The British Society of Gastroenterology

The 33rd annual general meeting of the British Society of Gastroenterology was held at Aviemore, Inverness-shire from 28 to 30 September 1972 under the Presidency of Professor W. I. Card. The programme included a very large number of communications of which the abstracts follow, and symposia on 'A new look at gastritis' and 'Gastrooesophageal reflex and its complications'. The Sir Arthur Hurst Memorial Lecture on 'Gut hormones—milestones and signposts' was given by Morton I. Grossman. A general report and a note on the annual business meeting, which was attended by honorary, senior, and ordinary members, is on page 858.

Hepatic Damage from Overdose of Paracetamol

R. P. H. THOMPSON, R. CLARK, R. A. WILLSON, V. BORIRAKCHANYAVAT, B. WIDDOP, R. GOULDING, and R. WILLIAMS (Liver Unit, King's College Hospital and Poisons Unit, Guy's Hospital, London) The increasing use of paracetamol as an analgesic has been followed by an increased incidence of overdoses. We have seen 46 patients during two years; 42 who took more than 13 g developed liver damage, and 14 died in hepatic failure. The prothrombin ratio and bilirubin level usually became abnormal within 24 hours, but peak levels were not reached until three to six days. An unusual finding was an initial unconjugated hyperbilirubinaemia. Hepatic histology at four to 26 days showed centrilobular reticulin collapse, congestion, and necrosis of varying extent, but with considerable recovery at three months, except in one in whom considerable fibrosis persisted. Coagulation tests were improved by intensive therapy with heparin and fresh-frozen plasma, and their effect is being assessed in a controlled trial.

A new approach to therapy was studied in pigs. Paracetamol administered to hepatectomized animals was completely cleared from the blood when passed in vivo through a column of activated charcoal. This may be an easy and effective method for removing this drug if the patient is seen early.

Factors Influencing Human Gallstone Dissolution in Monkey, Dog, and Human Bile

G. D. BELL, D. JUNE SUTOR, B. WHITNEY, and R. DOWLING (Departments of Medicine and Radiodiagnosis, Royal Postgraduate Medical School, Ducane Road, London W12, and Crystallography Unit, Department of Chemistry, University College, London) The influence of bile composition and of size and cholesterol and calcium content of gallstones on rates of dissolution has been studied in vitro and in vivo.

Selected human gallstones, removed at surgery, were analysed chemically and by x-ray diffraction and then exposed to flowing bile of rhesus monkeys with an intact enterohepatic circulation. Rapid gallstone dissolution was associated with (1) high gallstone cholesterol content; (2) bile undersaturated with cholesterol; (3) high surface area: weight ratio.

In vitro studies with dog bile showed that the presence of a radioopaque outer rim of calcium delayed gallstone dissolution.

Of 10 gallstone patients treated with chenodeoxycholic acid (0.75-1.5 g/day for three months) cholesterol solubility improved in nine. After six months' treatment, of two patients with radiolucent gallstones, complete gallstone dissolution occurred in one, and a significant reduction in stone size in the second.

Reference


Malignancy in Relatives of Patients with Adult Coeliac Disease

P. L. STOKES, P. ASQUITH, J. H. WATERHOUSE, AND W. T. COOKE (The General Hospital, Birmingham, B4 6NH) Previous reports have shown that patients with adult coeliac disease have an increased incidence of malignancy especially of lymphoma and cancer of the gastrointestinal tract. As adult coeliac disease frequently occurs in more than one member of a family it seemed appropriate to examine the families of patients with this disease to assess the incidence of malignancy.

A family history was obtained from 80 patients
with well documented adult coeliac disease. Data obtained by questionnaire were later confirmed in each case during a personal interview. Particular attention was paid to the causes of death of relatives with recourse to death certificates where possible, and to the Birmingham Regional Cancer Registry for confirmation of cancer and other deaths. The death of any family member was not included for analysis if the cause of death, age at death, or year of death were not definitely known.

From this information years-at-risk were obtained for all relatives and deaths from cancer and other causes noted. Computer programmes have been developed to provide the expected numbers of deaths from cancer of all sites and within each degree of relationship using the mortality rates of the Registrar-General. Preliminary results show that the numbers of deaths from cancer in first degree relatives of the propositi are greater than expected (p = 0.01) and further analysis is continuing.

The significance of these findings is discussed with emphasis upon the inheritance of the disorder and the predisposition to malignancy.

References


Essential Fatty Acid Deficiency Secondary to Intestinal Malabsorption

M. PRESS, H. KIKUCHI, AND G. R. THOMPSON (Department of Medicine, Royal Postgraduate Medical School, London) Malabsorption of essential fatty acids (EFA) must inevitably lead to EFA depletion since inadequate intake cannot be overcome by an increased rate of synthesis, as occurs with non-essential fatty acids. This paper reports an investigation into the fatty acid pattern of plasma lipids in a group of patients with steatorrhoea.

The fatty acid composition of lecithin, triglyceride, and cholesterol ester in fasting plasma was determined by GLC. The percentage of linoleic acid (18:2) in each of these fractions was significantly lower in 23 malabsorbers (15, 8, and 30%) than in 14 controls (27, 17, and 49%, p < 0.01). These changes, indicative of EFA depletion, were more severe in patients who had undergone intestinal resection than in those with malabsorption due to adult coeliac disease or other causes, even though the faecal fat excretion of the three groups was similar. The classical picture of EFA deficiency, characterized by the appearance of an abnormal fatty acid (20:3 ω 9) in plasma lecithin, was found in only three patients, all of whom had undergone intestinal resection. This was successfully treated by the intravenous administration of Intralipid.

The reason why resected patients are so prone to EFA deficiency is uncertain, but these observations may have clinical implications. EFA deficiency causes diarrhoea and dermatitis in human infants and gallstones in hamsters: its possible role should be considered in the pathogenesis of the watery diarrhoea and increased incidence of gallstones found after intestinal resection in man.

Effects of Cholecystokinin on Colonic Motility and Symptoms in Patients with the Irritable Bowel Syndrome

R. F. HARVEY AND A. E. READ (Department of Medicine, Royal Infirmary, Bristol) It has been shown that many patients with 'functional' food-induced pain have an abnormally marked colonic motor response to eating and this may be important in the production of their symptoms. Little, however, is known of the mechanisms involved in this response.

The effect of intravenous administration of cholecystokinin (CCK) on motor activity of the sigmoid colon was studied in 20 patients with abdominal pain believed to be due to the irritable bowel syndrome. Intraluminal pressure changes were recorded on a Devices M19 recorder, using miniature balloons placed 20—25 cm from the anus. After placing of the balloons, the patients rested quietly for at least 60 minutes, and were then given a slow intravenous injection of normal saline. Following this, motility was recorded for 30 minutes. CCK (6 CHR units/hour) was then given over a 10-minute period and motility recorded for a further 30 minutes. Motor activity during these two 30-minute periods was compared by measuring the percentage duration of pressure waves, their mean amplitude, and a motility index (multiple of the other two indices).

All three parameters of motor activity increased after CCK administration (% activity 22:2 to 33:7, p < 0.025; mean amplitude 9-0 to 11:1 cm H2O, NS; motility index 244 to 397, 0·05 < p < 0·10) but these increases were almost entirely confined to patients whose pain was usually precipitated by eating. In this group of eight patients the changes were much greater (13:7 to 41·3%, p < 0·001; 4·9 to 12·3 cm H2O, p < 0·02; 71 to 497, p < 0·02), and four of these eight patients developed a severe attack of their usual pain after CCK administration, at a time when markedly increased motor activity was seen.

These results suggest that the abnormally increased...
postprandial colonic motor response in patients with ‘functional’ food-induced pain may be mediated by cholecystokinin.

References


An Animal Model for Diverticular Disease

J. Hodgson (introduced by B. N. Brooke) (St. Georges Hospital, Tooting, SW17) An animal model using rabbits has been devised (Hodgson, 1972). After intra-colonic activity before and after neostigmine was measured, eight rabbits continued on normal pellet diet and eight rabbits were put on a pseudo-human diet of white bread, butter, milk, and sugar supplemented by Complan. Four months later pressures were measured again.

Pressures fell in the normal rabbits but rose in those on the special diet. The mean pre-dietary resting colonic motility index (CMI) of 147 rose to 1,287 \( (p < 0.05) \). After neostigmine the mean pre-dietary CMI rose from 8, 153 to 27, 569 \( (p < 0.0025) \).

Normal mean daily faecal weight was 80 g; on the special diet it was 3 g. Normal transit time was 24 hours; on the special diet it was 48 hours.

Neostigmine caused the regular occurrence of temporary intertaenial diverticula in the contracted colon of the special diet rabbits similar to those demonstrated by Painter (1962) in humans.

It is suggested that the colon, fixed only by the taeniae, can contract onto itself or contained faeces. In low residue states, contraction continues for a longer period than normal and may become permanent (Williams, 1965). More force is exerted by the hypertrophied muscle on a low faecal column and, such increased pressure would eventually lead to the formation of diverticula.

Study of Carcinoembryonic Antigen (CEA) in Gastrointestinal Cancers

A. K. Singh (introduced by B. Creamer) (St. Thomas's Hospital, Department of Haematology, London) The discovery of a tumour specific antigen, demonstration of its presence in the plasma of patients with gastrointestinal cancers, and the subsequent development of a quantitative measurement of the CEA in plasma has given rise to considerable optimism about the availability of a simple technique likely to be useful in the diagnosis and the assessment of treatment of gastrointestinal cancers. The present study was carried out to evaluate the role of CEA in the diagnosis of gastrointestinal cancers and examine its importance in assessing the efficacy of therapy and evaluate its possible function in early detection of recurrence of the disease. Plasma CEA levels were measured in a radioimmune assay system in normal subjects, patients with gastrointestinal cancers, and in related disorders. The findings show that CEA level is raised in the majority of patients with GI cancer and, thus, appears to be a useful diagnostic adjunct. It is, nevertheless, also shown that normal levels of plasma CEA do not exclude the presence of a malignant tumour of the gastrointestinal tract. Raised levels of plasma CEA were also found in certain liver diseases and megaloblastic and iron deficiency anaemias in the absence of a demonstrable malignancy of the GI tract. Considerably elevated CEA-like activity has also been observed in apparently normal gastric juice.

The physico-chemical nature of the CEA has been examined. Column chromatography has shown the presence of CEA activity in more than one fraction which appear to differ in their molecular size; similar studies have been carried out on gastric juice and plasma. Additional observations have shown an immunological resemblance between the CEA and blood group substances. It is likely that CEA may represent an incomplete or atypical blood-group substance-like product of the malignant tissues.

In view of these findings the values and limitations of the routine measurements of CEA level in patients with gastrointestinal disorders will be discussed.

Immunoglobulin Measurements in Jejunal Secretions of Patients with Adult Coeliac Disease and Dermatitis Herpetiformis

D. B. L. McClelland, R. R. Samson, R. C. Heading, R. St.C. Barnetson, and D. J. C. Shearmar (Gastrointestinal Section of the University Department of Therapeutics and the University Department of Dermatology, Royal Infirmary, Edinburgh) Jejunal immunoglobulin levels have been studied in normals (17), adult coeliac disease (8) and dermatitis herpetiformis (15) by immunodiffusion methods. Immunoglobulin levels in controls were similar to those...
already published (Douglas, Crabbe, and Hobbs, 1970). In adult coeliac disease (ACD) and dermatitis herpetiformis (DH), IgA levels were very high and usually exceeded 30 mg/100ml in ACD and 50 mg/100ml in DH. In five patients with DH, IgA levels exceeded 100 mg/100 ml. In both ACD and DH, IgG levels were very low but IgM levels were raised in DH.

Since the IgA levels in ACD and DH were much higher than previously reported, studies were carried out to confirm the validity of the immunodiffusion method for jejunal IgA. There was no interference from trypsin complexes (McClelland, Parkin, Samson, and Shearman, 1972). Although trypsic digestion may lead to an apparent increase in IgG levels, it did not affect secretory IgA levels. In addition, the molecular weight distribution of IgA in jejunal aspirate has been studied by agarose filtration and density gradient ultracentrifugation.

It is concluded that the method used for the measurement of jejunal IgA levels is valid and that very high levels of IgA occur in the jejum in dermatitis herpetiformis as well as in adult coeliac disease.

References

The Association between the Large Lymphocyte and the Small Intestine

A. R. Moore and J. G. Hall (introduced by J. C. Goliher) (University Department of Surgery, The General Infirmary, Leeds) It has been shown that about 30% of the large lymphocytes (immunoblasts) that appear in the thoracic duct of rats, after antigenic stimulation of their foot pads, 'home' to the lamina propria of the small intestine1,2.

We have studied the entry of immunoblasts into 'free' grafts of syngeneic foetal small and large intestine implanted subcutaneously as described by Zinzar et al3, and also the entry of xenogeneic immunoblasts into normally situated small intestine.

Histological studies show that implanted foetal intestine grows with a perfectly preserved structure.

After intravenous injection of 5-IODO-2 deoxyuridine labelled immunoblasts, the specific radioactivity of the 14 implants of foetal small intestine (corresponding to the number of labelled immunoblasts per unit length of small intestine) averaged 75% (SE 6-5) of the normal adult in situ small intestine.

Therefore although the foetal small intestine was isolated from the normal anatomical and environment influences it received a similar share of immunoblasts.

Although the entry of xenogeneic immunoblasts into the small intestine was somewhat less than entry of syngeneic cells the phenomenon was qualitatively similar. The localization of radioactivity in immunoblasts in intestinal tissues was confirmed with autoradiographs.

The possible importance of this primary association between the large lymphocyte and the lamina propria of the small intestine is discussed in relation to the immune defences of the small intestine and the diseases of this organ.

References

Circulating Immune Complexes in Ulcerative Colitis and Crohn's Disease

D. P. Jewell, I. C. M. MacLennan, and S. C. Truelove (Nuffield Department of Clinical Medicine, Oxford) When certain IgG antibodies combine with target cell antigens, determinants on the antibody molecule become available to react with receptors on the surface of non-immune lymphocytes. The interaction between such lymphocytes and the sensitized target cell leads to target cell destruction. Immune complexes are able to inhibit this form of cytotoxicity by competing for the receptor sites on the lymphocyte surface (MacLennan, 1972).

Using Chang liver cells labelled with 51Cr and sensitized with anti-Chang antibody as target cells, it has been found that serum from patients with ulcerative colitis or Crohn's disease inhibits the cytotoxicity or normal human lymphocytes to a greater extent than control sera. The difference is statistically significant. Inhibition of cytotoxicity showed a positive correlation with the clinical severity of the disease and, in the case of ulcerative colitis, with the degree of inflammation seen on sigmoidoscopy. There was no correlation with serum IgG concentrations.

The inhibitory factor was found in the globulin fraction following ammonium sulphate precipitation and, by fractionating the serum on Sepharose 6B, it was eluted in fractions of higher molecular weight than monomeric IgG but lower than that of IgM. These fractions, nevertheless, contained IgG measured by immunodiffusion. The inhibitory factor in patients' sera is therefore likely to be an immune complex containing less than five molecules of IgG.
Salazopyrin Metabolism in Ulcerative Colitis

K. M. DAS, M. A. EASTWOOD, J. P. A. MACMANUS, AND W. SIRCUS (Gastrointestinal Unit, Western General Hospital and University of Edinburgh) Though salicyl azo sulphapyridine (salazopyrin, SASP) is widely used in the treatment of chronic inflammatory bowel disease, our knowledge of its metabolism is largely obtained from normal volunteers.

We have studied 20 patients with ulcerative colitis, admitted to our Unit during the introduction of salazopyrin. Salazopyrin takes two to three days to reach a steady serum concentration, whereas its sulphapyridine metabolite takes three to seven days.

These patients have been followed for six months to one year and the serum concentration of salazopyrin and sulphapyridine metabolites are maintained at the concentration at discharge provided that the dosage remains the same. In addition, 68 patients in this steady 'state' have been studied at random to give a range of serum concentrations of SASP and its principle serum metabolites, free acetylated and hydroxylated sulphapyridine (SP).

Total sulphapyridine concentration, rather than salazopyrin or constituent sulphapyridine concentration equated best with remission. Ninety per cent of outpatients in remission had serum total SP concentrations in excess of 20 μg/ml. Yet 60% of outpatients with active colitis had concentrations of total SP of less than 20 μg/ml. A serum concentration of total sulphapyridine of more than 20 μg/ml appears to be best achieved with 3 g of salazopyrin/day.

Reference


Pathogenesis of Secondary Hyperoxaluria in Ileal Resection

V. S. CHADWICK, K. MODHA, AND R. H. DOWLING (Department of Medicine, Royal Postgraduate Medical School, London W12) Hyperoxaluria (and oxalate renal stones) may complicate ileal resection. To investigate the mechanism for this secondary hyperoxaluria, three hypotheses were tested. The first, that bile salt glycine, spilling into the colon because of ileal dysfunction, is liberated by bacterial deconjugation, converted to glyoxylate, absorbed and oxidized to oxalate, was tested by feeding choly1 glycine-1-14C. Results show that while breath 14CO2/24 hours was markedly increased after ileectomy (44% ± SEM 2.3) compared to controls (4% ± 0.7), both groups excreted only 0.003% of the dose as urinary oxalate/24 hours, thus excluding bile salt glycine as the oxalate precursor.

Secondly, in ileal resection, the increased demand on hepatic glycine for bile salt conjugation might be met by increased conversion from glycocolate through glyoxylate with an associated increase in oxalate production from glyoxylate. However, after intravenous 14C-glyoxylate, the conversion to bile salt glycine, CO2 and urinary oxalate was the same in controls and ileectomy patients.

Thirdly, since enhanced absorption occurs after resection, 14C-oxalate was fed to 10 controls, seven ileectomy patients without, and seven with, hyperoxaluria. The percentage of the dose in urinary oxalate/36 hours was 28, 29, and 52% respectively.

In conclusion, increased oxalate absorption explains, at least in part, hyperoxaluria after ileectomy.

References


Carcinoma of the Biliary Tract Associated with Ulcerative Colitis

JEAN K. RITCHIE AND P. R. HAWLEY (St. Mark's Hospital, London) In 1954, Parker and Kendall reported a case of a biliary tract tumour in a review of necropsy material from patients with ulcerative colitis. Since that time, there has been an increasing number of papers dealing with the rare coexistence of these two conditions amounting, according to some authors, to a definite association.

This study presents in detail eight new cases, only two of which have been mentioned briefly in earlier publications by one of the present authors.

In the cases described, the diagnosis of ulcerative colitis is authenticated in seven cases by histopathological reports of the excised colon and in the remaining patient by clinical and radiological evidence. Operative, necropsy, or histological data substantiate the diagnosis of malignant biliary tract tumour in all cases.

The present report shows that this association can occur not only in patients treated medically for ulcerative colitis but also many years after proctocolectomy.

A definitive survey of the literature is included;
particular attention has been paid to the management of the ulcerative colitis (medical or surgical) as well as to the location of the tumours within the biliary tract.

References


Abscess and Fistula in Crohn’s Disease

D. M. STEINBERG, W. T. COOKE, AND J. A. WILLIAMS (Nutritional and Intestinal Unit, General Hospital, Birmingham B4 6NH) Abscess and/or fistulae occurred in 18% of patients in a retrospective survey of 360 cases of Crohn’s disease followed up for a mean of 13 years. This incidence is less than in other reported series and the possible reasons for this are discussed.

Abscess

Abscesses can occur spontaneously but usually follow operation, sometimes many years later. Simple drainage of a superficial abscess almost inevitably has resulted in an external fistula. Deep abscesses are optimally treated by major excision.

Fistula

External fistulae comprised the largest group, usually following drainage of a superficial abscess. The majority of cases followed previous operation. There was a high incidence after appendicectomy (30%), bypass (13%) or diagnostic laparotomy (10%). The incidence was low after major resection (5%) which represented over 80% of the total operative experience in the series.

Fistulae do not close spontaneously and minor surgery has a poor record with a high recurrence rate. Major excision surgery with en bloc excision of the fistula and affected bowel has produced good results with minimal morbidity and mortality.

Conclusions

1. In a large series of Crohn’s disease the incidence of fistula and abscess has been low, possibly as the result of timely surgical excision before complications occur.

2. The results of the surgical treatment of fistulae compare favourably with early reports of immuno-suppressive drugs.

References


Observations on Experimentally Induced Colonic Pain

J. A. Ritchie, G. M. Ardran, and S. C. Truelove (From the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, and the Nuffield Institute for Medical Research, Oxford) Inflation of a balloon in the pelvic colon regularly produced pain, but its location and the degree of inflation required varied from one individual to another.

In most instances, the pain was felt either in the hypogastrium or in one or other of the iliac fossae, but sometimes it was anorectal and occasionally was felt in the back or in other areas of the abdomen. A few subjects experienced pain in different areas with repeated inflations or at different volumes of inflation.

Patients with diverticular disease or irritable colon syndrome were liable to develop pain at much lower levels of inflation than normal subjects. For example, only one out of 16 normal subjects developed pain at 60 ml inflation whereas more than half of the patients did so. The mean diameter of the balloon inflated to 60 ml was significantly less in patients with the irritable colon syndrome than in normal subjects; it was narrower still in patients with diverticular disease.

Observations on the mechanism of pain production suggest that increased tension in the wall of the gut is a crucial factor. However, the relationship of tension to the pain was different in the three clinical groups and this will be discussed.

Effect of Vagotomy and Pyloroplasty on the Interdigestive Myoelectrical Complex of the Stomach

I. H. Khan and B. S. Bedi (University Department of Surgery, Western Infirmary, Glasgow) There is good evidence of a close relationship between the electrical activity and the contractions of the stomach. Szurszewski identified a caudal moving band of large amplitude action potentials in the small bowel of fasted dogs. Carlson et al later showed that this interdigestive myoelectrical complex was controlled by the extrinsic nerves. The present experiments were designed to study the effect of vagotomy and pyloroplasty on the myoelectrical complex of the stomach in dogs.

Three mongrel dogs were used. Electrical activity was detected in healthy conscious dogs by using chronically implanted Ag-Ag CI electrodes. Prolonged recordings of the electrical activity showed periods with no action potentials (phase I) followed...
by periods (phase II, III, and IV) with action potentials. Each cycle (phase I—IV) lasted for 105 minutes and regularly recurred as long as the recordings were made (average eight hours). All dogs were studied for at least two months after vagotomy and a minimum of 10 myoelectrical complexes were recorded, in each dog, before and after vagotomy.

Pyloroplasty had no effect on these electrical complexes.

Vagotomy in dogs with previous pyloroplasty completely disrupted the regularly recurring complexes.

Reduction in the frequency of the pacemaker potential by an injection of insulin was abolished by vagotomy.

These experiments suggest that the vagus controls the myoelectrical complexes of the stomach.

References


The Two- to Four-Year Clinical Results of Highly Selective Vagotomy (Parietal-Cell Vagotomy) without a Drainage Procedure for Duodenal Ulcer

D. Johnston, J. C. Goligher, C. N. Pulvertaft, and B. E. Walker (Leeds/York Gastric Follow-up Clinic) and B. W. H and E. Jensen (Surgical Department I, Kommunehospitalen, Copenhagen, and the University of Arhus) Two years ago, we reported to the Society that the early results after highly selective vagotomy (HSV) were most encouraging, and last year we reported that it abolished postvagotomy diarrhoea.

We have treated 350 patients by HSV in the past 45 months, without operative mortality. There has been one proven recurrent ulcer, a gastric ulcer associated with gastric stasis. Three other patients were subjected to re-operation because of suspected recurrence, but no ulcer was found. Thus, to date, the incidence both of recurrence and of gastric retention is less than 1%.

Two hundred and six patients were reviewed, one year, and 105 patients, two years after HSV, the results being compared with those recorded in patients after vagotomy with drainage (V-D) or partial gastrectomy. Results in the two centres were in agreement. Results after selective V-D and truncal V-D were pooled, because they differed only slightly.

Comparing HSV with V-D, respective incidences were:—diarrhoea, 3% and 20% (p < 0.01); bile vomiting, 0% and 10% (p < 0.02); dumping, 6% and 14% (p < 0.05); perfect, Visick grade I clinical results, 62% and 40% (p < 0.02); and ‘fair’ (Visick grade III) results, 6% and 19% (p < 0.02).

Two to four years after operation, patients are faring significantly better after HSV than after vagotomy with a drainage procedure.

Reference


Is a Pyloroplasty Necessary with Proximal Gastric Vagotomy?

R. J. Clarke, B. M. Jaffe, B. J. Cledinnenn, and J. A. Williams (The General Hospital, Birmingham, The Department of Surgery, Washington University, St. Louis, USA, and The Royal Infirmary, Bristol) Holle concluded, from experimental work in dogs, that a pyloroplasty is always necessary with proximal gastric vagotomy (PGV) both to drain the stomach and to prevent excessive gastrin release and so excessive gastric secretion. This prospective trial assesses gastric acid secretion, serum gastrin, and gastric emptying in 20 patients before and three months after either PGV with (+P) or without (−P) pyloroplasty.

Acid secretion was measured after fasting, in response to insulin and to pentagastrin. Serum gastrin concentrations were measured by radioimmunoassay after fasting, insulin, and a standard meat extract drink. Gastric emptying of a hypertonic fluid meal was measured by double sampling dye dilution.

Acid secretion after insulin was reduced by 98% following PGV−P and by 93% following PGV+P and after pentagastrin by 67% following PGV−P and by 74% following PGV+P. Fasting gastrin levels increased by 56% after both operations. While the gastrin response to insulin was similar after both, the response to meat extract was twice as great after PGV−P. Gastric emptying is faster after than before operations, but PGV+P causes significantly more rapid gastric emptying than PGV−P.

Conclusions

After PGV the omission of a pyloroplasty results in more normal gastric emptying at the expense of an increased gastrin response to protein. It does not affect basal or maximal acid output.

References

Lysolecithin: A Factor in the Pathogenesis of Gastric Ulceration?

A. G. JOHNSON (Department of Surgery, Charing Cross Hospital Medical School, London) The regurgitation of bile salts into the stomach has been proposed as a cause of gastric ulceration. The phospholipid, lysolecithin, which is formed in the duodenum when phospholipase A in pancreatic juice hydrolyses the lecithin in bile, is also a strong detergent and highly toxic to cell membranes. This study was designed to determine whether in the night gastric juice of gastric ulcer patients, lysolecithin occurs in sufficient concentration to cause mucosal damage.

A nasogastric tube was positioned at 9.30 pm by a non-fluoroscopic method (Hassan and Hobsley, 1968) and 10 ml samples taken at two hourly intervals throughout the night. Lysolecithin was measured by silicic acid column chromatography (Borgstrom, 1957), and its purity confirmed by thin-layer chromatography.

Twenty-seven patients were studied. The mean of the concentrations of all night samples for gastric ulcer patients (212 μg/ml) was significantly higher (p < 0.001) than for normal control patients (23 μg/ml). Duodenal ulcer patients had normal or slightly raised levels (mean 69 μg/ml). The values found in gastric ulcer patients with peak levels up to 1369 μg/ml are in the range that causes considerable gastric mucosal damage under experimental conditions (Davenport, 1970) and it is concluded that lysolecithin may be as important or more important than bile salts in the aetiology of gastric ulceration.

References


The Effect of Antral Acidification on Gastric Secretion Stimulated by Pentagastrin

M. H. WHEELER AND A. P. M. FORREST (Department of Clinical Surgery, The Royal Infirmary, Edinburgh) There is some evidence that an antral inhibitory hormone and a nervous mechanism might be involved in the antral inhibition of gastric secretion. Such mechanisms might be relevant to both the medical and surgical management of duodenal ulcer. It has been suggested that preservation of an inhibitory reflex is an advantage of the operation of highly selective vagotomy.

A series of experiments have been performed in dogs to seek evidence for the existence of an antral inhibitory action not related to the control of endogenous gastrin release. Dogs were prepared with innervated antral and either innervated or denervated fundic pouches. Two series of tests were carried out in which submaximal doses of pentagastrin were infused intravenously and the acid secretory response was monitored. The antral pouches were perfused at pH 7.0 and pH 1.0 either in separate tests or in the course of a single test. There was no evidence of inhibition of acid or pepsin secretion.

As in these studies acid secreted by the main stomach could enter the duodenum, the duodenal inhibitory mechanism might have confused the interpretation of results by masking antral inhibition. Further antral acidification tests were therefore performed during which acid from the main stomach was diverted to the exterior by means of a gastric fistula. Again, no inhibition of gastric secretion occurred.

These studies provide no support for either a hormonal or neuronal antral inhibitory mechanism active against pentagastrin.

Gastric Metabolism of Histamine

C. F. CODE, W. E. R. GREEN, H. D. RITCHIE, J. F. SCHLEGEL, AND J. C. KENNEDY (Mayo Clinic and Mayo Foundation, Rochester, Minnesota, and Surgical Unit, The London Hospital, London, England) Recognizable products of histamine metabolism were compared in gastric juice collected from Heidenhain pouches in conscious dogs and from completely isolated and perfused canine stomachs. The experiments were designed to determine which products of histamine metabolism detectable in the gastric juice are the outcome of processes occurring in the stomach alone. 14C-labelled histamine was administered continuously, intravenously to the pouch dogs and intragastrically to the isolated stomachs. All gastric juice secreted by the pouches and the isolated stomachs was collected and the proportions of histamine, N-methylhistamine (NMH), N-dimethylhistamine (NDMH), 1-4 methylhistamine (1-4 MH), imidazoleacetic acid, 1-4 methylimidazoleacetic acid, acetylhistamine, and histaminol were determined by two-dimensional thin-layer chromatography after preparation of extracts of the juice. All of the primary products of histamine methylation, NMH, NDMH, and 1-4 MH, were present in the secretion of the isolated stomach in proportions similar to those in the juice from the pouches of the intact animals, while all of the other products were absent, or nearly so, in juice from the isolated stomach. Methylation is thus the sole route of metabolism of histamine in the stomach of dogs. This finding supports the concept that methylation...
in the stomach provides a mechanism for control of secretion.

This investigation was supported by grants from the Wellcome Trust, England, and the John A. Hartford Foundation, Inc., U.S.A.

Shock in Acute Pancreatitis and Hypovolaemia

P. FARRELL, P. FITZGERALD, O. FITZGERALD, K. MCGEENY, C. GEOGHEGAN, AND A. HEFFERNAN (Department of Surgery, Medicine, and Therapeutics, University College, Dublin) Shock in acute pancreatitis is indicative of a poor prognosis. In acute pancreatitis in dogs with hypotension, angiotensin II levels fell from 30 pg/ml to 6-4 pg/ml. Both parameters returned to normal on recovery. In acute pancreatitis without hypotension, angiotensin II remained stable, suggesting the activity of an angiotensinase in the shock of acute pancreatitis.

Trypsin when complexed with the plasma protease inhibitor alpha-macroglobulin possesses esterase activity (TPE). We have shown that this TPE in vitro behaves as an angiotensinase. With shock in canine acute pancreatitis TPE activity rises.

In canine hypovolaemia hypotension results in a rise in angiotensin II levels (16 pg/ml to 24 pg/ml). This reverts to normal on volume replacement. There was a concomitant moderate rise in plasma TPE activity.

Systemic kinin release in the shock of canine acute pancreatitis has not been shown. We conclude that TPE acting as an angiotensinase in vivo may form part of the aetiology of the shock in acute pancreatitis.

References


A Simultaneous Combined Pancreatic Test

S. NUNDY, J. H. BARON, J. S. M. BEALES, R. HEAF, J. P. LAVENDER, N. O'HIGGINS, AND E. PEARSE (Departments of Surgery, Diagnostic Radiology, and Diagnostic Cytology, Royal Postgraduate Medical School, London) To study pancreatic disease we have combined five standard procedures which can be performed in one morning and are without side effects: (a) near maximum bicarbonate and enzyme output, (b) maximum 75Se output, (c) scan, (d) cytology, (e) hypotonic duodenography.

The patient fasts overnight and a double-lumen Drelling tube is passed into the duodenum which is aspirated for three hours (12 x 15 min). After basal aspiration for 30 min a secretin-pancreozymin test is performed with an intravenous infusion of 0-25 u/kg-h secretin (GIH) and 16 u/kg-h pancreozymin (GIH) for 90 min and a single intravenous injection of 75Se selenomethionine 3 μci/kg is given. The pancreas is scanned with a gamma camera. Propantheline 30 mg is injected intravenously at the end of the tests and a hypotonic duodogram is performed using a standard double-contrast technique. The duodenal aspirates are analysed for volume, bicarbonate concentration, tryptic activity, and 75Se counts; Papanicoulo smears are made.

Four groups of patients have been studied: no pancreatic disease, acute pancreatitis (four weeks after the acute episode), chronic pancreatitis, and carcinoma of the pancreas.

In our first 50 patients: (a) a single secretion test has been of little value in distinguishing between different pancreatic diseases. (b) The cytological examination was most accurate and pancreatic scan least accurate. (c) The combined test distinguished patients without pancreatic disease from those with chronic pancreatitis and those with carcinoma of the pancreas.

An Appraisal of 75Se-Selenomethionine Scanning as a Test of Pancreatic Function: A Comparison with the Secretin-Pancreozymin Test

JOAN BRAGANZA, MAIR CRITCHLEY, H. T. HOWAT, H. J. TESTA, AND H. B. TORRANCE (Clinical Division of Gastroenterology and the Department of Medical Physics, Manchester Royal Infirmary, Manchester M13 9WL) Photoscans of the pancreas after the incorporation of 75Se-selenomethionine are interpreted in terms of both anatomy and function. Though the position of the pancreas and its distortion and involvement by tumours are now well defined, the assessment of the functional capacity of the pancreas by scanning remains empirical, being usually gauged by comparing the photoscan with the observer's appreciation of a normal scan. Few attempts have been made to correlate the photoscan obtained in pancreatic disease with reliable tests of pancreatic function.

In over 100 patients with and without pancreatic disease the isotope uptake in pancreatic scans, objectively determined, has been compared with pancreatic function assessed by the secretin-pancreozymin test, developed and used extensively in our division. The volume of duodenal juice after secretin stimulation shows a poor correlation to the uptake of 75Se selenomethionine. In chronic pancreatitis and cancer of the pancreas, photoscans correlate well with maximal bicarbonate concentration and post-secretin output of bicarbonate but less well with amylase output.
An Evaluation of a Breath Test to Detect Altered Bile Acid Metabolism

O. JAMES, J. E. AGNEW, RUBY LYDFORD, AND A. D. BOUCHIER (Department of Medicine and Physics, The Royal Free Hospital, London) Recently a test has been described1,3,3 claiming to be a convenient and reliable method of detecting bacterial deconjugation of bile acids. The test might therefore be thought to be useful in the investigation of bacterial overgrowth syndromes of the small bowel. In the test 14CO₂ specific activity of breath samples obtained after a meal containing cholyglycine-L¹⁴C are measured at intervals for up to 24 hours.

We report an evaluation of the breath test on 70 persons, including 20 normal subjects; from this group a normal range of 14CO₂ specific activity has been constructed. The patients comprised four principal groups: inflammatory bowel disease, ileal resection, recurrent cholangitis, and primary biliary cirrhosis, together with a range of other gastro-intestinal and hepatic conditions.

Markedly abnormal results were found in patients with terminal ileal resection, Crohn’s disease, gastro-colic fistula, bacterial overgrowth syndrome, and recurrent cholangitis. Minor abnormalities in the test, not previously described, have been found in primary biliary cirrhosis.

The shape of the 14CO₂ specific activity time curves and the reproducibility of the test will be discussed, and the results compared with the small bowel flora, radiology and other findings.

References

Bile Salt Absorption following Small Bowel Resection in the Rat

P. M. PERRY, JUNE WHITE, AND R. H. DOWLING (Departments of Medicine and Surgery, Royal Postgraduate Medical School, Ducane Road, London, and St. Bartholomew’s Hospital, London) The enterohepatic circulation (EHC) of bile salts (BS) ensures adequate concentrations of BS in the jejunum for the digestion and absorption of fat. In turn, this bile salt EHC is largely maintained by active BS reabsorption from the ileum and to a lesser extent by passive BS diffusion from jejunum and colon. Intestinal absorption depends on the number of epithelial cells and since small bowel resection causes mucosal hyperplasia (particularly in the ileum) we looked for (a) increased BS diffusion from jejunum and colon as compensation for loss of active transport following ileectomy, and (b) supranormal BS absorption by residual ileum after proximal small bowel resection.

Bile salt absorption was measured using an in vivo recirculation perfusion system in bile fistula sham-operated control rats and in animals three to six months after either proximal or distal small bowel resection. 14C monomer and micellar cholate and taurocholate absorption were measured both by fall in luminal BS concentration and by cumulative isotope excretion in bile.

Our results show: (1) in control rats, the ratio of ileal to jejunal BS absorption (per unit length of intestine) is 9:2:5:1; (2) after ileal resection, colonic absorption did not change but jejunal cholate (P<0.05) and taurocholate (P<0.01) absorption were both significantly increased; (3) following jejunectomy, active BS transport by hyperplastic ileum became supranormal, with expansion of the BS pool.

It was concluded that following ileal resection, compensatory increases in jejunal bile salt absorption partially conserve the EHC. Ileal mucosal hyperplasia produced by jejunectomy increases bile salt absorption.

Why are Primary Bile Acids Present in Cholera Diarrhoea?

M. A. EASTWOOD, J. M. FINDLAY, R. MACRAE, AND W. D. MITCHELL (Wolfson Gastrointestinal Laboratory, Gastrointestinal Unit, Western General Hospital and University of Edinburgh) We have recently shown that in patients who have ileal resection (I.R.) their faeces contain mainly primary bile acids and cholesterol1. An understanding of this phenomenon may affect management.

There may be several reasons. We had anticipated that transit time would be rapid, thus modifying bacterial activity. In eight patients (I.R.) the mean transit time2 (plastic markers) was 58 hours (range 25-120 hours). In eight normals the mean transit time was 61-4 hours (range 24-124 hours). The value of the use of plastic markers for transit time studies in diarrhoeal states was examined. Polyethylene glycol (water soluble) and chromium sesquioxide (solid phase) were administered for seven days. Recovery patterns suggest no 'streaming' effects justified the use of plastic markers.

In these patients the faecal extraction of bile acids is markedly increased. The homogenate of normal faeces was incubated anaerobically with taurocholate, glycocholate, and taurochenodeoxycholic acid. Whilst it was possible to influence deconjugation at 15 mM it was possible to abolish 7α-
dehydroxylation at concentrations found in diarrhoeal stool (> 4 mM).

It would appear that the presence of primary bile acids is due to inhibition of bacterial activity by bile acids rather than through altered transit time.

References


A New Technique for Examining Intestinal Biopsies

B. L. CHAPMAN, K. HENRY, F. PAICE, J. S. STEWART, AND N. F. COGHILL (Medical Department, West Middlesex Hospital, Department of Morbid Anatomy, Royal Postgraduate Medical School, and MRC Cyclotron Unit, Hammersmith Hospital, London) A new technique for measuring changes in the architecture of the small intestinal mucosa has been developed. Current techniques measure only single dimensions, or involve indices dependent on villous structure. They usually have overlapping ranges of values for control and flat mucosae, and at best only a threefold difference between the mean values.

We have used a modification of the technique of quantitative colour television image analysis to measure the areas occupied by the surface and crypt epithelial cells in proximal jejunal biopsies. From these measurements the ratios of surface to crypt cell areas were calculated. The mean ratio was 2.2 in 12 control mucosae. In 12 untreated flat coeliac mucosae the mean ratio was only 0.25. This ninefold difference, which was statistically highly significant, was greater than that for any measurement previously reported.

The technique was used to measure the progressive changes in the mucosae of coeliac patients treated with a gluten-free diet. The surface-to-crypt area ratio gradually increased in patients who kept to a strict diet. In some, a change was detectable at three or seven days. In both control and abnormal mucosae, the area ratios correlated very closely with the most accurate of the conventional measurements, the surface cell height.

Cell Production Rate in Mucosa of Untreated Coeliac Disease

N. A. WRIGHT, A. J. WATSON, A. R. MORLEY, D. R. APPLETON, AND JANET M. MARKS (Departments of Pathology, Medical Statistics and Dermatology, University of Newcastle upon Tyne) We have already established that the mitotic index in duodenojejunal crypt-cells is elevated in untreated coeliac disease, and that the production rate of crypt cells is increased \( \times 5 \) to \( \times 6 \). The validity of this conclusion depends on the assumption that there is no significant change in mitotic duration, a parameter upon which the value of the mitotic index heavily depends.

Mitotic index = mitotic duration

\[ \text{cell-cycle duration} \]

A shortened division cycle seems inherently more probable and has been postulated by others. Our earlier observations have been extended by using a stathmokinetic technique with vincristine. We have studied a patient with morphologically normal mucosa and another with the flat mucosa and total villous atrophy of untreated coeliac disease (associated in this instance with dermatitis herpetiformis). We find a small increase in mitotic duration in the coeliac mucosa but cell-cycle time is halved. These parameters have not hitherto been reported in coeliac disease. We also confirm that cell production rate is increased \( \times 5 \) to \( \times 6 \) and that crypt-cell migration rate is increased. These findings are in keeping with the existence of a hyperproductive mucosal state in untreated coeliac disease.

References


Two Types of 'Coeliac' Disease?

R. E. BARRY AND A. E. READ (Department of Medicine, University of Bristol) Although an association between malignant abdominal lymphoma and malabsorption has been known since 1937, it was not until shortly after the introduction of peroral jejunal biopsy in 1956 that some cases of lymphoma with malabsorption were shown to have the 'flat' jejunal biopsy characteristic of coeliac disease. In 1962 Gough, Read, and Naish suggested that malignant lymphoma may occur as a complication of coeliac disease, a suggestion subsequently supported by the publication of a study of a large series of cases of coeliac disease by Harris, Cooke, Thompson, and Waterhouse (1967).

We have recently studied the mucosal dynamics of the small bowel in the presence of malignancy and established the mechanism by which architectural changes may be produced. Because of the association
between coeliac disease (in which profound changes in the mucosal architecture occur) and malignancy of the lymphoreticular type, we have investigated 15 cases previously diagnosed as adult coeliac disease who presented with malabsorption and subtotal villous atrophy.

Studies of the mucosal dynamics as indicated by (1) epithelial cell (DNA) loss rate and (2) mucosal thickness and mitotic index suggest that these patients fall into two distinct groups, the mucosal changes in each group being produced by different mechanisms. The subsequent progress of these patients in their response to a gluten-free diet and development of grave complications suggest that the distinction between the two groups has direct clinical relevance. It is suggested that a consideration of mucosal dynamics in 'coeliac disease' is of considerable value in prognosis.

References


Change in Jejunal Structure and Function in Dermatitis Herpetiformis: Effect of Gluten-Free Diet and Corticosteroids

PARVEEN KUMAR, D. B. A. SILK, M. L. CLARK, AND M. DAWSON (Departments of Gastroenterology and Medicine, St. Bartholomew's Hospital, London).

Although there are similarities between coeliac disease and the enteropathy associated with dermatitis herpetiformis (DH), there is controversy over the response of the latter to a gluten-free diet. Prednisolone has recently been shown to improve the mucosal structure in coeliac disease. We have therefore investigated the response of DH enteropathy, both in terms of structure and function, to either gluten withdrawal or corticosteroid therapy. The function studies performed using a double-lumen perfusion technique were undertaken because of the claim that the lesion in this condition is patchy.

In the four patients studied so far we have shown a significant increase in surface cell heights and villous heights with a corresponding decrease in mucosal thickness. Absorption of glucose (from a 56 mM solution), and the amino acids glycine and alanine (from a mixture of glycine and alanine as well as the dipeptide glycylalanine) showed a dramatic improvement after treatment. Bicarbonate absorption (from a 35 mM solution) showed a less striking improve-

Intestinal Permeability in Coeliac Disease

I. S. MENZIES (Department of Clinical Chemistry, St. Thomas's Hospital, London) (introduced by B. CREAMER)

Lactulose (β-1-4 galactosido-fructose) is neither hydrolysed by the human small intestine nor metabolized significantly, and is quantitatively recovered from the urine after intravenous injection. The amount reaching the urine after ingestion therefore reflects the state of intestinal permeability. Müller, using an oral loading technique, found no difference in urinary lactulose excretion between normal subjects and patients with coeliac disease. However, because intestinal permeability temporarily increases when hypertonic solutions are ingested, this test was re-evaluated in relation to the tonicity of ingested solution, and different conclusions were obtained.

The excretion of lactulose, as measured by quantitative paper chromatography, was estimated in 20 healthy adults during five hours after both an isotonic (5g lactulose in 100 ml water) and a hypertonic (5g lactulose + 40g sucrose in 100 ml water) load. The excretion following the isotonic load was 23.5 ± 22 mg and following the hypertonic load was 25.7 ± 17.4 mg (mean ± 2 standard deviations). In 23 patients with coeliac disease, six of whom were untreated, the excretion of lactulose was greater than normal in 90% after the hypertonic load, but in only 25% after the isotonic load. All the untreated cases showed abnormal permeability following the hypertonic load.

In conclusion, the hypertonic lactulose test showed considerable potential as a screening procedure, and the isotonic test correlated well with the severity of the disease.

References


J. D. MITCHELL, P. BHATHAL, H. CORNELL, AND R. R. W. TOWNLEY (Introduced by C. C. BOOTH) (University of Melbourne, Departments of Paediatrics and Pathology, and the Gastroenterology Unit, Royal Childrens Hospital, Melbourne, Australia) The purpose of this study was to develop an in-vitro system for investigating coeliac disease. Small slices of single duodenal biopsies were maintained in vitro for 24 hours and used to study the effect on epithelial cell ultrastructure of the addition to the culture medium of a digest of gluten (peptic-tryptic-cotryzime (PTC) digest of gliadin): The culture medium was Eagle's (basal) medium containing foetal calf serum (10%), glucose to 2 mg/ml, antibiotics, and sodium bicarbonate. Tissue slices were placed in roller tubes on a slowly rotating drum situated inside an incubator at 37°C. A constant flow of a gas mixture of 95% O₂ and 5% CO₂ maintained the atmosphere within the incubator.

Cultures
Cultures of duodenal biopsy tissue from two normal controls and an infant with mucoviscidosis were compared with cultures of tissue from one young adult and two children with untreated coeliac disease. Individual slices of each biopsy specimen were maintained in medium alone and in medium to which 5 mg/ml PTC gliadin had been added. Tissue slices from five of the individuals studied were cultured in triplicate pairs and from one coeliac infant as only a single paired culture.

RESULTS
Results, based on an ultrastructural comparison of tissue before and after culture for 24 hours, indicated that 5 mg/ml PTC gliadin specifically inhibited maintenance of coeliac epithelial cell morphology in this in-vitro system. Mature enterocytes of non-coeliac origin maintained their ultrastructural characteristics both in the presence and absence of the gluten fraction. Coeliac tissue cultured in medium alone had epithelial cell morphology which tended, if anything, to approach the normal appearance as seen in treated coeliac disease. However, when cultured for 24 hours in medium containing PTC gliadin, coeliac enterocytes showed marked loss of microvilli with marked blunting and fusion of those remaining. Epithelial cell height was reduced and variable intracellular ultrastructural changes occurred.

This system shows promise as an in-vitro model for the study of coeliac disease and has the advantage that portions of a biopsy obtained primarily for diagnostic purposes can be used.

Vagotomy and Gastrin Secretion

D. BYRNE AND T. SCRATCHERD (Wolfson Gastrointestinal Laboratories and Teaching and Research Centre, Western General Hospital and University of Edinburgh) It has generally been assumed that gastrin release during insulin-induced hypoglycaemia is mediated solely by the vagus nerves. The present study was undertaken to determine if gastrin secretion during hypoglycaemia was abolished by surgical vagotomy.

Using a sensitive radioimmunoassay gastrin estimations were determined on serum samples taken before and during insulin-induced hypoglycaemia from 11 patients, six months after surgical vagotomy. The gastric contents were continuously aspirated during the procedure. Studies were also performed on dogs to determine the gastrin response to hypoglycaemia following cholinergic and adrenergic blockade.

Following 'complete vagotomy' (six patients) serum gastrin levels were significantly elevated (130 ± SE 35 pg/ml, normal 49 ± SE 8 pg/ml). A decrease in mean gastrin concentration occurred during the basal hour (130 ± SE 35 to 98 ± SE 31 pg/ml). After administration of insulin there was a latent period of 30 minutes followed by a consistent rise in serum gastrin above the basal level. A similar gastrin response during hypoglycaemia was observed in two patients with histologically proven gastrinomas.

These studies demonstrate a non-vagal release of gastrin during insulin-induced hypoglycaemia. Possible mechanisms for this release will be discussed.

Antral G-cell Hyperplasia with Hypergastrinaemia Producing a Zollinger-Ellison Syndrome

R. Y. WILSON, B. E. BOYES, B. H. STagg, M. R. LEWIN, JULIA M. POLAK, A. G. E. PEARSE, I. W. DYMOCk, AND D. J. COWLEY (Departments of Surgery and Medicine, University Hospital of South Manchester, Department of Surgery, University College Hospital, London, and Department of Histochemistry, Royal Postgraduate Medical School, London) It has recently been postulated that some patients with the Zollinger-Ellison syndrome have hypergastrinaemia and hyperplasia of the antral G-cells but no tumour. This subgroup has been classified as Z-E syndrome type I. We have treated such a patient by vagoctomy and antrectomy with subsequent return of fasting plasma gastrin and acid secretion to normal.

A 17-year-old male had a four-year history of duodenal ulcer confirmed radiologically. Gastric secretion tests showed acid hypersecretion (BAO 13-6 m-equiv/h, basal acidity 92 m-equiv/l, PAO
pentagastrin 47.8 m-equiv/h). Fasting plasma gastrin was 8350 pg/ml (normal 50-170 pg/ml). Pancreas scan and angiography showed no abnormalities.

At laparotomy duodenal ulceration was confirmed but no pancreatic or other tumours were found. Truncal vagotomy and antrectomy was performed with distal pancreatectomy. Immunofluorescent staining showed hyperplasia of G cells in the resected antrum but with a normal pancreas and duodenum.

Since operation he has been symptom-free and two months later fasting plasma gastrin was <50 pg/ml and the acid secretion was reduced by 92% (BAO 0.45 m-equiv/h, PAO pentagastrin 4.8 m-equiv/h).

This report confirms that type I Z-E syndrome is a clinical entity and suggests that it may be treated by a less radical operation than total gastrectomy.

Reference


Acid Secretion, Plasma Gastrin Levels and the Diagnosis of the Zollinger-Ellison Syndrome

M. R. LEWIN, B. H. STAGG, AND C. G. CLARK (Department of Surgery, University College Hospital Medical School, London) Fasting plasma gastrin levels have been determined by radioimmunoassay for 75 patients with suspected Zollinger-Ellison syndrome. Fifty-two patients had gastrin levels within the normal range (50—170 pg/ml), and 23 patients had gastrin levels in the range 800—9500 pg/ml. A diagnosis of Zollinger-Ellison syndrome was confirmed in 16 of the latter, the remaining seven patients being lost to follow up. Acid secretion studies were carried out on the majority of patients, and the secretory patterns evaluated to determine their usefulness in the diagnosis of the syndrome.

The patients could be divided into three main groups. Group 1 consisted of 23 patients referred with a short history of severe dyspepsia associated with high acid secretion and/or multiple ulceration. Group 2 consisted of 39 patients referred with recurrent ulceration after previous surgery. Group 3 consisted of nine patients with a variety of symptoms, some of which occur in the Zollinger-Ellison syndrome. Hypergastrinaemia was observed in eight patients in group 1 and 15 patients in group 2, but in none of the group 3 patients. Acid secretory patterns were suggestive of the disease in less than 50% of the patients with the Zollinger-Ellison syndrome, but the radioimmunoassay gave unequivocal results.

The Relationship between the Rate of Gastric Emptying and Release of Insulin after Partial Gastrectomy and in the Idiopathic Lag Storage Curve

G. H. TOMKIN AND A. M. CONNELL (Royal Victoria Hospital, Belfast, and Division of Gastroenterology, University of Cincinnati, Cincinnati, Ohio) In a recent paper1 pyloroplasty, but not partial gastrectomy, was associated with raised insulin levels after a glucose load, suggesting that a major insulin releasing factor(s) in the antrum was removed by partial gastrectomy.

This study examines the relationship between gastric emptying, glucose absorption, and insulin release in (1) controls, (2) newly diagnosed mild diabetics, (3) patients with an 'idiopathic' lag storage curve, and (4) patients with a lag storage curve after partial gastrectomy.

RESULTS

Group 4 emptied faster than group 1 (t = 3.5, p < 0.01). There was no difference between the emptying times of groups 1 and 3 (p > 0.05). The insulin response to the glucose load was greater in group 4 than in group 3 (t = 3.26, p < 0.05) and in group 4 but not in the other groups and the insulin response correlated with the emptying rate (r = 0.94, p < 0.005).

These studies demonstrate that the idiopathic lag curve is not related to rapid gastric emptying whereas there is a correlation between insulin release and rate of emptying in the postgastrectomy patients. Removal of the antrum is not associated with a diminished insulin response after a glucose load. It is concluded that insulin stimulation by gastrointestinal releasing factor(s) depend on the length of time that glucose is in contact with the body of the stomach and/or the upper small bowel.

Reference


A Radioimmunoassay for Secretin Using Antibodies Raised to Pure Natural and Synthetic Hormone

J. D. TEALE, K. D. BUCHANAN, AND G. HARPER (introduced by A. H. G. LOVE) (Department of Medicine, The Queen's University of Belfast) A radioimmunoassay for secretin has been established. Iodination of synthetic secretin (Squibb) to specific activities of 40 to 75 mCi/mg has been achieved using a modification of the procedure of Hunter and Greenwood (1962). Antibodies were raised using as little as 5 µg of pure natural secretin
(Jorpes) in the unconjugated form and adsorbed onto carbon (Boyd and Peart, 1968). Higher antibody titres were achieved by immunization with 25 μg of unconjugated synthetic secretin or 30 to 90 μg of natural hormone conjugated to ovalbumin.

Standard curves were constructed and pure natural, synthetic and crude (Boots) hormone preparations were found to inhibit binding of the labelled hormone to antibodies. Antisera from animals immunized with either natural or synthetic secretin showed equal reaction with both natural and synthetic standards. The immunoassay could detect an absolute amount of 40 pg of secretin in buffer solution. No cross-reaction was observed with insulin, pancreatic and gut glucagon, gastrin, and cholecystokinin-pancreozymin.

Immunoreactive secretin has been detected in acid-alcohol extracts of duodenum and upper and mid parts of jejunum of pig. None was found in the stomach, pancreas, liver, spleen, lower jejunum, ileum, and colon.

References


Secretin and Pancreozymin Effect on Salivary Amylase Concentration in Man

H. MULCAHY, O. FITZGERALD, AND K. F. McGEENEY (Department of Medicine & Therapeutics, University College, Dublin 4) During serum enzyme evocative tests using secretin and pancreozymin (PZ-CCK) a rise in salivary amylase concentration was observed.

Fasting subjects were given secretin IV 1·5 units/kg, and following a 30-minute interval 1·5 units/kg PZ-CCK. Saliva was collected before secretin (control period) and then at 30-minute intervals, a total of five samples being taken from each subject. In each of seven subjects a rise in salivary amylase concentration was noted following administration of secretin. This rise was augmented in each case by PZ-CCK.

In pure parotid saliva an increase in amylase concentration in response to the two hormones was also observed.

The parotid duct of fasting subjects was covered with a Curby cup and the basal secretion collected for one hour. Secretin and PZ-CCK were given as before and parotid saliva was collected at 30-minute intervals. A rise in amylase concentration in response to secretin was again augmented following PZ-CCK. The maximum rise observed was 50% of the resting value (5 × 10⁶ iu).

From our experiments on the conscious human, it would appear that the gastrointestinal hormones exert an effect on the composition of human saliva, unlike the situation in the dog.

Reference


Double-contrast (Air-contrast) Radiology of the Stomach and Duodenum

W. G. SCOTT-HARDEN (Cumberland Infirmary, Carlisle) This paper describes our experience of routine double-contrast radiology of the stomach and duodenum. The decision to replace the traditional barium meal by air-contrast studies six years ago was the result of critical assessment of the shortcomings of the traditional method, by endoscopy in patients not submitted to surgery, and by the findings at laparotomy.

The traditional barium meal relies upon tangential irregularities and irregularities en face demonstrated by palpation at the time of screening. Both are increasingly difficult to achieve when the stomach lies obliquely and become impossible when it is horizontal. Furthermore an error of observation at the time of screening is too often irretrievable by study of the film series.

The double-contrast method suffers none of these difficulties and it has been proved that minute ulcers are demonstrable. Progress of an ulcer to complete healing can be defined and the mucosal characteristics of malignancy are clearly demonstrable.

The double-contrast technique must be simple to permit routine use within the work load of the National Health Service. A simple method is described.

This contrast method has also been used throughout this period in the acute bleed with very obvious advantage and illustrations of these cases are included in this paper.

References


Enterokinase Levels in Intestinal Mucosa from Normal Subjects and Patients with Coeliac Disease

J. F. WOODLEY and ROSALEEN KEANE (introduced by C. F. MCCARTHY) (Department of Biochemistry, University College, Galway, Ireland) Enterokinase levels were measured in peroral biopsy specimens of intestinal mucosa from coeliac patients and from
normal and symptomatic controls. The levels of enterokinase were compared with those of sucrase and lactase, expressed as specific activities (mIU/mg of protein). The results were divided on the basis of anatomical location, ie, duodenal or jejunal, and on histological appearance, ie, normal or total villous atrophy. In the series of biopsies from the duodenum, 15 with normal histology and 10 showing a 'flat' mucosa, typical of coeliac disease, were analysed. The biopsies from the coeliac patients had levels of sucrase and lactase which were 75% lower than normals, whereas there was no significant reduction in the enterokinase levels. Results from jejunal biopsies showed a similar trend. In the 33 normal and nine coeliac biopsies studied, the sucrase and lactase levels were reduced 80-90% in the coeliac samples, with no significant change in the enterokinase levels.

These results do not support the hypothesis (Holmes and Lobley, 1970; Nordstrom and Dahlqvist, 1971) that enterokinase is a 'brush border' enzyme like sucrase and lactase, but would be consistent with the idea that it is adsorbed to the cell membrane after secretion.

References

Enterokinase in Human Duodenal Juice Following Secretin and Pancreozymin and its Relationship to Bile Salts and Trypsin

S. MOSS, R. W. LOBLEY, AND R. HOLMES (Department of Gastroenterology, The Royal Infirmary, Manchester)

Enterokinase has been localized to the brush border of the epithelial cell of small intestinal mucosa, and it is also present in fluid aspirated from the duodenum in humans. Both bile salts and trypsin release enterokinase from guinea pig brush borders in vitro, and it has been suggested that in vivo enterokinase is released from the brush borders of intact epithelial cells by the action of bile salts and of trypsin present in duodenal fluid.

The duodenum was intubated in humans and the amount of enterokinase in aspirated juice estimated after removing trypsin by gel filtration. Following the administration of both secretin and pancreozymin there was a significant rise in the output of enterokinase in duodenal juice similar to that observed for alkaline phosphatase, but only negligible amounts of disaccharidases were detected. The postsecretin rise in enterokinase output also occurred when bile salt levels remained low, and in one patient with complete biliary obstruction enterokinase output rose following secretin stimulation although bile salts were undetectable throughout. Duodenal fluid from a patient with pancreatic atrophy contained virtually no trypsin, yet the rise in enterokinase output still occurred after secretin and pancreozymin stimulation.

Thus the rise in output of enterokinase in duodenal juice after secretin and pancreozymin stimulation is independent of bile salt concentration, and does not appear to require the presence of trypsin.

Clinical Relevance of Endoscopic Retrograde Cholangio-pancreatography

P. B. COTTON AND J. S. M. BEALES (St. Thomas’ Hospital, London) Endoscopic cannulation of the papilla of Vater has succeeded in 80 out of our first 100 attempts, and relevant retrograde cholangiograms and/or pancreatograms have been obtained in 72 patients. In many patients where cannulation failed, duodenal fluid alone provided useful visual or histological diagnostic information. Significant complications have so far been confined to two cases of septicaemia (successfully treated). However, the procedure is not simple and requires the cooperation of endoscopist, radiologist, assistant, and patient for up to one hour. Is it worth while?

Where preoperative diagnosis is sought in a patient with obvious obstructive jaundice, transcatheter cholangiography (in experienced hands) is simpler and better. In the differentiation of medical from surgical jaundice, however, the retrograde route may be equally valuable since both normal and abnormal duct systems can thereby be outlined. This is also the case in patients with biliary type symptoms, particularly after cholecystectomy, in whom standard intravenous or infusion cholangiography has failed.

Much remains to be learnt concerning the range of normality, and the specificity of abnormality in pancreatic duct radiographs. Retrograde pancreatography promises to be a useful guide to the operative approach in patients with known chronic pancreatitis, for instance in the localization of strictures; however, similar strictures may be seen in carcinoma.

Pancreatography has not yet been shown to be more discriminating than already available diagnostic tests in patients with suspected pancreatic disease.
The Natural History of Hepatitis-associated (Australia)-antigen (HAA)-positive Chronic Liver Disease

F. J. DUDLEY, P. J. SCHEUER, AND S. SHERLOCK (Departments of Medicine and Pathology, Royal Free Hospital, London) Fifty-nine patients with HAA-positive chronic liver disease have been studied. Onset was varied. Continued hepatic injury after acute hepatitis was documented in 30 (51%). Seven others (12%) gave a history of acute hepatitis but were asymptomatic for a variable period before chronic liver disease was diagnosed. The other 22 (37%) had no history of acute hepatitis and presented as chronic liver disease.

Corticosteroid therapy was commonly used early in the course of the original episode of acute hepatitis. Its subsequent withdrawal and reintroduction was often associated with exacerbations and remissions of disease activity. Such therapy markedly accentuated natural fluctuations in activity. Patients with established cirrhosis also improved both symptomatically and biochemically from steroid therapy.

Six patients presented initially as primary liver cell carcinoma and all have died. Thirty-three other patients have been followed for an average of 23 months (range six—99). Three have died, two from complicating primary liver cell carcinoma, and one from haematemesis and hepatocellular failure. Only two other patients have shown any clinical or biochemical deterioration during the follow-up period. The other 28 (85%) have either improved or remained static.

Liver biopsies of all 59 patients were reviewed. Diagnoses included acute hepatitis with possible transition to chronic hepatitis, chronic persistent, lobular, or aggressive hepatitis, cirrhosis, and primary liver cell carcinoma. Excluding patients with cancer, follow-up biopsies were available in 21 patients, seven showing a significant change in the type of hepatitis, usually toward a more active lesion.

Asymptomatic Liver Disease in Australia-antigen-positive Blood Donors

I. L. WOOLF, B. E. BOYES, I. W. DYMOCK, P. H. RENTON, AND F. STRATTON (Department of Medicine, University Hospital of South Manchester, and the National Blood Transfusion Service, Manchester) Routine testing of donor blood for the hepatitis-associated antigen and antibody has been carried out for some time. Twenty-two donors were found on this routine screening to be HAA positive. These have been reviewed clinically and in some cases more detailed investigations carried out. Three of the donors had received either blood or plasma. Three had been extensively tattooed and six had had contact with hepatitis. Three donors became antigen negative during the period of review.

Six of the 22 had abnormal liver function tests. Bromsulphathalein retention tests were carried out on nine donors and in four abnormal retention was found. In nine donors liver biopsy was performed and in only two was histology considered normal. The abnormalities encountered were a chronic aggressive hepatitis in two donors, chronic persistent hepatitis in two donors, focal parenchymal necrosis in two donors, and a resolving viral hepatitis in one donor.

Twelve donors were found to have the antibody to Australia antigen and in two of these the liver function tests were mildly abnormal. One liver biopsy was carried out and the histology was within normal limits.

Australia Antigen in the Urine of Patients with Acute Australia-antigen positive Hepatitis and their Household Contacts

E. J. L. HEATHCOATE, A. TSIAINIDES, AND SHEILA SHERLOCK (Department of Medicine, Royal Free Hospital, London, England) The Australia antigen was looked for in concentrated urine samples using the complement-fixation test. Twenty-three patients were studied during their acute hospital admission; only four showed urinary antigen. However, 15 of these patients and their household contacts were studied at monthly intervals for six months, dating from the time of the hospital admission, and 13 showed transitory urinary antigen, only one having been positive whilst in hospital. Sixty per cent of the 43 household contacts also developed Australia antigen in their urine during this time but none had clinical or biochemical evidence of hepatitis. Urines from 50 healthy controls were found to be negative.

In summary, Australia antigen may be detected in the urine of patients with acute, Australia-antigen-positive hepatitis, most commonly during the period of their convalescence, when the antigen was no longer present in the serum. Despite no evidence of recent hepatitis a high proportion of household contacts also had Australia antigen in their urine.

Hepatitis-associated, Antigen-induced Lymphocyte Transformation in Chronic Hepatic Disease

N. PETTIGREW AND R. I. RUSSELL (Departments of Pathology and Gastroenterology, Royal Infirmary, Glasgow) Recent work has demonstrated that
lymphocytes from patients who have recovered from hepatitis-associated, antigen-positive hepatitis can be transformed when stimulated in vitro by hepatitis-associated, antigen-positive sera (Yeung Laiwah, 1971).

This finding has been confirmed. The transformation was expressed as the ratio of \(^{3}H\)-thymidine uptake in triplicate cultures of lymphocytes in the presence and absence of antigen. The mean lymphocyte transformation ratio (with SD) in a series of 12 normal control subjects was 1·31 ± 0·23; in six patients with a history of serum hepatitis 2·97 ± 0·98; in nine patients with biopsy-proven primary biliary cirrhosis 1·20 ± 0·36; and in five patients with chronic active hepatitis 1·30 ± 0·52.

In seven chronic alcoholic patients with hepatic disease, the mean ratio was 2·07 ± 0·58. Alcoholics without hepatic disease behaved like normal controls. The lymphocyte transformation ratio was significantly different from that of normal individuals in the patients who had recovered from serum hepatitis \((t = 5·6; P < 0·001)\) and in the chronic alcoholic patients with hepatic involvement \((t = 3·9; P < 0·01)\).

These observations suggest that serum hepatitis virus may be important in the pathogenesis of alcoholic liver disease.

Reference

Serum Alkaline Phosphatase Isoenzymes in Liver Disease

T. W. Warnes, Pauline M. Hine, and G. H. Kay (Department of Gastroenterology, Manchester Royal Infirmary) Alkaline phosphatase isoenzymes were separated by heat, urea, and L-phenylalanine inhibition tests, and the results compared with acrylamide gel disc electrophoresis, on which intestinal and origin bands may be found, in addition to the main band. Band width and position were measured and expressed in such a manner that the results could, for the first time, be placed on a semiquantitative basis, thus permitting a statistical analysis. The main 'bone' band is significantly slower and broader than the 'liver' band, whilst two main bands are seen in normal serum.

An intestinal band was found in 50\% of normals, in only 19\% of patients with bone disease, and in 45\% of patients with liver disease. When the latter group was analysed, an intestinal band was found in 55\% of patients with an intrahepatic lesion, but in no patient with an extrahepatic lesion.

In contrast, an origin band, which was found in 80\% of the liver disease group, was present in both intra- and extrahepatic lesions. This origin band was found in only 7\% of patients with bone disease, and in no normal subject.

The liver isoenzyme can often be demonstrated in the serum of patients with liver disease who have normal liver function tests, including a quantitatively normal alkaline phosphatase concentration, and alkaline phosphatase isoenzyme studies represent a sensitive and specific new test of hepatocellular integrity.

The Diagnosis of Gilbert's Syndrome: Role of the Reduced Caloric Intake Test

D. Owens and S. Sherlock (Department of Medicine, Royal Free Hospital, London) The effect of a 400 calorie diet for 72 hours on plasma bilirubin concentration was studied in 12 normal subjects, 10 with Gilbert's syndrome, in 12 patients with chronic liver disease, and in three with haemolytic anaemia.

There was a significant increase in the unconjugated bilirubin concentration in both normal subjects and in patients with Gilbert's syndrome. It occurred within 24 hours of starting the diet. Continuation for another 48 hours was not associated with further increase in the bilirubin concentration. The increase was significantly higher in Gilbert's syndrome than in normal subjects. There was no significant increase in the patients with chronic liver disease and in the three patients with haemolytic anaemia.

The cause of the elevation is unknown. It may be related to decreased hepatic glucuronyl transferase activity which was shown to be present in seven normal rats fasting for 72 hours.

Intestinal Blood Flow and Sodium Transport

A. H. G. Love, J. G. W. Matthews, and N. Veall (Departments of Medicine and Surgery, The Queen's University of Belfast, and the Radioisotopes Division, MRC Clinical Research Laboratories, Harrow, Middlesex) Intestinal blood flow not only supplies the metabolic needs of the mucosa but also transports absorbed materials. The relationships between absorption and blood flow are poorly defined. No relationship between net sodium absorption and total blood flow has been demonstrated (Goldberg and Fine, 1945).

In the present study in dogs using small bowel perfusion bidirectional sodium ion fluxes were measured using double isotope labelling. Total blood flow to the intestine was measured using an electromagnetic flow meter. \(^{188}\)Xenon clearance from the intestine was recorded as an estimate of functional blood flow.
The mean transit times of sodium tracer and xenon from the lumen to the blood were almost identical at varying blood flow rates. At low flow rates bidirectional sodium fluxes were depressed but net absorption was not impaired until blood flow fell below 10% of control values.

It appears that the relationship between bidirectional sodium fluxes across the intestinal mucosa and functional blood flow is closer than previously suspected. This may be important in the pathogenesis of diarrhoeal states.

Reference

The Effect of Intravenous Prostaglandin F2\alpha on Small Intestinal Function

J. H. CUMMINGS, G. J. MILTON-THOMPSON, J. A. BILLINGS, A. N. NEWMAN, AND J. J. MISIEWICZ (Medical Research Council Gastroenterology Unit, Central Middlesex Hospital, London, and Royal Naval Hospital, Haslar, Gosport, Hants) Oral and parenteral prostaglandins may cause diarrhoea1,2 but the effect of circulating prostaglandins on small intestinal function has not been studied.

We have measured the net movements of water and electrolytes, the transit time and motor activity in the small intestine of 13 normal male volunteers. Using a three-lumen tube, the intestine was perfused with an isoosmotic solution before and during intravenous administration of PGF2\alpha. Intraluminal pressures were recorded with open-ended tips and transit with a dye injection technique.

In six out of seven jejunal studies at doses of 0.28 to 0.81 μg/kg/min of PGF2\alpha no significant change in net movements of water and electrolytes were noted. In one jejunal study at the highest dose net water and electrolyte secretion into the lumen was observed. However, jejunal motility was inhibited at the two highest doses.

By contrast, in four out of six ileal studies in a similar range of doses, significant net secretion of fluid into the lumen occurred (p < 0.01). Pressure activity was inhibited (p < 0.001) but transit times remained unchanged.

These results suggest that circulating prostaglandins affect water and electrolyte transport, and the motility of the small intestine. They also indicate that the ileum is more sensitive and that motility and absorption are affected independently.

References

The Effect of Glucagon and Secretin on Salt and Water Transport in the Human Jejunum

T. HICKS AND L. A. TURNBerg (Division of Gastroenterology, Manchester Royal Infirmary) The influence of glucagon and secretin on salt and water transport in the human jejunum was investigated in healthy volunteers using a triple-lumen tube perfusion technique. Intravenous infusions of glucagon (0.7 μg/kg/hour) significantly reduced absorption of NaCl, by an average of 0.29 m-equiv/hour/cm and of water by 2 ml/hour/cm of jejunum and in some subjects this resulted in a net secretion. The mean transit time was increased by 100%, mean jejunal diameter by 50%, and jejunal volume by 130% in response to glucagon. Higher doses of glucagon did not increase its effects on transport or motility. All subjects developed marked diarrhoea, while those given doses greater than 3 μg/kg/hour also developed nausea and vomiting.

Intravenous infusions of physiological doses of pure secretin (0.5 μg/kg/hour) influenced ion transport only in the most proximal jejunum (90 cm from teeth) where it reduced absorption of NaCl by a mean of 0.3 m-equiv/hour/cm of jejunum and it was ineffective in the mid jejunum (120 cm from teeth). Higher doses did not increase its effect on the proximal jejunum. Transit times were not clearly altered by secretin.

The possible relevance of these findings to the physiological control of jejunal ion transport and to the diarrhoea associated with some pancreatic adenomata will be discussed.

Absorption of Amino Acids and Peptides in Man

D. B. A. SILK, D. PERRET, AND M. CLARK (Departments of Gastroenterology and Medicine, St. Bartholomew's Hospital, London) Absorption of peptides may occur either by hydrolysis at the brush border followed by absorption of the released amino acids, or by direct uptake of the peptide into the cell with subsequent intracellular hydrolysis. Using a double-lumen perfusion technique in man, we have studied the absorption of the amino acids glycine and alanine and their two dipeptides glycyl-alanine and alanyl-glycine.

Alanine was absorbed faster than glycine from an equimolar amino acid mixture. Glycine was absorbed faster from both dipeptides than from the amino acid mixture, and this was greatest when the dipeptide glycyl alanine was perfused. Alanine, on the
other hand, was absorbed at comparable rates from all three solutions. Free amino acids were seen in the lumen during perfusion of both dipeptides—higher concentrations of both glycine and alanine were present during perfusion with alanyl-glycine. These results suggest that by altering the amino acid configuration, the dipeptides are handled differently. This difference in handling would be compatible with both suggested modes of peptide transport. On the one hand, direct uptake of glycylalanine with minimal hydrolysis at the brush border; on the other hand, alanyl-glycine transport probably involves both superficial hydrolysis and direct uptake.

The Effect of Salazopyrin on Water and Electrolyte Transport in the Human Colon Measured in vivo and in vitro

J. HARRIS, E. Q. ARCHAMPPONG, AND C. G. CLARK (Department of Surgery, University College Hospital Medical School, London) One of the principal functions of the human colon is to absorb water and electrolytes from its lumen. Its ability to do this is markedly impaired in both ulcerative colitis and Crohn's disease so that the large intestine becomes less absorptive and more secretory in function.

To study the action of salazopyrin on the net transport and unidirectional fluxes of sodium, potassium and water, two methods of investigation have been used: (1) the in-vivo technique of Duthie et al. (1964), and (2) a modification of an in-vitro procedure described by Ussing and Zerahn (1951). Measurements have been made in 18 patients (10 controls, four ulcerative colitis, and four Crohn's disease).

Both the in vivo and in vitro studies show that control subjects absorb sodium and water and secrete potassium into the lumen. In ulcerative colitis and Crohn's disease net secretion of sodium and water is found and potassium secretion is increased. The addition of salazopyrin to the test solution significantly increases the absorption of sodium and water from the healthy colon but has no effect on potassium transport. The effects of salazopyrin are even more marked on the diseased bowel, for in all cases net sodium and water secretion is converted into net absorption within 10 minutes. These changes are accompanied by an alteration of the unidirectional fluxes across the mucosa.

These results suggest that salazopyrin, in addition to its immunosuppressive action, also has a local direct effect on both healthy and diseased colonic epithelial cells.

References
1 Harris and Shields (1970), Gut, 11, 27.

Comparison of Bowel Function after Colectomy and Ileostomy or Ileorectal Anastomosis for Inflammatory Bowel Disease

C. R. NEWTON (introduced by J. E. LENNARD-JONES) (Research Department, St. Mark's Hospital, London)

A large fluid effluent from the small bowel can be a problem after colectomy for inflammatory bowel disease. This study was carried out to see if patients with a large output differed from those with a smaller output in gut transit time or biochemical composition of the effluent, and if the output after ileostomy differed from that after ileo-rectal anastomosis. Transit times were determined with polythene shapes, and 24-hour ileostomy or stool outputs were weighed, homogenized, and analysed for pH, dry weight, sodium, potassium, calcium, magnesium, chloride, lactic acid, short chain fatty acids (with D. Gompertz, Royal Postgraduate Medical School, London), and faecal fat.

Twenty-eight inpatients were studied after colectomy and ileostomy and 19 after ileo-rectal anastomosis for inflammatory bowel disease. The average ileostomy output was 697 g/24 hours, which was significantly greater than the average stool output of 414 g/24 hours after ileo-rectal anastomosis (p<0.05). Average daily sodium losses were 92 m-equiv after ileostomy and 45 m-equiv after ileo-rectal anastomosis (p<0.02). The mean sodium concentration in the ileostomy effluent was 127 m-equiv/l as compared with 113 m-equiv/l after ileo-rectal anastomosis (p<0.05) and conversely, the potassium concentration was 11·8 m-equiv/l after ileostomy and 21·2 m-equiv/l after ileo-rectal anastomosis (p<0.05). Similar results were obtained in 21 unselected, healthy outpatients, 11 with ileostomy and 10 with ileo-rectal anastomosis, who had had a colectomy for ulcerative colitis more than six months previously. In both ileostomists and patients with ileo-rectal anastomosis, 24-hour outputs correlated with transit times and sodium and chloride losses but not with pH, potassium, calcium, magnesium, lactic acid, short chain fatty acid, or faecal fat excretions.

These results suggest that a large fluid effluent is associated with rapid transit and inadequate absorption of sodium chloride and water. Ileo-rectal anastomosis may confer a biochemical advantage over ileostomy due to the sodium and water absorbing capacity of the rectal remnant.
Does Oral Metoclopramide Increase Cardiac Sphincter Pressure?

J. B. DILAWARI AND J. J. MISIEWICZ (Medical Research Council Gastroenterology Unit, Central Middlesex Hospital, London) Oral metoclopramide (Maxolon) is frequently prescribed for heartburn. Although intravenous metoclopramide increases the lower oesophageal sphincter (LES) pressure in normal people, it is not known what is the magnitude and duration of response following oral administration to patients with heartburn or regurgitation. We have measured pressures in the oesophagus, the LES, and the stomach of 23 such patients before and after the ingestion of a placebo (five patients) or 10 mg of metoclopramide (18 patients).

Intraluminal pressures were measured with perfused open-ended tips, positioned so that two tips were in the gullet, one in the LES, and the fourth in the stomach. Pressures were recorded for 30 minutes before and for 90 minutes after, the drug.

The placebo had no effect. Oral metoclopramide raised the LES pressure (r < 0.01 to < 0.001) within 30 minutes in all but two of the patients. Although in individuals at the time of maximal effect the LES pressure rose two or more times above basal for 0 to 80 minutes (mean 22 ± 6 min), the average increase in the group amounted to only 6 mm Hg. Amplitude of oesophageal peristaltic waves was increased whilst gastric activity was stimulated in half the patients. These results suggest that oral metoclopramide increases the cardiac sphincter pressure.

Reference


The Interpretation of Colonoscopic Biopsies of Polypoid Lesions in the Large Bowel

R. H. RIDDELL AND T. MUTO (introduced by B. C. MORSON) (St. Mark’s Hospital, London) Of over 800 colonoscopic biopsies examined histologically at St. Mark’s during the past 18 months, 250 have been from polypoid lesions. In addition, over 50 excision biopsies of polyps have been examined since the introduction of the colonoscope diathermy snare. The success of these biopsies in the diagnosis of polyps and the relative merits of the different colonoscope biopsy forceps are discussed.

The majority of single polyps sampled proved to be adenomatous, but metaplastic, inflammatory, and benign lymphoid polyps were frequent. Lymphoid polyps of the terminal ileum must be distinguished from chronic inflammatory bowel disease. One submucous lipoma and a single case of malignant transformation of an adenomatous polyp were seen. Cases with multiple adenomas, metaplastic polyps, or Peutz-Jeghers polyps were also examined.

It is concluded that accurate differential diagnosis of colonic polyps is possible from biopsies obtained using the available biopsy forceps. The use of spiked forceps was helpful for sampling large polyps but less desirable for small polyps. There are also limitations on interpretation of colonoscopic biopsies and not all frank carcinomas biopsied actually showed unequivocal carcinoma on forceps biopsy. Close correlation between the clinician, radiologist, and pathologist is never better exemplified than in these cases.

Comparative Study of the Principal Gastric Glycoproteins Isolated from Gastric Aspirates of Normal, Neoplastic, and Foetal Gastric Mucosae

J. SCHRAGER (The Group Laboratory, Royal Albert Edward Infirmary, Wigan) Proteolysed four normal, 20 neoplastic, and six foetal gastric mucosae were investigated. The procedures of isolating the glycoproteins and the determination of their carbohydrate and amino acid composition and the method used to study structural features of the isolated glycoproteins have been described.

The carbohydrate and amino acid composition of the glycoprotein isolated from the normal gastric mucosae was virtually the same as the principal gastric glycoprotein obtained from gastric aspirates. Galactose, fucose, glucosamine, and galactosamine were present in approximate molar ratios of 4:3:3:1. Superimposed on the basic common structure were additional sugar residues associated with blood group specificity which was the same as that of the host red cells.

The acid hydrolysates of the 20 glycoproteins isolated from gastric neoplastic mucosae contained the same range of sugars but also revealed significant differences: (a) The quantitative relationships of the carbohydrate components of the neoplastic glycoproteins showed variations dividing the samples investigated into four groups, each group with a distinctive and constant carbohydrate composition:—

<table>
<thead>
<tr>
<th>Group</th>
<th>galactose/glucosamine/galactosamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1:1:1 (1 case)</td>
</tr>
<tr>
<td>2</td>
<td>2:1:1 (1 case)</td>
</tr>
<tr>
<td>3</td>
<td>3:2:1 (9 cases)</td>
</tr>
<tr>
<td>4</td>
<td>4:3:1 (9 cases)</td>
</tr>
</tbody>
</table>

The British Society of Gastroenterology
(b) The blood group specificity of 11 out of the 20 cases investigated differed from that of the hosts' red cells.

The extracts of the gastric mucosae from the two foetuses 16 weeks and the four foetuses 20 weeks old showed the same carbohydrate composition which had the same quantitative relationship as the neoplastic glycoproteins of group 1 (1:1:1) and group 2 (2:1:1) respectively. The amino acid composition of all foetal glycoproteins were similar to that of the normal and neoplastic glycoproteins.

It is suggested that the mutation of the normal mucous cell to a neoplastic cell has changed the enzymic system synthesizing the glycoprotein, the change consisting in the varying losses of the number of repeating units glucosamine-galactose dividing the specimen investigated into groups with respect to the number of units composing the carbohydrate side-chains, the groups differing in one or multiple units of the disaccharide glucosamine-galactose (except group 1 which differed from group 2 by only one galactose residue).

The change in the blood group specificity involved all four blood groups. It is interesting to note that the change from blood group O to A would involve the introduction of a new enzyme linking the terminal galactosamine to the carbohydrate side chain.

The results of this investigation would suggest that the foetal mucous cell at 16 and 20 weeks after gestation has not yet developed the full complement of enzymes needed to synthesize the complete side chain hence its shortness and difference from the normal glycoprotein.

References