The British Society of Gastroenterology

The 30th Annual General Meeting of the British Society of Gastroenterology was held in Manchester on 6, 7, and 8 November 1969, with the President, Dr H. T. Howat, in the Chair.

The Sir Arthur Hurst Memorial Lecture 'Digestion and Absorption at the Brush Border Membrane: A Lesson in Functional Organisation' was given by Dr Robert K. Crane (Rutger's Medical School, New Jersey, USA).

The meeting was exceedingly well organized by Dr H. T. Howat, Dr R. Holmes, and Dr John Lennard-Jones, and the social events included a reception given by the Vice-Chancellor and Council of the University of Manchester, and the annual dinner of the Society, when the President took the Chair, and later invested Dr N. F. Coghill as President. Dr H. T. Howat welcomed many guests from home and overseas, and particularly those from the University of Manchester which had shown them such warm hospitality.

At the Annual General Meeting of the Society the following elections were made:—

**PRESIDENT** Professor A. A. Harper

**EDITOR OF Gut** Professor Sheila Sherlock

**MEMBERS OF COUNCIL** M. Atkinson and A. M. Connell

**HONORARY MEMBERSHIP** A. M. Ugolev

**CORRESPONDING MEMBERSHIP** L. Dembling, S. J. Goulston, K. Heinke, J. Landor, and J. Myren.

Seventy-one Associate members were elected.

**TRANSMUCOSAL ELECTRICAL POTENTIALS OF HUMAN RECTUM AND PELVIC COLON**

C. J. Edmonds and R. C. Godfrey (MRC Department of Clinical Research, University College Hospital Medical School, London) introduced by D. A. W. Edwards In a variety of animal species it has been shown that the mucosal epithelium of the colon is electrically polarized, the outer surface being positive with respect to the lumen. This electrical potential difference (pd) appears to be generated by active absorption of Na ions from the gut lumen. We have recently developed a simple method for measuring the pd in man which can be performed rapidly during routine sigmoidoscopy. In 30 normal subjects, the pd was measured at various points along the rectum and sigmoid colon up to 16 cm from the anus. The pd varied little along this length of intestine in any one subject, although there was considerable variation between subjects. The values obtained ranged from 4 to 51 mV, the mean of all observations being 25 mV. The pd was elevated within four hours of administration of aldosterone and reached a maximum in six hours when the pd ranged from 37 to 101 mV, the overall mean being 60 mV. By 18 hours, the pd had returned to normal. Stool fluid obtained after aldosterone administration showed a reduced Na and raised K concentration. Preliminary observations have also been made on subjects with bowel disease and will be discussed.

**ELECTROLYTE TRANSPORT IN THE HUMAN ILEUM**

L. A. Turnberg, F. A. Bieberdorf, and J. S. Fordtran (Dallas, Texas, and Manchester Royal Infirmary) introduced by R. Holmes Sodium, chloride, and bicarbonate transport in the human ileum was studied using a triple-lumen perfusion technique. It was observed that both sodium and chloride were absorbed against electrochemical gradients. During absorption of chloride, luminal bicarbonate concentrations rose, suggesting the possibility of chloride/bicarbonate, anion exchange mechanism. Changes made in the concentration of either anion in the perfusion solution altered the rate and direction of transport of the other anion, lending support to the idea of an exchange process. Sodium absorption from 'chloride-free' solutions was associated with a fall in pH of luminal contents in contrast to the rise in pH which occurs in the presence of chloride. The luminal acidification associated with sodium absorption reduced the luminal bicarbonate concentration. This observation may explain the finding that a 1 to 1 chloride/bicarbonate exchange relationship was observed only when sodium absorption was zero, luminal bicarbonate concentrations being influenced by both chloride and sodium movements. Neither anion nor cation transport was associated with a change in electrical potential difference measured between ileal lumen and skin.

One model which successfully predicts all our observations is a double exchange process of chloride for bicarbonate and sodium for hydrogen, and the evidence in favour of such a model will be discussed.

**SMALL BOWEL PERMEABILITY AND MOLECULAR SIZE**

C. A. Loehry, P. J. Hilton, A. T. Axon, and B. Creamer (St. Thomas's Hospital, London) Studies on losses from the small bowel by exudation and cell exfoliation had indicated that most molecules pass swiftly from blood to gut lumen and some cross later in shed cells. The early
phase of exudation was studied further with a series of substances of known molecular weight: urea, creatinine, glucose, fructose, vitamin B₁₂, and inulin. Following intravenous infusion of these substances the whole small intestine of the rabbit was perfused with saline and the substance estimated by established methods. The results show that there is a relationship between molecular weight and plasma clearance of the substance by the small intestine, the exception being glucose which did not increase in passage from blood to gut with increasing concentrations. Similarly the passage of isotopically labelled PVP was studied both from blood to gut and gut to blood. By elution on a Sephadex column the pattern of molecular passage across the gut wall was shown to be related to molecular size and to be the same in both directions.

THE VAGUS AND ACHALASIA

J. B. ELDER AND G. GILLESPIE (Department of Surgery, Western Infirmary, and Gastrointestinal Centre, Southern General Hospital, Glasgow) introduced by I. E. GILLESPIE.

Iordanskaia¹ and Woolam, Maher, and Ellis² reported abnormal vagal nerve function on insulin testing in almost 50% of patients with achalasia of the cardia. In addition Woolam et al³ suggested that the maximal acid output of the stomach was reduced in achalasia.

In this study 13 patients with achalasia of the cardia were submitted to both insulin and pentagastrin tests. Most had undergone successful Heller’s operations without vagotomy one to 10 years previously. Using Hollander’s criteria,⁴ three gave no response to insulin, one had a late positive response, i.e., in the second hour after insulin, and the remaining nine had early positive responses occurring in the first hour after insulin. The mean maximal acid output of the entire group was within the normal range.

Iron, vitamin B₁₂, and folate indices were also investigated to see whether there might be any other evidence of disordered upper gastrointestinal function. Serum iron and total iron-binding capacity were normal in 12 patients. Serum B₁₂ and serum folate levels were likewise normal in 10 patients.

The finding of an abnormal insulin response in 30% of the present series is in keeping with the view that impairment of vagal nerve function may be a feature in a significant proportion of patients with achalasia of the cardia. However, there was no evidence of other significant gastric disturbance.

REFERENCES


OESOPHAGEAL REFLUX AND GASTRIC SECRETION

A. S. WARD (Queen Elizabeth Hospital, Edgbaston, Birmingham), introduced by G. SLANEY. Most hiatus hernia patients exhibit reflux and the presence of acid in the lower oesophagus has been shown to stimulate gastric secretion.¹ A vicious circle is envisaged in which acid reflux produces increased gastric secretion, which in turn leads to further reflux. The response appears to be particularly marked in patients with oesophagitis and may be important in initiating and maintaining the inflammatory process. This paper reports an investigation of these findings in 20 preoperative hiatus hernia patients, 12 patients after operation, and nine controls.

Barium swallow and oesophagoscopy were carried out in all patients before gastric analysis. The basal secretory rate was measured for one hour, then 20 ml 0·1N hydrochloric acid was instilled into the oesophagus and the collection continued for a further hour. The instilled acid was subsequently identified in the gastric aspirate by using polyethylene glycol as marker.

The results confirm that gastric secretion is increased following oesophageal acidification. The response is greater in hiatus hernia patients than in controls and repair of the hiatus reverses this trend. There is no evidence that oesophagitis is associated with excessive gastric stimulation; basal acid output is lower and the perfusion response less in this group than in patients without inflammatory change. A reduction in response occurs in both groups after hiatal repair.

REFERENCE


HISTOCHEMICAL DEMONSTRATION OF THE GASTRIC LIPASE OF THE RAT

J. BARROWMAN AND S. JANE DARNTON (Department of Physiology, The London Hospital Medical College, London) Recently, it has been shown that rat gastric mucosal homogenates contain an enzyme capable of hydrolysing medium-chain triglycerides.¹ In this same study results were obtained which suggested that fats in the stomach might stimulate the production of lipolytic enzymes in the mucosa.

A histochemical method has been devised for the demonstration of pancreatic lipase based on the use of a bile-salt stabilized emulsion of long-chain triglyceride.² This method has been modified to demonstrate gastric lipase activity by substituting trioctanoin for triolein as substrate. Fatty acids produced by hydrolysis of the triglyceride are precipitated as calcium soaps; the calcium ions are exchanged with lead ions and a lead sulphide precipitate forms the final reaction product.

Samples of gastric mucosa were taken from fasting rats with chronic pancreatic-biliary fistulae. These specimens showed no trioctanoinase activity. Feeding 2 ml of olive oil 20 minutes before taking the specimens resulted in the appearance of a large amount of lipolytic activity in gastric mucosal epithelium, the greatest concentration being present in the deeper layers of the fundic mucosal part of the glandular stomach. In studies where oleic acid and preparations of triolein freed of fatty acid
were fed, results were obtained which suggest that it is free fatty acid in the gastric lumen which is responsible for the observed effects.

REFERENCES


THE CONVERSION OF HAEMATIN TO BILE PIGMENT BY THE FOETUS

PAUL M. SMITH, ROGER LESTER, HELMUT F. J. RAUSCHECHER, GEORGE J. PIASECKI, AND BENJAMIN T. JACKSON (Boston University Medical School, Boston, Massachusetts, USA) Although neonatal haemolytic jaundice is a major clinical problem, relatively little is known about the conversion of haematin to bilirubin in the foetus and newborn. Advanced techniques for intrauterine surgery were used to study haematin degradation in foetal sheep, which were prepared in utero with indwelling jugular, carotid, and biliary canulats. 14C-haematin was administered intravenously to the foetus, and plasma disappearance, biliary excretion, placental transfer, and tissue distribution of radioactivity were measured over an eight-hour period.

Eight to 23 per cent of the 14C-label was recovered in foetal bile, half as 14C-bilirubin and half as unidentified 14C-haematin derivatives. Four to 25 per cent was transferred across the placenta, appearing in maternal bile entirely as 14C-bilirubin. Excretion of 14C-label thus totalled 30 to 34%. For comparison, six adult sheep infused with 14C-haematin excreted 23 to 44% of the dose in the bile, one third as bilirubin.

At the end of the foetal studies, 16 to 46% of the radioactivity was found in the foetal liver, no significant radioactivity being found in other foetal or maternal tissues. Total recovery of 14C-label averaged 75%.

It is concluded that foetal sheep have an efficient mechanism for the hepatic catabolism of haematin, a large fraction being excreted in the bile as bilirubin. Another fraction is transferred across the placenta, probably after prior conversion to bilirubin. The remainder is catabolized to other end products, total excretion being approximately as effective as in the adult.

This study directly demonstrated that foetal sheep can readily produce bilirubin from haematin breakdown, and can eliminate this bilirubin efficiently.

ADRENERGIC INNERVATION OF RAT INTESTINAL SMOOTH MUSCLE

J. D. MAXWELL AND J. S. GILLESPIE (Department of Medicine, Royal Infirmary and Department of Pharmacology, University of Glasgow) introduced by ROGER WILLIAMS.

There is still no generally accepted view of the organization of pre- and postganglionic nerves in intestinal smooth muscle and enteric plexuses, as previous historical studies on bowel innervation have lacked specificity.

The classical view that sympathetic (adrenergic) postganglionic nerves directly innervate intestinal smooth muscle cells has had to be modified following the development of a histochemical technique (formaldehyde-induced catecholamine fluorescence) which has provided a highly specific and sensitive method of localizing adrenergic fibres.1 Using this technique dense networks of fluorescent adrenergic terminals surrounding intramural ganglia have been reported1 but there has been uncertainty as to whether adrenergic fibres directly innervated intestinal smooth muscle, and no information on innervation at sphincter areas.

Adrenergic innervation was investigated at various sites between the lower oesophagus and internal anal sphincter in both transverse sections and stretch preparations of rat bowel. The presence of a network of adrenergic fibres surrounding intramural ganglia was confirmed. There was a low but fairly constant density of adrenergic innervation of smooth muscle cells proper (in addition to fluorescence around ganglia and vascular smooth muscle). At the pyloric and internal anal sphincters, however, the pattern of adrenergic innervation was quite different with a five to six-fold increase in innervation density compared with non-sphincteric smooth muscle.

The significance of these findings is discussed in relation to current concepts of intestinal innervation.

REFERENCES


THE INSULIN TEST IN THE UNOPERATED SUBJECT

J. H. BARON, L. V. GUTIERREZ, J. SPENCER, J. TINKER, AND R. B. WELBOURN (Department of Surgery, Royal Postgraduate Medical School, London) Recent studies in one individual1 have suggested that peak gastric acid output in response to insulin (PAO) is greatest with doses of insulin from 0.1 to 0.3 units/kg and that extreme hypoglycaemia depresses gastric secretion. The optimum dose of insulin for this test is that dose which in the highest proportion of subjects lowers the blood glucose sufficiently to elicit maximum vagal acid response without producing such a low blood glucose concentration that acid secretion is depressed. The desirable range of blood glucose levels appears to be from 13 to 25 mg/100 ml.

In the first part of the present study volunteers were given 0.1, 0.2, and 0.4 u/kg insulin on different days. In each of eight patients with duodenal ulcer PAO after 0.2 units/kg (mean 37.3 m-equiv/hr) was higher than after 0.1 units/kg (mean 23.4 m-equiv/hr), and the mean of the differences was significant (p = 0.008). In five of the seven patients with duodenal ulcer PAO after 0.2 units/kg (mean 38.9 m-equiv/hr) was higher than after 0.4 u/kg (mean 38.0 m-equiv/hr), but the mean of the differences was not significant (p = 0.9). The optimum dose of insulin was therefore considered to be 0.2 units/kg.

This dose was used in a standard test designed to measure in one morning all known gastric secretory responses. This four-hour test consisted of: basal 4 × 15 min; insulin, 0.2 u/kg iv, 8 × 15 min; penta-
gastrin, 6 μg/kg im 4 × 15 min. Patients with peptic ulcer, and patients with x-ray-negative abdominal pain and healthy controls were studied. The results have been analysed in terms of the ratio of the peak acid outputs after insulin and pentagastrin (PAO₁/PAO₂PG) as an index of the vagal 'drive' on the parietal cells. In 50 men with duodenal ulcer PAO₁ (34:1 m-equiv/hr) was significantly less than PAO₂PG (43:2 m-equiv/hr) and the mean PAO₁/PAO₂PG ratio as a percentage was 82% ± SD 32, insignificantly different from this percentage in 10 women with duodenal ulcer (76 ± 27), but significantly greater than this percentage in 10 men with gastric ulcer (57 ± 22). These results are consistent with the hypothesis that there is an increased vagal 'drive' on the parietal cells in duodenal ulcer.

REFERENCE

THE LONG-TERM STABILITY OF THE INSULIN RESPONSE AFTER VAGOTOMY
G. GILLESPIE, J. B. ELDER, I. E. GILLESPIE, A. W. KAY, AND G. F. CREAN (Department of Surgery, Western Infirmary, and Gastrointestinal Centre, Southern General Hospital, Glasgow) It is generally agreed that after vagotomy a positive insulin response according to the concentration criteria of Hollander indicates incompleteness of the vagal nerve section, and the absence of a response, complete vagotomy. While it has been shown that there is no significant change in the maximal acid response to histamine up to three years after vagotomy, it is not known whether the insulin test exhibits similar long-term stability.

In this study 74 patients, who had previously undergone vagotomy and drainage for duodenal ulcer and whose immediate postoperative insulin responses were known, were retested one to four years after surgery. Of 31 patients originally insulin negative, only 14 remained so at follow-up; 17 patients exhibited positive responses. Of 43 patients initially insulin positive, 39 remained so at retesting. Four gave subsequent negative responses.

These results indicate that the response to insulin tests performed in the second week after vagotomy may change with the passage of time, and the trend is towards increasing positivity. However, comparison of initial and follow-up maximal acid outputs showed no significant difference.

REFERENCES

GASTRIC EMPTYING AND TRANSIT TIME AS FACTORS IN POSTVAGOTOMY DIARRHOEA
S. T. D. MCKELVEY, A. M. CONNELL, AND T. L. KENNEDY (Department of Surgery, Queen's University, Belfast) Gastric emptying and transit time of both a 600 ml water meal and a 600 ml balanced food fluid meal were measured by a modification of the double sampling technique. Patients who had vagotomy and drainage were compared with patients undergoing medical treatment of uncomplicated duodenal ulcer.

The 600 ml water meal was given to 12 preoperative and 30 postoperative patients. In the 12 preoperative patients the mean emptying time for the water meal at 43:8 minutes differed from that of the fluid food meal at 203:9 minutes. In 35 postoperative patients the mean emptying time for the water meal at 22:1 minutes was not significantly different from that of the balanced meal at 29:9 minutes, demonstrating loss of chemical regulation of gastric emptying following vagotomy and pyloroplasty.

The effect of posture on the emptying of a balanced meal before operation was estimated by measuring gastric emptying in 10 preoperative patients sitting upright and then lying on the left side. There was only a small difference due to change in posture. Postoperatively, in 10 patients the mean emptying time in the sitting position was 31:6 minutes and lying on the left side 138:9 minutes.

Patients with a more frequent bowel habit postoperatively and those with episodic postvagotomy diarrhoea emptied their stomachs faster than those whose bowel habit remained unchanged. Patients with postvagotomy diarrhoea had very rapid transit times and explosive diarrhoea following ingestion of a fluid meal. Following ingestion of water, transit time was normal and no diarrhoea occurred.

There was no difference in the rate of gastric emptying following selective vagotomy compared with truncal vagotomy.

REFERENCE

THE EFFECT OF VAGOTOMY AND DRAINAGE ON BOWEL HABIT AND SMALL BOWEL FLORA IN THE IMMEDIATE POST-OPERATIVE PERIOD
G. G. BROWNING, C. MACKAY, AND K. A. BUCHAN (Department of Surgery, Western Infirmary, Glasgow) introduced by A. W. KAY The cause of diarrhoea in the period immediately following vagotomy and drainage is not known. The aim of this investigation was to study (1) bowel habit, and (2) small bowel flora during the first 10 days following vagotomy and drainage.

Upper jejunal juice was aspirated preoperatively and on alternate days postoperatively. The postoperative specimens were obtained using the feeding jejuno-stomy limb of a Kay's gastrostomy tube. The specimens were cultured qualitatively and quantitatively and counts greater than 10⁴/ml of faecal type organisms regarded as indicating significant colonization. The number of bowel motins was recorded and four or more per day were regarded as diarrhoea. The maximal acid responses to pentagastrin were measured before and after operation.

The preoperative incidence of colonization was 11%; postoperatively the incidence in 32 patients increased progressively from 47% on the second day to 69% on the
The incidence was the same whether pyloroplasty or gastrojejunostomy was used as the drainage procedure. Comparison of the colonized with the non-colonized groups after operation revealed no significant difference in preoperative acid production; there was, however, a significantly higher maximal pentagastrin response post-operatively in the non-colonized group (9.48 ± 2.06) compared with the colonized group (4.99 ± 0.72).

Diarrhoea developed in eight of 49 (16%) patients, and the type of drainage procedure did not influence its occurrence. The incidence of colonization in the diarrhoea group was 100% compared with 76% in the non-diarrhoea group.

The findings suggest that alterations in bacterial colonization of the upper small intestine may be related to the postvagotomy diarrhoea.

**HAUSTRAL MOVEMENT IN THE HUMAN COLON**

J. A. Ritchie, G. M. Ardran, and S. C. Truelove (The Nuffield Department of Clinical Medicine and the Nuffield Institute for Medical Research, Oxford) The 'hastral pattern' of the human colon as seen radiographically after ingestion of a contrast medium frequently shows the colonic lumen divided into a number of functional segments or haustra. The intervening constrictions are referred to as interhastral folds.

The shape and size of the hastral sacs are known to change with activity of the bowel. However, there is no general agreement as to whether, after they have been obliterated by muscular contraction, the hausta re-form in the same anatomical situation. In other words, it is not known whether the interhastral folds are fixed structures.

Isolated diverticula containing opaque material act as anatomical markers of the bowel wall. We have observed instances in which variations of the hastral pattern can be seen in relation to these markers. It is clear from time-lapse cinefluorograms at one-minute intervals that diverticula which are visible at first to one side of a hastral mass of bowel contents may come to be associated in subsequent frames of the film with different points of the hastral and interhastral outline. This indicates that, after a contraction of the colon, the hastral sacs need not re-form at the same sites. Our cinefilms also suggest that interhastral constrictions can move progressively along the bowel.

**INFERIOR MESENTERIC ARTERIOGRAPHY IN CARCINOMA OF THE COLON**

H. Herlinger (Leeds) Carcinoma produces a distinctive angiographic pattern which can be differentiated from normal appearances, from diverticulitis, and uncomplicated ulcerative colitis. Aspects of techniques will be briefly mentioned. Lesions as far as the middle of the transverse colon can be outlined by inferior mesenteric injection.

 Inferior mesenteric arteriography may be used in the diagnosis of colonic carcinoma in the following circumstances:—(1) The differential diagnosis of diverticular disease and carcinoma; (2) in suspected malignancy in the recto-sigmoid area where a barium enema may fail to be helpful; (3) the possibility of recurrence after resection; (4) the evaluation of a short stricture in ulcerative colitis; (5) the differential diagnosis of a benign versus a malignant polyp; and (6) in the occasional geriatric patient in whom a barium enema may fail completely.

**A COMPARISON OF THE EFFECTS OF CAERULEIN AND CERTAIN PEPTIDE ANALOGUES OF CAERULEIN ON CATS**

JOAN BRAGANZA, F. B. BESWICK, H. T. HOWAT, A. I. MORRIS, AND J. M. MORLEY (Manchester) Caerulein1-3, the decapeptide amide isolated from the skin of Hyla caerulea, has in common with gastrin II, a N terminal pyroglutamyl, a sulphated tyrosinyl residue, and a carboxyl terminal tetrapeptide amide. The same tetrapeptide amide is present in pancreozymin (cholecytokinin) as is the sulphated tyrosinyl residue. Pharmacologically the decapeptide possesses to a high degree certain attributes of both gastrin and cholecystokinin-pancreozymin; caerulein is much more potent on a weight basis than gastrin in stimulating acid by the stomach than cholecystokinin in contracting the gall bladder and than pancreozymin in increasing the enzyme output of the pancreas.

We have extended the study of Beswick, Howat, and Morris4 on the effects of peptide analogues related to gastrin on cats by comparing the action of desulphated caerulein, and two desulphated peptides which are altered by substitution of the methionine residue in the active C terminal tetrapeptide sequence.

Neither caerulein or any of these derivatives has a stimulant action on the resting pancreas of the anaesthetized cat, but caerulein potentiates the fluid output of the secretin-stimulated pancreas. Desulphation results in loss of cholecystokininetic activity and effectively reduces both acid and pepsin output of the stomach. Enzyme production by the pancreas is virtually lost.

REFERENCE


**THE ACTION OF ETHANOL ON THE PANCREAS OF THE RAT**

H. Sarles, F. Tasso, and Catherine Figarella (Unité de Recherches de Pathologie Digestive, Marseille) It is not possible from the conflicting statements in the literature to determine whether alcohol is toxic or not to rat pancreas. This work was planned to test the hypothesis that the action of ethanol was different according (1) to the protein and lipid level of the diet, and (2) to the frequency and mode of administration of ethanol.

One hundred and twenty-four Wistar male rats weighing from 50 to 120 g were allocated by chance to two groups, one of which received freely 20% alcohol, the other water to drink. Each group was then divided into subgroups of from eight to 12 rats, each of which were given four different diets comprising respectively
5 to 6% or 17 to 18.5% of the total proteins in the form of casein and 10%, 33 to 35% and 59.5% of the calories in the form of arachis oil. Experiments lasted from two to 21 months. At the end of the experiment, trypsin, chymotrypsin, amylase, lipase, total protein, and DNA were measured, together with the diameter and the number of subcellular constituents. Differences were calculated by the method of Mann and Whitney. The effect of ethanol depends on the quantity of ingested protein and lipid: (a) on 17 to 18.5% of protein and 10% lipid, amylase and chymotrypsinogen are significantly reduced, but with the same regime and 35% of fat, amylase, lipase, and chymotrypsin are increased; (b) with 5 to 6% protein, alcohol moderately decreases the enzyme irregularity.

In no case was a histological lesion of the pancreas observed. (a) Alcohol associated with a balanced diet of protein increases the number of lipid inclusions and lysosomes, and diminishes the number and diameter of mitochondria as well as the number of zymogen granules, which is not in keeping with the increase of enzymes under the same conditions and leads us to suspect that the alcohol increases the concentration of protein both in zymogen granules and in pancreatic juice. (b) Associated with deficient protein intake, whatever the intake of fat, alcohol decreases the number and diameter of mitochondria, the mean diameter of the nucleus, and the area of cytoplasm.

Twenty Wistar rats divided by chance into two groups, received daily by stomach tube either 20% alcohol or an identical volume of an isocaloric sucrose solution. During the first eight days, the animals received 3 g of pure alcohol/100 g, for eight days 4 g alcohol/100 g, and finally 9 g. The animals receiving sucrose remained well and normal; the pancreas was normal. Nearly all the animals given alcohol died during the course of the experiment without having developed pancreatic lesions. It does not appear possible to induce alcoholic pancreatitis in the rat. With a diet rich in protein and in fat, similar to that observed in patients suffering from chronic pancreatitis, alcohol leads to an increase of zymogen granules enzyme concentration, which in the concentration of proteins may play a role in the formation of the intracanalicular precipitates which appear to cause alcoholic chronic pancreatitis.

**ALKALINE PHOSPHATASE IN DUODENAL JUICE FOLLOWING SECRETIN AND PANCREOZYMIN**

T. W. Warnes, P. Hine, and G. Kay (Manchester) introduced by H. T. Howat. Histochromically small intestinal mucosa can be shown to contain large quantities of alkaline phosphatase. Fresh specimens of pancreas obtained at operation when stained by modern histochemical techniques can be shown to contain alkaline phosphatase in both the islets and in the acini in the form of discrete granules.

The biochemical properties of the intestinal and pancreatic iso-enzymes have been compared with those of bile alkaline phosphatase by means of heat inactivation, urea denaturation, and inhibition with L phenylalanine. Small intestinal alkaline phosphatase is 78.9% inhibited by L phenylalanine, compared with negligible inhibition of bile and pancreatic alkaline phosphatase (10.7% and 11.5% respectively); it is also much more heat stable. The iso-enzymes have been further characterized by acrilamide gel (5%) disc electrophoresis, the enzyme bands being located by a diazo coupling technique. After preincubation with neuraminidase the electrophoretic mobility of the pancreatic iso-enzyme is reduced, showing that it differs from small intestinal alkaline phosphatase in containing neuraminic acid.

The output of alkaline phosphatase in duodenal juice in normal and pathological states has been measured in the course of secretin-pancreozymin tests of pancreatic function. From a study of patients with complete biliary obstruction and with complete pancreatic obstruction it is concluded that both secretin and pancreozymin increase the output of the intestinal iso-enzyme in duodenal juice. It can be calculated that about 30% of the alkaline phosphatase output in duodenal contents is derived from bile.

**THE RELATIONSHIP BETWEEN THE BACTERIAL CONTENT OF ILEAL EFFLUENT AND THE METABOLISM OF BILE SALTS IN PATIENTS WITH ILEOSTOMIES**

I. W. Percy-Robbs, W. A. Telfer Brunton, K. N. Jalan, J. P. A. McManus, J. C. Gould, and W. Sircus (University Department of Clinical Chemistry, Royal Infirmary of Edinburgh, and Gastro-Intestinal Unit and Central Microbiological Laboratories, Western General Hospital, Edinburgh) Bile salt metabolism has been studied in patients with ileostomies allowing assessment of ileal function in isolation from the colon. Proctocolectomy had been carried out for ulcerative colitis. Some patients had had ileal resection, allowing more specific consideration of the role of the ileum *per se*. It has been previously reported that patients with ileal resection show a greatly shortened biological half-life of the bile salt pool, and this is associated with reduction of the intraluminal concentration of bile salts and with increased fat excretion. Whereas deconjugated bile salts were found in the ileal effluent in four out of five patients, deoxycholic acid could not be demonstrated by thin-layer chromatographic techniques either in bile or in ileal effluent. Deconjugation and dehydroxylation of bile salts are functions of bacterial action. Since it is known that the bacterial microflora of ileal effluent and of faeces are qualitatively similar, we have studied the microflora of the ileal effluent under aerobic and strictly anaerobic conditions. Various organisms were isolated, including *E.coli*, *streptococci*, *Veillonella*, *Clostridium welchii*, and Bacteroides in counts of $10^9$ to $10^8$/ml. Anaerobic lactobacilli were not isolated from culture. Pure cultures of the strict anaerobes were incubated in the presence of $^{14}C$-taurocholate. Deconjugation of taurocholate occurred with bacteroides and clostridia but not Veillonella. On the other hand none of these bacteria was shown to be capable of dehydroxyating cholic acid liberated from conjugate. The significance of these findings will be discussed since it has been shown by Hill and
Drasar et al. that some bacterial species (Bacteroides, Streptococci faecalis, Veillonella, and Clostridium welchii) are capable of dehydroxylating bile acids, whereas Midvedt and Norman were unable to demonstrate dehydroxylation by these organisms.

This study was supported by a grant from the Scottish Home and Health Department (ACMR 845).

REFERENCES


EFFECT OF ONE MEAL ON ENTEROHEPATIC CIRCULATION OF BILE SALTS

T. S. LOW-BEER, L. LACK, AND M. P. TYOR (Department of Medicine and Department of Physiology and Pharmacology, Duke University Medical Center, Durham, N.C., and Department of Medicine, University of Bristol) introduced by A. E. READ The half life of a bile salt in ileectomized patients may be less than 24 hours. It has therefore to be measured over a shorter time period and by a method which does not require the bile salt pool to remain in a steady state. In the present studies, enterohepatic return of the two major primary human bile salts after a standard meal was studied in such patients and compared with normal subjects.

The experimental design was as follows: 24-14C-labelled glycocholate or glychenodeoxycholate was injected intravenously at 4 p.m. Three hours later the subject ate a standard meal. After an overnight fast, the same bile salt, labelled with 3H, was injected intravenously; three hours later duodenal contents were aspirated over a period of 75 to 100 min during two separate infusions of cholecystokinin, and glycocholate or glychenodeoxycholate was isolated by thin-layer chromatography. The ratio of 14C:3H was determined and compared with the ratio of 14C:3H injected. These ratios, obtained in four ileectomized patients, indicated a return of glycocholate to the hepatobilary space after a single meal which averaged 3% (range 0-11%). In contrast, the return was 70% (range 92-54%) in seven studies on six healthy volunteers. Similarly, the return of 14C-glychenodeoxycholate in three ileectomized patients was 2%, contrasting with 84% (range 71-93%) in three healthy volunteers. It is concluded that ileectomized patients may lose 90% or more of the glycocholate and glychenodeoxycholate available in the hepatobilary space in the course of a single meal. Thus, the proximal small intestine contributes only minimally to the economy of these bile salts in these patients.

REFERENCE

duodenum is due to secretion of bicarbonate and the significant transmucosal passage of hydrogen ions does not occur.

In all subjects, the bicarbonate response to duodenal acid was less than the response to 0.25 CU/kg/hour pure secretin. The abnormally low bicarbonate response in duodenal ulcer was due to defective release of secretin and, to a lesser extent, high pancreatic threshold to secretin and in some subjects inhibition of the action of secretin on the pancreas by acid in the duodenum.

Much of the acid infused into the duodenum was regurgitated into the stomach or aspirated. Acid in the lower small intestine is a near maximal stimulant of bicarbonate secretion into the duodenum in normal subjects, due probably to the release of both secretin and pancreozymin. In patients with duodenal ulcer, the bicarbonate response to jejunal acidification was significantly less than normal. The release of small intestinal hormones is an interesting new test of small intestinal function, as well as shedding new light on the pathological physiology of duodenal ulcer.

THE SOURCE OF PANCREATIC JUICE BICARBONATE

T. SCRATCHERD AND R. M. CASE (Department of Physiology, Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU) Pancreatic juice bicarbonate can have two origins: CO₂ in the blood or CO₂ generated by oxidative metabolism in the pancreatic cell. Using the saline-perfused preparation of the cat's pancreas, attempts have been made to determine this source in a number of ways.

A linear relationship exists between the perfusate bicarbonate concentration and pancreatic secretory rate. When all bicarbonate is omitted, secretion completely or almost completely ceases, suggesting that plasma bicarbonate acts as the chief source of juice bicarbonate. Furthermore, if [¹⁴C] bicarbonate is incorporated into the fluid perfusing the gland it appears in pancreatic juice at a concentration four to five times that in the perfusate. These two observations suggest that about 95% of juice bicarbonate is derived from the plasma and 5% from the cell. However, acetazolamide inhibits secretion from the perfused gland to the same extent as in vivo, an observation which mitigates against all bicarbonate being derived from plasma. Observations on the pH and PCO₂ of the perfusate clarify these inconsistencies. There is a fall in pH and a rise in PCO₂ in the perfusion fluid leaving the gland during secretion, indicating that hydrogen ions pass from the gland into the perfusate thus increasing the production of CO₂ from circulating bicarbonate. This CO₂ diffuses into the cell, is rehydrated (partly under the influence of carbonic anhydrase) and finally is secreted, thus establishing the necessary gradient for the continued diffusion of CO₂ into the cell.

REFERENCE

1. Supported by the Medical Research Council.

THE ISOLATED PERFUSED CANINE STOMACH-DUODENUM PREPARATION

1. D. HARDCASTLE AND MANSEL AYLWARD (The London Hospital) A perfused preparation of the dog's stomach, duodenum, and pancreas has been developed, which makes it possible to study gastric secretion and motility on the whole stomach in isolation.

In this paper, which is based on data obtained from 84 such preparations, the technique of perfusion and the function of the preparation is described. The stomach is perfused with heparinized autologous blood at a rate of 0.5 to 0.6 ml per gram wet weight/minute using only mechanical pumps and oxygenation. The blood electrolytes, gas tensions, pH, osmolality, temperature, and perfusion pressure can be maintained within carefully controlled limits.

Gastric secretion in response to intraarterial histamine, pentagastrin, and caerulein has been measured. The maximum acid output in response to 20 μg histamine per minute was 180-200 μ-equiv/minute and was maintained throughout the 90-minute period of observation. The maximum concentration of acid was 155 m-equiv per litre. Compared with histamine the onset of acid secretion in response to caerulein (0.5 μg/minute) was slower and the maximum acid output lower (130 to 135 m-equiv/min). The maximum concentration was 132 m-equiv/litre. The response to pentagastrin was very similar to that of caerulein.

The motility of the stomach and duodenum has been monitored by a combination of open tip tubes and balloons. The electrical activity has been studied by multiple subserosal differential electrodes placed in the antrum and duodenum.

When the stomach was filled with saline at a constant hydrostatic pressure of 5 to 8 cm regular contractions occurred at a rate of 1 or 2 per minute in the fundus, 3 or 4 per minute in the antrum, and 14 to 18 per minute in the duodenum. The gastro-duodenal region has been studied in detail. A characteristic type of motility has been demonstrated in the junctional area between stomach and duodenum and the length of this zone defined by a pull-through technique. Gastric emptying has been investigated and has been found to be intermittent and related to the motility of the antrum and junctional zone.

AN IMMUNOLOGICAL APPROACH TO THE DIAGNOSIS OF REJECTION OF LIVER TRANSPLANTS

A. L. W. F. EDDLESTON, M. G. M. SMITH, J. DOMINGUEZ, ROGER WILLIAMS, AND R. Y. CALNE (From the Liver Unit, King's College Hospital, London, and the Department of Surgery, University of Cambridge) The diagnosis of rejection of a liver transplant can be difficult as changes in conventional liver function tests are non-specific. Serum hepatitis, extrahepatic obstruction, and vascular lesions can all cause jaundice in the postoperative period. Rejection is probably mediated by sensitized lymphocytes and if these could be detected in the peripheral blood the diagnosis of rejection might be made with more certainty. Changes in the migration of leucocytes

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in the presence of a specific antigen has been shown, in man, to be a measure of delayed hypersensitivity. In a preliminary report we described the development of an in-vitro test for rejection based on the changes observed in the migration of peripheral blood leucocytes (obtained from the patient) when exposed to foetal liver homogenate in a tissue culture chamber.

We have now used this test to follow the changes in the cell-mediated immune response to liver and histocompatibility antigens in five patients after liver transplantation. Changes in leucocyte migration preceded changes in conventional liver function tests during rejection episodes in all the patients studied and gave a clear indication of recovery from rejection whether this occurred spontaneously or after increased doses of immunsuppressive agents.

Early episodes of inhibition of leucocyte migration were associated with marked changes in liver function tests but similar episodes occurring some months after operation in two long-term survivors were associated with little, if any, biochemical evidence of organ dysfunction. This is in keeping with the reported findings after renal transplantation in the dog and may mean that the transplanted organ becomes partially protected from immune attack by the development of 'graft' adaptation to the host.

REFERENCES


AUSTRALIA ANTIGEN AND SMOOTH MUSCLE ANTIBODY IN ACUTE AND CHRONIC HEPATITIS

RALPH WRIGHT, R. W. MCCOLLUM, AND GERALD KLATSKIN (Nuffield Department of Clinical Medicine, Oxford, and Yale University School of Medicine) Sera from patients with biopsy-documented liver disease including acute viral hepatitis (78 patients), prolonged viral hepatitis (13 patients), subacute hepatic necrosis with progression to cirrhosis (15 patients), and chronic active hepatitis (23 patients) were examined for Australia antigen and smooth muscle antibody. In acute viral hepatitis Australia antigen was present in over half the patients early in the course of the disease and disappeared with recovery, whereas smooth muscle antibody was present much less frequently, intermittently and usually only at low titre. In prolonged viral hepatitis the Australia antigen could be detected for months or years, but was not associated with the development of antibody to the Australia antigen or of smooth muscle antibody. In subacute hepatic necrosis with progression to cirrhosis and in chronic active hepatitis, the Australia antigen was detected in one quarter of the patients, and those who did not have the antigen in their serum frequently had smooth muscle antibody at high titre.

The implications of these findings will be discussed.

RAVOCARBON ESTIMATION OF LACTOSE ABSORPTION: A SURVEY OF 104 PATIENTS WITH SKIN DISEASE

P. R. SALMON, A. E. READ, AND R. WARIN (Departments of Medicine and Dermatology, Bristol Royal Infirmary)

A method of estimating intestinal lactase activity by autoradiography of expired air following the ingestion of lactose-14C has been described. This technique has been applied to the study of a series of 104 patients admitted to hospital with skin disease. The patients fell into four main diagnostic categories: (1) controls (23), patients who were chiefly treated for gravitational ulcer; (2) psoriasis (30); (3) generalized eczema (19); (4) contact dermatitis (10). Seven patients failed to complete the test.

Comparison of the two-hour radiocarbon excretion, which has been shown to separate normals from those with alactasia (p = < 0.001), showed that only those with contact dermatitis and positive patch tests differed significantly from the control group.

A correlation was, however, demonstrated between the extent of the rash in those with psoriasis and radiocarbon excretion (r = -0.725, p < 0.001). There was no significant correlation between age, sex, length of history, and radiocarbon excretion.

These findings are discussed in relation to current concepts of dermatogenic enteropathy. Radiocarbon estimation of lactose absorption provides a suitable means of screening large numbers of patients for evidence of brush-border damage.

REFERENCES


HYPOLACTASIA AND THE IRritable Colon SYNDROME

A. S. PENA, S. C. TRUELOVE, K. LUMSDEN, AND R. WHITEHEAD (The Radcliffe Infirmary, Oxford) From a large number of patients diagnosed as suffering from the irritable colon syndrome according to the criteria of Chaudhry and Truelove, 52 were selected for study of the small-intestinal disaccharidases because they had some clinical features suggesting the possibility of hypolactasia. All had a jejunal biopsy performed and the disaccharidases were assayed by the method of Burgess, Levin, Mahalanabis, and Tonge. In patients with a lactase activity of less than 2 units per gram wet weight, the presence of hypolactasia was confirmed by a lactase barium meal or by a lactose tolerance test. Eight of these 52 patients were of foreign birth and came from countries in which hypolactasia is common; all eight showed hypolactasia. One of these patients had hyposucrasia in addition to hypolactasia, a rare combination of deficiencies; there was a past history of bloody diarrhoea in India, diagnosed as dysentery, and though there was no direct evidence of protozoal or parasitic infestation at the time of examination, the small-intestinal biopsy specimen showed minor villous abnormalities and a definite increase of inflammatory cells in the lamina propria. In the other seven patients, the small-intestinal mucosa was microscopically normal. Among these eight patients, symptomatic relief was obtained simply with a lactose-free diet in only two;
several of the remainder had a good symptomatic response when a standard regime for the irritable colon syndrome was added to the dietary treatment.

Among the 44 patients of British birth, there were eight with hypolactasia. One of these patients developed his symptoms after an attack of 'food poisoning' affecting all members of his family; he responded to a lactose-free diet, but when re-examined six months later he showed a normal level of small-intestinal lactase and he was then able to return to a normal diet without getting symptoms. Among the other seven patients, some responded well to a lactose-free diet but others derived no benefit. All but one of the 44 patients had small-intestinal biopsy specimens which were structurally normal by dissecting and light microscopy; the exception was a girl with mild partial villous atrophy but with normal enzyme levels.

We conclude that, among patients of British birth who develop the features of irritable colon syndrome, there is a minority with hypolactasia and in some of these a lactose-free diet on its own will relieve the symptoms. Hypolactasia is possibly more common among patients presenting with the irritable colon than it is in the general population; for example, we have studied 28 patients with simple iron-deficiency anaemia and found only two to have hypolactasia. However, the striking fact is that most patients with the irritable colon syndrome do not have hypolactasia and, even when this is present, it does not always account for the symptoms.

REFERENCES


SOME OBSERVATIONS ON THE ACTIONS OF PURE UROGASTRONE

E. L. GERRING (Imperial Chemicals (Pharmaceuticals) Ltd., Alderley Park) introduced by H. T. HOWAT Urogastrone is a potent inhibitor of gastric acid secretion found in the urine of man and certain animals. The pure substance was highly effective in inhibiting acid secretion in denervated pouch dogs in doses of 1 to 2 μg/kg intravenously. It was similarly effective against histamine, pentagastrin, or test meal-stimulated secretion. In the innervated stomach somewhat larger doses were required. Acid concentration was unchanged during the inhibition, except in the case of histamine stimulation of the innervated stomach, where a significant reduction in acid concentration was observed following urogastrone. Urogastrone was without effect on pancreatic exocrine secretion, salivary secretion, or gastric motility in animals.

EFFECTS OF SECRETORY INHIBITORS ON MUCOSAL BLOOD FLOW IN NON-SECRETING HEIDENHAIN POUCHES

DAVID J. COWLEY AND C. F. CODE (Mayo Clinic) introduced by ALAN G. COX Resting gastric mucosal blood flow was measured by a modification of the aminopyrine clearance technique.1 In this modification the plasma level of aminopyrine was kept constant and the amount cleared into the non-secreting Heidenhain pouches of conscious dogs was measured. The pouches were kept filled with 16 ml of N/10 HCl which was changed at 30-minute intervals throughout the test. After three control periods secretory inhibitors were administered: pentagastrin, 50 μg, as a single rapid intravenous injection, or one of the following by intravenous infusion for 90 minutes; pitressin 4 units/hr, noradrenaline 0.5 μg/kg/min, adrenaline 1 μg/kg/min. Pentagastrin, pitressin, and noradrenaline reduced the resting mucosal blood flow by a mean of 47%, 73%, and 45% respectively. Adrenaline increased mucosal blood flow by a mean of 140%. In no tests did the pouches secrete acid. These findings suggest that the method provides a valid index of changes in mucosal blood flow. An increase of mucosal blood flow is not necessarily a stimulus to secretion. Inhibition of secretion by a single rapid injection of pentagastrin may be caused by the reduction of mucosal blood flow.

REFERENCE


THE RELATIONSHIP OF PENTAGASTRIN-STIMULATED PEPSIN SECRETION TO DUODENAL ULCERATION

C. W. VENABLES (Department of Surgery, University of Newcastle upon Tyne) The maximal acid and pepsin response to intramuscular pentagastrin (6 μg/kg intramuscularly) was measured in one hundred and fifty-three patients. A washout technique was used in all the tests to improve the accuracy of collection and reduce losses in peptic activity before collection.1

The patients were divided into three groups following investigation or operation. Group I consisted of 75 patients who had an active ulcer at operation with a well defined crater or thickening and stippling of the duodenum. Group II consisted of 24 patients in whom only a scar was found at operation with no evidence of recent inflammation. Group III were 54 patients with either no indigestion or dyspepsia with no radiological evidence of duodenal ulceration. No patients in this group had laparotomy.

The correlation between acid and pepsin output was significant in each group (I, 0.65, II, 0.70, III, 0.67).

The output of pepsin was increased in the group with active ulceration and the difference in the regression lines between the active and inactive groups was significant (p < 0.01). The mean difference in pepsin secretion between the groups was 42 mg/hr. There was no difference between the regression lines of groups II and III.

These findings suggest that the activity of duodenal ulceration is associated with increased pepsin secretion and is not related to acid output.

REFERENCE

CORTICOSTEROIDS (INCLUDING ACTH) IN CROHN'S DISEASE

J. F. FIELDING AND W. T. COOKE (Nutritional and Intestinal Unit, The General Hospital, Birmingham). Of three hundred patients with Crohn's disease followed by one of us between 1944 and 1968, 124 have received corticosteroids and/or ACTH: 66 of 197 patients with small bowel disease, 25 of 49 patients with combined small and large bowel disease, and 33 of 51 with large bowel disease. Forty-seven patients have received continuous therapy for two years or more.

In the six months following the initiation of therapy, 16-0% were rendered symptom free, 60% showed improvement, and 24% were not benefited. These clinical results were paralleled by the biochemical and, to a lesser degree, the haematological findings.

The patients were twice as likely to undergo excisional or bypass surgery at any time between four and 20 years after the time of diagnosis as those that did not receive steroid therapy (p < 0.001). The mortality rate in the steroid-treated group was four times that of a matched group of the general population and double that of the whole group of 300 patients. Side effects from therapy which may have contributed to this mortality rate are discussed.

THE EFFECT OF DIVERSION OF INTESTINAL CONTENTS ON THE PROGRESS OF CROHN'S DISEASE OF THE LARGE BOWEL

J. H. BURMAN, J. A. WILLIAMS, H. THOMPSON, AND W. T. COOKE (The General Hospital, Birmingham). Preliminary reports have suggested that in Crohn's disease faecal stream diversion may allow the disease in the defunctioned bowel to heal sufficiently to permit subsequent restoration of intestinal continuity.1,2

We present a study of 24 patients with Crohn's disease followed up between 12 and 200 months since faecal stream diversion.

An assessment is made whether (1) diversion results in improvement in the systemic signs of disease; (2) there is cessation of disease activity in the defunctioned bowel; and (3) the diverted bowel is able to resume useful function after restoration of continuity.1

1 All but one patient showed improvement in general health; most gained weight and the majority of those in whom regular measurements were made showed improvement in levels of haemoglobin, serum albumin, and seromucoids.

2 No patient has shown evidence of complete cessation of disease activity in the defunctioned bowel. Twelve patients have had a subsequent resection and in all there was macroscopical and microscopical evidence of continued disease. Of those patients who retain their defunctioned bowel, there is sufficient evidence in five of disease activity to preclude restoration.

3 Four patients have had restoration of continuity. Two are well with minimal sigmoidoscopic evidence of rectal inflammation. One required proctectomy after three months and one died after some years of fistulae of unrelated small bowel infarction.

These results suggest that there is little chance of 'resting' Crohn's disease in the expectation of subsequent re-use of the bowel.

REFERENCES


IRON ABSORPTION AND RETENTION IN CHRONIC RENAL FAILURE

J. B. HAWKINS, H. G. SAMMONS, B. J. SMITS, AND B. H. B. ROBINSON (East Birmingham Hospital and United Birmingham Hospitals) Observing that oral iron therapy failed to correct the biochemical picture of iron deficiency in patients on maintenance dialysis, a group (15) of these patients and a second group (14) of patients with advanced renal failure were tested for their ability to absorb iron from the alimentary tract. Plasma iron levels in both groups were below normal; the mean iron-binding capacity in the second group was slightly above normal and in the dialysis group was higher still.

Two methods of assessment were used. Radioiron retention was measured by giving 55FeCl3, in N/10 HCl as a drink during the course of a standard meal containing 6 mg of food iron. Retention at 14 days was determined by whole-body counting. Oral iron absorption was measured by giving a freshly prepared solution of 100 mg FeSO4 in 250 ml distilled water to the fasting patient. Blood for plasma iron was taken at 0, half, one and a half, two, and three hours and analysed automatically by the method of Young and Hicks.1

Both groups showed depressed alimentary iron absorption by both methods of assessment compared with patients who had similarly low plasma iron levels but no renal disease. In a few patients maintenance dialysis appeared partially to have reversed this trend. Most of the dialysis patients became less anaemic when given parenteral iron dextran.

Possible reasons for the malabsorption of iron will be discussed. It is suggested that apparent iron deficiency in renal failure patients should be treated with parenteral iron, albeit cautiously, as excess iron tends to accumulate uselessly in extramedullary tissues.

REFERENCE

1 Young, D. S., and Hicks, J. M. (1965), J. clin. Path., 18, 98.

COMPARISON OF ABSORPTION OF A POLAR AND NON-POLAR LIPID FROM MICELLAR SOLUTIONS AND EMULSIONS

M. MACMAHON AND G. R. THOMPSON (Royal Postgraduate Medical School, London) Simmonds, Redgrave, and Willix1 have suggested that fatty acids are absorbed as efficiently from emulsions as from micellar solutions. The present study further explores this concept, by similarly comparing the absorption of a long-chain fatty acids.
acids and a fat-soluble vitamin. This was done by intraduodenal administration to lymph fistula rats of \textsuperscript{14}C-oleic acid and \textsuperscript{3}H-a-tocopherol in mixed micellar solutions or emulsions (9.6 or 48 mM fatty acid in 20 mM taurocholate). The percentage absorption of oleic acid into 0-24-hour lymph was similar from micelles (57\%) and emulsions (65\%), but tocopherol was better absorbed from micelles (45\%) than from the emulsion (29\%). To avoid intraluminal conversion of emulsions into micelles, the labelled lipids were next administered to lymph and bile duct cannulated rats in identical micelles, or as emulsions containing 9.6 mM fatty acid in 2.5 mM taurocholate. The results were as before, with equal absorption of oleic acid from both solutions (67 and 63\%) but better absorption of tocopherol from micelles (19\%) than from the emulsion (5-5\%). These results suggest that micelle formation is important for the absorption of an insoluble non-polar lipid, such as \alpha-tocopherol, but not for a polar lipid, such as oleic acid.

**REFERENCE**


**THE INCIDENCE AND CLINICAL SIGNIFICANCE OF FAECAL HYDROXY FATTY ACIDS**

T. D. Kellock, Joy R. Pearson, R. I. Russell, J. G. Walker, and H. S. Wiggins (MRC Gastroenterology Research Unit and Department of Gastroenterology, Central Middlesex Hospital, London) In 12 normal subjects hydroxy stearic acid (produced by bacteria from dietary fat) was less than 3\% of the total faecal fatty acids. No less than 43 out of 75 patients with gastrointestinal disorders exceeded this level, the maximum found being 23\%.

The patients studied were in the following categories: ileal resection (10), partial gastrectomy (12), vagotomy and pyloroplasty (15), pancreatic steatorrhoea (7), adult coeliac disease (7), ileal disease (6), diffuse small bowel disease (8), and a miscellaneous group (10).

The eight patients with gross steatorrhoea who were excreting more than 30 g/day of faecal fatty acids from whatever cause had a mean proportion of 14\% (range 9 to 21\%). Of the cases with less severe steatorrhoea hydroxy fatty acids were present in increased amounts, particularly in the ileal resection group. The maximum faecal fatty acid excretion for this group was 17 g/day and six out of 10 in this group had more than 10\% hydroxy stearic acid compared with two of 42 (both with coeliac disease) in all other disease groups with the same range of steatorrhoea.

In addition to hydroxy stearic acid, a C18 unsaturated hydroxy fatty acid chemically similar to ricinoleic acid has been detected in samples with high levels of hydroxy stearic acid.

**THE DIGESTION AND ABSORPTION OF GLYCINE OLIGOPePTIDES**

T. J. Peters, K. Modha, and M. T. MacMahon (MRC Intestinal Malabsorption Group, Royal Postgraduate Medical School, London) introduced by C. C. Booth In a previous communication,\(^1\) it was shown that dipeptidase activity was predominantly localized to the soluble fraction of intestinal mucosa and only small amounts (5 to 10\%) were present in the brush border region. Tripeptidase activity, however, was found to be significantly (20 to 45\%) localized to the brush border region of the enterocyte.

The subcellular localization of peptidase activity was studied using a series of glycine oligopeptides (up to and including hexaglycine). All the peptides except diglycine were hydrolysed by the brush borders in vitro. The relative rates and mechanism of hydrolysis of the various peptides by the brush border enzymes were also studied.

Glycine peptides (100 mM) were infused into the duodenum of fasted splenectomized rats. Portal and femoral artery blood was sampled and analysed for glycine and glycine peptides by ion exchange chromatography. During the infusion of di-, tri-, or tetracycline both portal and systemic blood showed a chromatographic peak which was identified as diglycine. No tridecaglycine was detected.

It is suggested that triglycer and longer peptides are partially hydrolysed at the brush border. Dipeptides are, at least in part, absorbed directly into the enterocyte where intracellular hydrolysis occurs, although a small proportion of the dipeptide enters portal blood.

**REFERENCE**


**NEONATAL PYLORIC HYPERTROPHY AND DUODENAL ULCERATION PRODUCED BY PENTAGASTRIN**

J. A. Dodge (Nuffield Department of Child Health, The Queen's University of Belfast) introduced by I. J. Carré. Prolonged administration of gastrin has been shown to produce duodenal ulcers in experimental animals. Pentagastrin has similar physiological effects to the natural hormone, and was administered in depot form to two pregnant bitches and some of their offspring, as well as to the pups of an untreated mother. The preparation contained 8 mg pentagastrin/100 ml of a 10\% mixture of beeswax in arachis oil.

The pregnant animals were each given 2 mg of the depot pentagastrin, twice daily for the three weeks before delivery. Newborn puppies of both these mothers had pyloric hypertrophy at birth, in one case with superficial ulceration in the pyloric canal. Others of the offspring were given further pentagastrin (1 mg, bd, for variable periods) and in several instances large duodenal ulcers were produced. In some, but not all cases, marked pyloric hypertrophy developed, resembling the 'tumour' of human infantile pyloric stenosis. Muscular hypertrophy was less marked in puppies born to the untreated mother, who were given pentagastrin postnatally, although they also developed duodenal ulcers.

In one case, a pup which had been exposed to pentagastrin both before and after birth died at the age of 38 days from a perforated oesophageal ulcer. A duodenal ulcer and pyloric 'tumour' were also present.

These findings indicate that chronic pentagastrin...
stimulation of the parietal cells in puppies, and in adult dogs, may produce duodenal ulceration. Moreover, pyloric hypertrophy may also be produced in young puppies, and in at least one instance appears to have occurred as a result of prenatal administration of pentagastrin to the mother. One would expect transplacental passage of the relatively small pentagastrin molecule to occur, and it is known that at least in humans the foetus is capable of producing considerable amounts of gastric juice prior to birth, possibly in response to maternal or autogenous gastrin. The association of pyloric hypertrophy with duodenal ulceration in the human infant has previously been demonstrated on rare occasions, and postulated as a frequent occurrence. Under experimental conditions the lesions may evidently coexist in young puppies.

Factors Affecting the Mortality in Haemorrhage from Benign (Pep t ic) Lesions of the Stomach and Duodenum

A. MCEWEN, S. JOHNSTON, C. D. NEEDHAM, P. F. JONES, AND J. KYLE (Aberdeen) During the years 1967 and 1968 a prospective study was carried out on all patients bleeding from benign (peptic) disease of the stomach and duodenum who were admitted to hospital in the north-east region of Scotland (population 440,000). There were 566 such patients admitted, of whom 50 died, a mortality of 8.8%. The factors determining a fatal outcome were then analysed. The sex of the patient and delay in admission to hospital were not important, nor was a history of previous haemorrhage or of recent ingestion of aspirin. Mortality was significantly lower among patients who had had previous episodes of bleeding. The age of the patient, further bleeding after admission and the amount of blood lost were most important factors. Erosive gastritis had a mortality more than twice that of duodenal ulceration; surprisingly there were no deaths in the stomal ulcer group. The presence of major associated diseases was twice as common among those who died as it was in the survivors, but mostly there was little correlation between such diseases and the eventual cause of death. Almost half of the fatal cases received 4 litres or more of transfused blood, but frequently too little was given too slowly in the early stages. The mortality among the 175 patients treated operatively (13%) was higher than among those managed medically throughout; the operation group contained the most serious cases, but some of the deaths are attributed to errors in timing and surgical technique.

Water and Electrolyte Imbalance in Pyloric Stenosis

J. A. GRAHAM (Department of Surgery, Western Infirmary, Glasgow) introduced by A. W. KAY The changes in extra- and intracellular water and electrolyte contents in patients with pyloric stenosis have been measured using a muscle biopsy technique. Comparison has been made between the serum and intracellular electrolyte concentrations in these patients in whom the usual disturbance is a hypochloremic alkalosis with a variable loss of sodium and potassium. The patients have been divided into three groups according to the duration and severity of their clinical symptoms.

The acute cases were all clinically dehydrated and had gross serum electrolyte abnormalities. Despite this, the total biopsy water content was normal, but there was a marked reduction in extracellular water, and an increase in intracellular water. Biopsy sodium and chloride contents were greatly reduced, but the potassium content was normal. The loss of sodium and chloride causes a reduction in the extracellular osmotic pressure, and the shif t of water into the cell is probably necessary to restore osmotic equilibrium across the cell membrane.

In subacute and chronic cases the biopsy water and electrolyte contents were either normal or showed an increase in extracellular water and sodium contents, as found in 'starvation'.

In all the patients the biopsy potassium contents were within normal limits, despite low serum potassium concentrations in most cases. This is probably due to the well known effect of extracellular alkalosis preventing loss of potassium from the cell.

References


The Production of Indole by Bacteria In Vitro

G. Neale, R. A. Lambert, and S. Gorbach (Royal Postgraduate Medical School, London) Although the excretion of urinary indican, an end product of intestinal bacterial action on 1-tryptophan, is higher than normal in most conditions causing steatorrhoea, the degree of indicanuria depends on the type of malabsorption. Patients with bacterial proliferation in a stagnant loop of small intestine commonly produce high levels of indicanuria even when they have little steatorrhoea. In coeliac disease and after intestinal resection the degree of indicanuria is usually less and is presumably due to a 'spillover' of unabsorbed tryptophan into the colon. Patients with diarrhoea due to severe pancreatic insufficiency or due to disaccharidase deficiency often excrete less indican than normal subjects.

To study the mechanisms for the variable levels of indican excretion in patients, the production of indole by bacteria has been examined in vitro with the following results. (1) Indole is produced more readily by E. coli than Bacteroides, and the presence of non-indole-producing bacteria does not influence its formation. (2) Indole production falls progressively as the pH of the medium is reduced from 8.3. Below a pH of 5.5 no indole is produced. (3) At concentrations of 1 g/100 ml, glucose, fructose, and lactose inhibit completely the production of indole by E. coli in 1% peptone water. At a concentration of 0.1 g/100 ml these sugars delay the production of indole. Galactose inhibits indole production to a lessee
degree and maltose and sucrose have no effect. (4) The addition of pancreatic enzymes to meat broth and albumin solution facilitates the production of indole by E. coli.

These findings are applied to an analysis of indican excretion by patients with gastrointestinal disease and help to explain some of the difficulties in the interpretation of indicanuria.

PYRIDOXINE DEFICIENCY IN COELIAC DISEASE AND THE DETECTION OF NEUROPSYCHIATRIC DISORDERS

JOHN S. MORRIS, A. B. ADUKIEWICZ, and A. E. READ (Department of Medicine, University of Bristol) Neurological disorders have been reported in association with adult coeliac disease. The nature of the relationship is unknown, although disordered metabolism of pyridoxine may be important. The availability of a microbiological assay method for the estimation of serum levels of pyridoxine has stimulated this investigation into the relationship between neurological disorder and adult coeliac disease.

Thirty patients with adult coeliac disease were investigated. Their ages ranged from 21 to 76 years. Fourteen patients (10 female) had been on a gluten-free diet for a period of from 11 months to 15 years; 10 patients (five female) had been on a low fat diet with supplementary vitamins for a period of from one to 15 years and six patients (four female) were undergoing investigation before starting treatment. In 28 patients the diagnosis had been made by the finding of a subtotal villous atrophy on peroral jejunal biopsy; in the two remaining patients there had been a favourable response to dietary gluten restriction. One female patient had diabetes.

All patients were examined by one of us (J.S.M.). Peripheral nerve conduction studies were performed and serum levels of calcium, folate, vitamin B₁₂ and pyridoxine estimated as well as the haemoglobin.

Depression requiring psychiatric supervision occurred in three patients. Two patients had experienced transient loss of consciousness, one patient being left with a transient hemiplegia. Paraesthesia was a prominent symptom in nine patients. Muscle wasting, with loss of reflexes and sensory impairment occurred in only one patient. A slowed nerve conduction velocity was seen in only one patient, a 64-year-old man not on a gluten-free diet.

No apparent relationship existed between depression, transient losses of consciousness or paraesthesia with anaemia, folate or B₁₂ deficiency. Serum calcium levels were lower in patients with paraesthesia (mean 9·1 mg %) compared with those without (mean 9·5 mg %) but this difference was not statistically significant. Pyridoxine levels were higher in those patients on a gluten-free diet. Of the whole group 15 patients had lowered levels of serum pyridoxine. The mean nerve conduction velocities in these patients, however, was only slightly lower than in those patients with a normal level of pyridoxine.

REFERENCE


STRUCTURAL AND FUNCTIONAL CHANGES IN RAT JEJUNUM AND ILEUM AFTER SURGICAL EXCLUSION FROM NORMAL INTESTINAL CONTINUITY

M. H. GLEESON, J. CULLEN, JUNE COLLINS, AND R. H. DOWLING (Departments of Medicine and Morbid Anatomy, Royal Postgraduate Medical School, London) Following small bowel resection in the rat, the residual intestine undergoes anatomical and functional compensation, which occurs to a much greater extent in ileum than in jejunum. The greater ileal compensation appears to be due to increased intraluminal nutrition. A corollary is that intestine deprived of intraluminal nutrition should undergo atrophy. To study this, we excluded two-thirds of either proximal or distal small bowel from intestinal continuity by creating Thierry-Vella fistulae and examined the morphology and function of the bypassed segments.

Macroscopically, the bypassed intestine became narrowed, but histological measurements of villous height and total mucosal thickness were normal. However, on dissecting microscopy, villi in bypassed jejunum changed from normal adult ridges to 'leaves'; bypassed ileum changed from normal adult leaves to finger-like villi.

Mean jejunal glucose absorption (mg/cm intestine/hour measured in vivo) in 16 control rats was 1·93 (±SEM 0·12). In 16 animals with proximal bypass, glucose absorption from comparable segments of excluded jejunum was normal up to six weeks after surgery (2·10 mg) but fell to 1·66 mg at six to nine weeks and from 10 weeks onwards absorption was significantly depressed to 1·06 (±SEM 0·11) (p < 0·001).

Ileal glucose absorption in nine animals with distal bypass 1·13 ± SEM 0·14 was the same as in controls 1·13 ± SEM 0·15 and did not vary with time.

These results support the concept that for glucose absorption in the rat (1) basal (ileal) absorptive capacity is unaffected by intraluminal nutrition. (2) Proximally sited small bowel, whether jejunum or ileum, is stimulated by intraluminal nutrition and removal of such stimulus reduces absorption to basal levels.

REFERENCE


TREATMENT OF SECONDARY HEPATIC TUMOURS BY LIGATION OF THE HEPATIC ARTERY AND PERFUSION OF THE PORTAL VEIN WITH CYTOTOXIC DRUGS

IAIN M. MURRAY-LYON, J. L. DAWSON, M. O. RAKE, L. M. BLENDIS, J. W. LAWS, AND ROGER WILLIAMS (From the Liver Unit and Departments of Surgery and Radiology, King's College Hospital, London) Secondary hepatic tumours derive their blood supply largely from the hepatic artery and surgical ligation of the hepatic artery would be expected to cause ischaemic necrosis of the bulk of the tumour tissue. However, cells in the periphery of the tumour deposits are also supplied by the portal vein. The aim of the present study was to follow hepatic artery ligation by portal vein perfusion via a catheter placed at operation so as to achieve a high concentration of cytotoxic drug in areas of surviving tumour tissue. Results in eight patients are presented—four with

REFERENCE

secondary carcinoma, two with hepatic metastases from a melanoma some years following removal of a primary tumour in the orbit, and two with the carcinoid syndrome.

Immediately following the operation there was a rise in serum aspartate aminotransferase (SGOT) in all patients but in only one was there a rise in serum bilirubin. Severe flushing and hypotension occurred following hepatic artery ligation in the first patient with the carcinoid syndrome. The second patient was, therefore, given cytotoxic drugs through a percutaneous hepatic artery catheter for a period before the ligation in an attempt to control the release of 5-hydroxytryptamine.

All the patients were improved symptomatically with loss of abdominal pain and gain in weight. Symptoms of the carcinoid syndrome were abolished. Shrinkage of the tumour mass was demonstrated on serial liver scans and parallel improvement in liver function occurred. Remission of symptoms has been maintained for up to 10 months.

PROLONGED SURVIVAL WITH INTRAHEPATIC PORTAL HYPERTENSION

R. ZEEGEN, A. STANSFELD, A. M. DAWSON, AND A. H. HUNT (St Bartholomew's Hospital, London) An unexpectedly large group of 44 patients with chronic intrahepatic portal hypertension, not due to hepatic cirrhosis, was found while reviewing the clinical and pathological features of over 250 patients who had undergone a portal decompression operation. Although these patients had been previously labelled as portal cirrhosis, the histological features consisted of minor changes in hepatic lobular and vascular patterns, sometimes with slight portal fibrosis. Nodular regeneration and marked fibrosis were conspicuously absent. The histological changes were similar to those described elsewhere.1,2

Clinically the group could not be distinguished from hepatic cirrhosis for 10 patients had cutaneous stigmata, and 11 had ascites. Routine liver function tests for the group tended to be within the normal range, and even the ascitic patients had a serum albumin above 30 g/100 ml. In the individual patient, however, there was little preoperatively with which to differentiate from the patient with hepatic cirrhosis. At operation the liver was firm with a smooth or granular surface, sometimes covered with a fine capsular fibrous network. Occasionally the liver was shrunken and wrinkled. Extrahepatic portal venous abnormalities were present in 13 patients, and these included partial thrombosis, sclerosis and calcification. A patent umbilical vein was present in three cases.

This series has demonstrated the importance of making the distinction from nodular cirrhosis, for there was a striking difference in prognosis: 83% were alive five years, and 77% were alive 10 years after portal decompression, as compared with 43% at five years and 22% at 10 years for our group of cirrhotic patients. It would, therefore, seem that these patients, with non-cirrhotic intrahepatic portal hypertension, are ideal candidates for portal decompression operations. The very large proportion of this type of case in the present series, as compared with others, is probably due to the fact that mainly good risk patients, ie, those who had survived a bleed or bleeds elsewhere, and were then fit for transfer, were available for operation.

REFERENCES