate. In 148 general medical patients without gastrointestinal disease, the positive rate (11.5%) was also not significantly different.

The data show that salicylate ingestion is common and the clinical history unreliable. They do not support a particular association with peptic ulceration or gastritis.

Reference


Drugs as associated factors in primary acute pancreatitis

J. B. BOURKE, M. B. MCILMURRAY, G. M. MEAD, AND M. J. S. LANGMAN (University Departments of Surgery and Therapeutics, The City and General Hospitals, Nottingham) Since 1 March 1973, careful drug histories have been taken in patients admitted with primary acute pancreatitis to the City and General Hospitals in Nottingham. To date, 81 patients have been studied and six of these have so far been matched for age and sex with patients admitted with acute abdominal pain of non-pancreatic cause.

Nine of the total group gave a history of excess alcohol intake (11%) and 20 were taking thiazide or related diuretics (25%). Ten (12%) of the total groups were receiving digoxin at the time of admission. Six (9%) in the patient group of 66 compared with none in the control group gave a history of excess alcohol intake. Sixteen out of 66 (24%) of the matched disease group were taking thiazide or related diuretics compared with seven out
of 66 control group (11%). Seven patients (10%) compared with three controls (4-5%) were taking digoxin. Twenty-one out of 66 (32%) patients compared with 37 out of 66 (56%) controls were receiving no drug therapy.

These results suggest that there may be a significant and frequent association not only with alcohol but also with thiazide and related diuretic intake and the occurrence of primary acute pancreatitis.

Role of insulin and source of calories in intravenous feeding

R. V. HEATLEY, A. M. J. WOOLFSON, AND S. P. ALLISON (General Hospital, Nottingham)

It is believed that changes in insulin secretion and activity play an important part in the catabolic changes which are associated with acute illness. The provision of exogenous insulin may be effective in reversing protein catabolism in this situation, but proof has been lacking that insulin has a specific effect over and above the provision of carbohydrate calories.

In this study catabolic patients, many of whom were undergoing surgery for gastrointestinal disease, have been infused intravenously with constant amounts of amino-acids, and calories in the form of glucose, or sorbitol and fat. Three-day crossover studies were performed comparing isocaloric regimes with and without insulin. The effect of these various caloric sources on the catabolic response to acute illness has been assessed by measurement of the urea production rate.

This study has demonstrated that in non-catabolic starved patients a standard intravenous feeding regime of 10 g nitrogen together with 200 calories/g nitrogen, in the form of fat and carbohydrate, is entirely satisfactory for nutritional purposes. However, in more catabolic patients in whom the urea production rate rises above 12-15 g a day, glucose is more protein sparing than fat, and the provision of exogenous insulin further decreases the catabolic rate.

INFLAMMATORY BOWEL DISEASES followed by ABSORPTION/MALABSORPTION

Pulmonary function in patients with inflammatory bowel disease

O. E. EADE, C. L. SMITH, AND P. J. WHORWELL (Southampton University Hospitals, Southampton, Hants) Occult pulmonary disease has been found in some chronic inflammatory disorders. Also, pulmonary disease with ulcerative colitis and sulfasalazine has been suggested. We have investigated the pulmonary function of 32 patients with inflammatory bowel disease (21 with ulcerative colitis, 11 with Crohn's disease) compared with 32 age/sex matched healthy controls. The FEV₁, FVC, and DCO (transfer factor) were measured. The mean observed DCO (as a percentage of the predicted value) for patients with inflammatory bowel disease was 71-2, which was significantly lower (p < 0.01) than that of the control group (mean 80-2). The severity of the reduction in DCO was greater with extensive disease than with limited disease. The severity of the reduction also correlated with the duration of the disorder. There was no difference in FEV₁ or FVC between patients and controls. Also there was no difference in any of the pulmonary function tests between those taking sulfasalazine and the rest.

It is probable that the change in lung function is due to systemic involvement in the disease process, similar to the other extraintestinal manifestations, and not a consequence of drug therapy.

References


Abnormal jejunal surface pH in Crohn's disease—new evidence that Crohn's disease is a diffuse lesion of the gastrointestinal tract

B. T. COOPER, M. L. LUCAS, F. H. LEI, J. A. BLAIR, AND W. T. COOKE (Nutritional and Intestinal Unit, The General Hospital, Birmingham, and Department of Chemistry, University of Aston in Birmingham) There is increasing evidence that Crohn's disease is a diffuse lesion of the gastrointestinal tract. The presence of an acidic layer on the proximal jejunal luminal surface has been demonstrated in healthy subjects and it has been suggested that this jejunal acid microclimate is produced by hydrolysis of ATP by mucosal adenosine triphosphatase. Reduction in enzyme activity would decrease jejunal surface acidity. The present study examines the proximal jejunal luminal surface pH (pHs) in patients with Crohn's disease apparently confined to the large or distal small bowel.

Proximal jejunal mucosa was obtained by peroral biopsy from 15 patients with Crohn's disease and 17 normal controls. Samples were immediately incubated in buffer and the pHs was measured with pH-microelectrodes.

In the normal controls, the pHs was 5.95 ± 0.05 which was significantly different to the buffer pH of 6.97 ± 0.03 (p < 0.001) and it remained stable over one hour's incubation in the presence of 10 mM glucose. The pHs in the patients with Crohn's disease was significantly different to that of the normals at 6.21 ± 0.04 (p < 0.01). There was no correlation between pHs and the site of macroscopic disease, disease activity, length of history, or jejunal cellular infiltration. Incubation of jejunum in the presence and absence of glucose showed that the pHs was only maintained in the presence of glucose.

In conclusion, the pHs is abnormal in patients with Crohn's disease, suggesting jejunal mucosal enzyme abnormalities, and providing further evidence for the concept that Crohn's disease is a diffuse lesion of the gastrointestinal tract.

References


Influence of inflammatory bowel disease on intestinal microflora

M. R. B. KEIGHLEY, Y. ARABI, F. DIMOCK, D. W. BURDON, AND J. ALEXANDER-WILLIAMS (The General Hospital, Birmingham) There is a high incidence of sepsis after intestinal resection in patients with inflammatory bowel disease which may be due to large numbers of bacteria in the bowel at the time of operation.

We have therefore studied the intestinal flora of 22 patients with non-obstructive inflammatory bowel disease: Crohn's disease (n = 14), ulcerative colitis (n = 4), and pseudomembranous colitis (n = 4). All diagnoses were confirmed histologically and, with the exception of pseudomembranous colitis, none of these patients had received antibiotics within three weeks of sampling. The results have been compared with patients requiring operation for gallstones or peptic ulcer (n = 25). Samples were either collected at sigmoi-
scopy or at operation and were taken immediately into an anaerobic chamber. Viable counts were measured by inoculating serial dilutions of intestinal fluid on selective media.

In Crohn's disease there were increased numbers of Escherichia coli and Bacteroides fragilis in the jejunum, ileum, and colon by a factor of between 100 and 10,000 compared with controls. In ulcerative colitis small intestinal counts did not differ from controls but there was a modest increase in the number of bacteria in the colon. However, there was no evidence that pseudomembranous colitis was associated with decreased numbers of intestinal bacteria.

These early results suggest that patients with Crohn's disease are particularly at risk from developing postoperative sepsis because of the increased numbers of bacteria in the small and large intestine.

Reference


Impaired immunity in ulcerative colitis with hyposplenism: the response to the intravenous antigen ëX174

F. P. Ryan, C. D. Holdsworth, and J. Verrier Jones (Department of Medicine, The Royal Infirmary, Sheffield, and Department of Medicine, Southmead Hospital, Bristol) We have found hyposplenism to be quite common in ulcerative colitis. As impaired immune response to an intravenous particulate antigen has been associated with hyposplenism in patients with coeliac disease, we have investigated the ability of patients with ulcerative colitis to mount an immune response to the same antigen.

The immunological response to both primary and secondary intravenous injections of the bacteriophage ëX174 was measured in eight patients with extensive ulcerative colitis, of whom four had normal and four markedly subnormal splenic function.

The primary response was normal in three of the four patients with normal spleens, being reduced in one patient who had a low serum IgM level, but was severely impaired in all four patients with hyposplenism. The secondary responses showed an even more marked difference, with a mean maximum titre of phage-neutralising antibody in those with normal spleens of 22,000, compared with only 220 in those with hyposplenism. One patient with hyposplenism showed no response to either the primary or secondary injection.

This severely impaired response to intravenous particulate antigen may be partly responsible for the frequency of post-operative septicemia and disseminated intravascular coagulation in patients with ulcerative colitis and hyposplenism.

References


Ulcerative colitis and malignancy

J. C. MacCartney, H. Thompson, W. T. Cooke, and Robert Allan (The Nutritional and Intestinal Unit, General Hospital, Birmingham) Malignancy complicating ulcerative colitis is well recognised, and is commonly assumed to be a frequent association. We have reviewed 707 patients with ulcerative colitis followed on this unit between 1944 and 1975. All clinical and pathological data have been reviewed, and where feasible repeat barium enema examinations have been done. Forty-eight patients have developed carcinoma—33 (4-6%) in the colon or rectum, seven in the biliary tract (0-9%), and eight in other organs. Tumours of the large bowel were identified in the rectum and sigmoid colon (36%), ascending or transverse colon (33%), multifocal (18%), descending colon (3%), and not recorded (9%). Four of the six patients with multifocal carcinoma had precancerous change elsewhere in the colon. All but two of the carcinomas were associated with total colitis.

The mean age at onset of colitis symptoms was 31-6 years with a mean interval of three years to diagnosis, and 15-8 years (range 0-45 years) to the diagnosis of carcinoma in the large bowel. Two distinct groups were identified. A short survival group (19 patients) average 11-3 months (0-41 months) and a long survival group (12 patients) average 12-9 years (range six-23 years). The long survival group included half the patients with multifocal carcinoma. Data relating the incidence of carcinoma of the large bowel and survival rates with the rates in the general population, matched for age, sex, and years at risk are being computed.

Carcinoma of the large bowel complicating ulcerative colitis is an uncommon complication and nearly always occurs in the presence of total colitis. These patients could be divided into two distinct survival groups.

Treatment of haemorrhoids in patients with inflammatory bowel disease

P. J. Jeffery, Jean K. Ritchie, and A. G. Parks (St. Mark's Hospital, London) Haemorrhoids and inflammatory bowel disease are conditions seen commonly at St. Mark's Hospital; occasionally they may occur in the same patient. Little advice exists for clinicians confronted with this problem, so a retrospective review has been undertaken of patients with this dual diagnosis to see if any guide-lines for treatment can be laid down.

Sixty-two patients seen between 1935-75 inclusive in whom treatment of haemorrhoids and inflammatory bowel disease was undertaken have been studied. A diagnosis of ulcerative colitis was made in 43, Crohn's disease in 19.

Both conservative (injection, banding) and operative treatment for haemorrhoids was relatively trouble free in patients with ulcerative colitis. Only six patients developed complications after treatment; anal pain (two); secondary haemorrhage (two); exacerbation of colitis (one), and a complex anal fistula leading to rectal excision (one).

Conservative and operative management of haemorrhoids before and after the diagnosis of Crohn's disease was followed by frequent complications, especially severe after surgery; six patients came to rectal excision later.

For the first time, data concerning coincidental haemorrhoids occurring in inflammatory bowel disease are available. In ulcerative colitis treatment of haemorrhoids is usually safe and can be recommended for patients with troublesome symptoms, while in Crohn's disease it would be wise to pursue an ultraconservative regime. It is essential to make a histological diagnosis in any patient with proctitis and symptomatic haemorrhoids.

Dual action of cholera toxin on electrolyte and non-electrolyte transport in the mucosa of canine jejunum and ileum

J. W. L. Robinson, V. Mirkovitch, F. V. Sepulveda, H. Menge, and Professor H. Dowling (Département de Chirurgie
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Dog ileum, unlike that of most mammals, exhibits a larger net absorption of sodium and water than the jejunum. Furthermore, this net movement can be stimulated more extensively by glucose in ileum than in jejunum. In the presence of glucose, the net absorption of sodium and water in the ileum is so great that it cannot be reversed by cholera toxin; only a considerable reduction is observed when mucosal adenylyl cyclase is significantly stimulated.

In the jejunum, without luminal glucose, a characteristic reversal of net water and electrolyte absorptions is elicited by cholera toxin. However, in both jejunum and ileum, treatment of the mucosa in vivo with cholera toxin enhances the steady-state accumulation of amino-acids and monosaccharides in vitro during a subsequent incubation. The initial rate of entry of these substrates into the mucosa in vitro is not affected by pre-treatment with the toxin, nor are the ionic contents of mucosal scrapings, examined immediately after excision of the treated intestine. Therefore, pre-treatment of mucosa with the toxin may reduce the efflux of non-electrolytes, accumulated in vitro; perhaps a cholera-toxin-induced collapse of intercellular spaces could be responsible for this phenomenon.

**Consequences of the destruction of the villus epithelium by ischaemia or Triton X-100**

J. W. L. Robinson, V. Mirkovitch, and H. Menge (Département de Chirurgie Expérimentale, Centre Hospitalier Universitaire Vaudois, CH-1011 Lausanne, and Medizinische Universitätsklinik, D-3550 Marburg/Lahn) After one hour of complete normothermic ischaemia of canine ileum, the whole villus epithelium was destroyed, but the crypts remained intact; this was accompanied by a large net secretion of water and electrolytes into the lumen and abolition of the active transport of sugars and amino-acids in vitro. Preloading the blood of these animals with phenol red did not lead to loss of dye into the lumen after ischaemia, suggesting that the secretion was not caused by simple filtration through the capillary network.

On the other hand, perfusion of the ileum in vivo for one or two hours with 1% Triton X-100 in Krebs bicarbonate buffer containing glucose caused destruction of the enterocytes only at the villus tips; all net water and electrolyte absorption in vivo was abolished, glucose absorption in vivo was reduced, and the active transport of sugars and amino-acids in vitro was diminished.

The above results are interpreted in terms of a balance between absorption and secretion of electrolytes in the epithelial cells at different levels along the villus, and suggest that the crypt cells possess principally a secretory capacity, whereas the mature cells at the villus tips absorb more than they secrete.

**Fructose absorption and the effects of other monosaccharides on its absorption in the rat jejunum in vivo**

P. J. Millan, J. E. J. Oyesiku, D. P. R. Muller, and J. T. Harris (Institute of Child Health and The Hospital for Sick Children, Great Ormond Street, London) Current evidence suggests that fructose is absorbed from the small intestine by a carrier-mediated transport system; in addition, there is evidence that at least two membrane carriers may participate in the transport of glucalocytes into the enterocyte. It has been our clinical impression for several years that infants with diarrhoea often tolerate mixtures of glucose and fructose better than either monosaccharide alone, and this prompted us to examine that mixture.

The absorption of fructose and the effects of other monosaccharides on its absorption has been studied in the rat jejunum using an in vivo perfusion technique. The perfusates contained 20 mM fructose alone, or a mixture of 20 mM fructose and one other monosaccharide (glucose, galactose or 3-O-methylglucose); these three monosaccharides were added at a concentration of either 2 or 56 mM.

Low (2 mM) concentrations of glucose and galactose stimulated fructose transport (p < 0.01) but higher concentrations (56 mM) had no effect; neither concentration of 3-O-methylglucose had a significant effect. Fructose also stimulated glucose (2 mM) absorption (p = 0.02). When perfused alone fructose increased (p < 0.001) the transmural potential difference (PD): phlorizin (0.1 mM) abolished this PD increment as well as markedly inhibiting (p < 0.001) fructose transport. At the same concentration phlorizin also inhibited fructose absorption (p < 0.002) and abolished the PD from perfusates containing mixtures of fructose and glucose (2 mM).

These results suggest that fructose is transported by an electronegic phlorizin-sensitive carrier, and that fructose and certain other monosaccharides are more efficiently absorbed when presented to the mucosa as mixtures; the data support our original clinical impression. We suggest that the results are also compatible with the concept of multiple membrane carriers for monosaccharides by the enterocyte.

**Reference**


**‘One swallow’ test for the investigation of malabsorption and diarrhoea**

R. H. Taylor and Susan Waterman (Introduced by Dr. T. D. Kellock) (Department of Gastroenterology, Central Middlesex Hospital, London) In the investigation of malabsorption and diarrhoea tests requiring several small bowel intubations are commonly used. These include a Lundh test, a jejunal biopsy, and an aspiration of small bowel juice for culture, microscopy, cytology, and biochemical examination.

A technique has been developed in which all these investigations can be done in one outpatient session using a specially designed tube. The tube has an outer aspiration channel and a central triggering channel for the biopsy capsule. The sterilised tube is positioned at the ligament of Treitz under fluoroscopy. The initial aspiration is taken from microscopy, cytology, and culture, and a Lundh test is done in the standard way, and, after two hours, a jejunal biopsy is taken. The tube is well tolerated by patients.

In 35 consecutive patients referred we diagnosed three cases of coeliac disease and three of partial villous atrophy. There were three cases of giardiasis, one of hookworm, and one of bacterial colonisation. Fungal hyphae were found in three patients. One patient had pancreatic exocrine insufficiency. One patient could not swallow the tube and in two it failed to pass the pylorus.

There were positive findings in 47% of completed tests compared with 28% for biopsy alone.

**Short chain fatty acid absorption in the human large bowel**

N. I. McNeil, J. H. Cummings, and W. P. T. James (Dunn Nutritional Laboratory and Addenbrooke’s Hospital, Cambridge)
Short chain fatty acids (SCFA) are produced in the human large bowel, probably by microbial digestion of dietary fibre. In faeces, SCFA are the major anion. In animals they are absorbed from the large bowel, but in man their fate is unknown; they are often considered to be unabsorbed and responsible for faecal bulking.

We have studied acteate absorption by the normal rectum using Edmonds' technique in which dialysis tubing on a stiff catheter is introduced into the rectum. Fifteen obese non-fasting subjects were studied. The test solution contained Na⁺ 98 mmol/l, K⁺ 40 mmol/l, CH₃COO⁻ 97 mmol/l, HCO₃⁻ 7 mmol/l, Cl⁻ 33 mmol/l at pH 7.21. Faecally stained dialyses were discarded, leaving nine for analysis.

After one hour fluid loss from the dialysis bags was 0.30 ± 0.4 g (SEM) with a final composition of Na⁺ 8.5 ± 1.5 mmol/l (p < 0.001), K⁺ 42.5 ± 2.1 mmol/l (NS), CH₃COO⁻ 64.2 ± 2.5 mmol/l (p < 0.001), HCO₃⁻ 35.6 ± 4.0 mmol/l (p < 0.001), Cl⁻ 26.9 ± 1.2 mmol/l (p < 0.001), and pH 7.86 ± 0.07 (p < 0.001).

The subjects were studied for a second hour with a new solution at pH 5.5 containing Na⁺ 98 mmol/l, K⁺ 39 mmol/l, CH₃COO⁻ 97 mmol/l, Cl⁻ 50 mmol/l. Eight were suitable for analysis. The loss of fluid was 0.34 ± 0.07 g with a final dialysate concentration of Na⁺ 83.5 ± 2.0 mmol/l (p < 0.001), CH₃COO⁻ 62.9 ± 3.1 mmol/l (p < 0.001) and pH 7.66 ± 0.11 (p < 0.001).

We conclude that there is marked absorption of acetate from the rectum in man with secretion of bicarbonate, in addition to absorption of sodium and chloride. Acetate absorption seems unaffected by initial pH. Proposed mechanisms for faecal bulking after fibre feeding need revising, as does the concept of fibre as an 'unavailable' source of energy.

References

Improved fat absorption with synthetic detergents in patients with bile salt deficiency

R. F. G. J. King, J. Kelleher, P. D. Howdle, G. P. Hall, and M. S. Losowsky (Department of Medicine, St. James's Hospital, Leeds) Bile salt deficiency, due to liver disease or ileal disease, causes fat malabsorption not corrected by standard therapy. Replacement of bile salts by non-ionic detergents has been suggested, and Tween improves bile salt deficient steatorrhoea in the rat, but careful assessment of its place in therapy has not been reported.

The effects of Tween were studied in 12 patients with bile salt deficient steatorrhoea.

After five days' equilibration on constant fat intake and marker, faecal fat was measured on diet alone and on diet plus Tween given with meals. In five patients jejunal intubation was conducted using meals with or without added Tween. Bile salts, free fatty acids (FFA), and phospholipids (PL) were measured in whole jejunal contents and in the micellar phase.

Jejunal bile salt levels were low in all subjects. With Tween, micellar FFA and PL were increased in four out of five patients (mean increases 100% and 260%). With Tween the micellar PL and FFA per mole of bile salts were increased. Regular Tween produced a mean decrease in faecal fat of 33%, with best effects in patients with severe steatorrhoea.

The results suggested that in steatorrhoea due to bile salt deficiency Tween causes increased micellisation of ingested fat and improvement in fat absorption. Thus non-ionic detergents may find a place in therapy.

References

Interrelationships between motor activity and transmucosal transport in the human small intestine in vivo

A. I. Morris, K. A. Pimbblett, L. Hall, and L. A. Tarnberg (Department of Medicine, Hope Hospital (University of Manchester, School of Medicine), Salford) The complex interrelationships between motor activity of, and rate of transit through, the intestine, and between these and its absorptive activity are ill understood. Since autonomic nervous activity influences both motility and transmucosal transport processes, we have investigated the effects of parasympathetic agonists and antagonists on these small bowel activities using in vivo intubation techniques in normal volunteers.

Atropine intravenously (1 mg.h⁻¹) significantly delayed intestinal transit in the jejunum and clearly inhibited motor activity as indicated by intraluminal pressure measurements. The parasympathetic agonists betahaneol (25 mg.l⁻¹) and neostigmine (15 mg.l⁻¹) intraluminally also delayed transit but here pressure wave activity was apparently increased. Thus intestinal transit cannot be predicted simply from measurements of pressure wave activity.

We examined the influence of these agents on transmucosal transport during the same experiments. Atropine inhibited absorption of Na⁺, Cl⁻, K⁺, HCO₃⁻, and H₂O in the jejunum but neither betahaneol nor neostigmine influenced transport in jejunum or ileum.

These results suggest that (1) parasympathetic activity influences both motor and mucosal transport activity of the small intestine, (2) there is no simple relationship between pressure wave activity and intestinal transit, and (3) changes in intestinal transit or in motor activity do not necessarily correlate with transmucosal transport.

Control of iron absorption in pregnancy

R. G. Batey (Department of Medicine, Royal Free Hospital, London) The effect of pregnancy on iron absorption has been studied in rats at various stages of gestation. Intestinal iron transport (T), expressed as the percentage of a 40 μg dose of ⁵⁹Fe entering the carcass in 20 minutes, from a closed duodenal loop was measured. Values were compared with the half-life of ⁵⁹Fe in serum (t½ ⁵⁹Fe).

T remained constant from days one to 15 of gestation, 18.9 ± 1.8% (mean ± SE) but increased significantly from day 16, to a maximum value of 44.0 ± 6.6% at term (p < 0.01), coinciding with the phase of fetal iron accumulation. The t½ ⁵⁹Fe fell from control values, 72.1 ± 2.4 min to 59.2 ± 2.7 min at day 19 (p < 0.05). In the subsequent 24 hours t½ ⁵⁹Fe fell to 37.2 ± 3.4 min (p < 0.01). This rapid fall preceded the increased intestinal transit of 18 h. The t½ ⁵⁹Fe was minimal immediately prepartum, 19.4 ± 2.1 min (day 20-21). Hysterecemy at day 20-21 produced a significant rise in t½ ⁵⁹Fe to 58.2 ± 4.7 min (p < 0.01) within five hours. Intestinal T did not fall to control.
values, 22.6 ± 2.6% until 18 hours after hysterectomy.

In contrast, animals fetectomized at day 20-21 demonstrated values for T of 37.4 ± 3.4% and $t_1/2^{55}Fe$ of 27.8 ± 2.5 min which were not significantly different from those in day 20-21 pregnant rats.

The results demonstrate that control of intestinal iron absorption during the latter third of gestation is dependent on placental function.

**Intestinal absorption in relation to nutrition in old age**

R. D. MONTGOMERY, I. N. ROSS, M. R. HAENEY, H. G. SAMMONS, A. V. BARFORD, AND L. S. CULANK (Frazer-Squire Metabolic Research Unit, East Birmingham Hospital, Birmingham) Although there have been many studies of nutritional deficiencies in old age, little attention has been paid to the functional efficiency of the ageing small intestine and the possible role of malabsorption.

Fifty subjects aged 65 to 92 years gave informed consent to detailed nutritional and absorption studies as inpatients in a metabolic unit. Seventeen were symptomless volunteers, and 33 presented with anaemia, chronic diarrhoea, or bone pains, for which no cause was immediately apparent. In addition to a clinical, haematological, and biochemical assessment of nutritional state, intestinal function tests included blood xylose and iron absorption curves, a double isotope Schilling test, faecal fat, urinary indican, and small bowel radiology, with duodenal aspiration and jejunal biopsy in some cases.

On the basis either of steatorrhoea or at least two other abnormal parameters of absorption, there were 15 cases of malabsorption. Four of these had duodenal diverticulosis, two had the post-gastrectomy syndrome, and one had calcific pancreatitis. Malabsorption in the remaining eight cases was unexplained. The age range of this group was 70 to 86 years. In the main they presented with mixed anaemia; five complained of diarrhoea and four had steatorrhoea. Three had suggestive evidence of pancreatic insufficiency, which might well be of ischaemic origin. The role of 'silent' mesenteric ischaemia in the remainder remains speculative.

At least half such cases of malabsorption in the elderly require treatment for multiple deficiencies. A factor calling for further study is the possibility of serious malabsorption of drugs.

**Assessment of xylose absorption by correcting one hour blood xylose levels for body surface area**

L. S. CULANK, M. R. HAENEY, R. R. MONTGOMERY, I. N. ROSS, AND H. G. SAMMONS (Frazer-Squire Metabolic Research Unit and Department of Clinical Chemistry, East Birmingham Hospital) D-xylose absorption is a standard test of intestinal absorption which has been criticised for its dependence on renal function and for inadequate discrimination between healthy and abnormal subjects.

Two hundred and seventeen subjects aged 14 to 92 years were given orally 5 g D-xylose. Blood absorption curves were studied over a three hour period and urine collections to two and five hours were made.

We have shown that in subjects without evidence of malabsorption the peak blood xylose level occurs in most subjects at one hour. The one hour blood values give maximum discrimination between these subjects and patients with proven small intestinal malabsorption.

This discrimination is enhanced by correction of the blood concentrations to a constant body surface area. We have shown that such a correction allows for the partial dependence of blood levels on variability of body size and gives results independent of age, sex, and mild renal impairment.

A one hour blood xylose level corrected for surface area gives a better and simpler estimate of jejunal absorption than other measurements of D-xylose in blood or urine, and the normal range for this method is greater than 0.65 mmol/l.