British Society of Gastroenterology

The one-day scientific spring meeting of the British Society of Gastroenterology was held in Sheffield on 15 April 1971 under the Presidency of Professor A. A. Harper, and with the local arrangements having been made by Professor Duthie. The meeting was held at Ranmoor House, one of the university students' residences. The meeting started with a symposium on polypeptide synthesis and protein turnover in the liver and gastrointestinal tract, and was followed by short papers. Dr J. S. Morley (ICI Research Laboratories, Alderley Park, Cheshire) gave an introductory paper on gastrointestinal hormones, and put the subject initially in an evolutionary perspective and brought out the role of the alimentary tract and its associated organs not only in relation to digestion but also in the production of vital polypeptide hormones and mucoid substances. Over the aeons, divergent mutations had built up what would now be seen as a closely knit interlocking pattern of polypeptide control of alimentary function. There had been much initial confusion from the multiple target sites of action of gastrin, CCK (pancreozymin), glucagon, and secretin, but this was now being resolved and indeed correlated with the basic similarities of the polypeptide patterns of these alimentary hormones. The biomolecular concept of the active tetrapeptide amide (TRP-MET-ASP-PHE) was described with special reference to the development of analogues. It seems that while changes could be made in relation to those amino acids concerned with binding sites (TRP, MET, and PHE), any change to the aspartic fraction caused inactivation, as this one took an active part in the final chemical process. Similar studies have been made in relation to the C terminal heptapeptide and of gastrin II, CCK, and caerulein, and the important role of the sulphated tyrosine for gallbladder activity was demonstrated, and also its spatial relation to tryptophane. The secretin polypeptide molecule was entirely different and no fragments of the 27 amino acid residue had been found to be active. It seemed possible that a special three-dimensional configuration with a double twist was essential to its chemical activity.

Professor A. G. E. Pearse (Royal Postgraduate Medical School, London) further elaborated the evolutionary history of the digestive tract as an endocrine organ. He defined the stem cells of the so-called APUD cell system, based on certain staining and fluorescent characteristics. These were polypeptide-secreting cells which had a common ancestor, being originally nerve cells migrating from the neural crest. This group of cells had differentiated chemically to produce the various polypeptide hormones. It was particularly interesting to note that they could retain some function relating to nerve cells, and, for example, the G cells producing gastrin in the stomach had microvilli which acted as sensors and responded to local change in environment liberating their secretion.

Professor P. N. Campbell (Department of Biochemistry, Medical School, Leeds), with the help of chains of coloured beads and balls, gave a graphic and memorable picture of basic mechanisms of protein synthesis with the ribosomes picking up the messenger RNA strands and building up the genetically determined sequence of amino acids. The intracellular protein production was being made either for export from the cell or in some cases for cell replacement. Many controlling factors existed, but as yet little was known about them.

Dr A. S. Tavill (Northwick Park, Harrow, Middx) gave a picture of the continuous process of synthesis and catabolism of proteins with special reference to liver cells—a process which was independent of the supply of nutrients. The liver protein synthesis amounted to about 10 g daily.

Dr R. Holmes (Royal Infirmary, Manchester) followed on with an account of protein turnover in intestinal mucosa, and this was apparently concentrated in the crypt cells, and appeared to cease in the cells which were travelling up the villi, with the exception of some continued protein production of enzyme subunits in the brush border. The glycoxylic, or layer of glucopolysaccharides, behaved as a dynamic digestive surface to the villi and seemed to help with the concentration of enzyme activity, and bile salts also probably played an important role in relation to the glycoxylic.

Dr R. N. Melmed (Courtauld Institute of Biochemistry, Middlesex Hospital, London) then discussed protein synthesis within the pancreas. This was a very active organ producing 10-30 g daily, mainly as digestive enzymes. The pancreatic acinar cell was particularly well suited for study, as there was a regular sequence of protein production from the base to the apex through the Golgi apparatus which passed on the synthesized proteins into the condensing vacuoles which later reached the apex where they were discharged, the whole process taking about one hour.

This symposium gave a vivid picture of the lessons of molecular biochemistry and electronmicroscopy in relation to protein synthesis by the digestive organs, and, as Professor Duthie commented, was notable not only for its great interest but also for the skill of the contributors in tempering their expertise to the biochemically shorn lambs—the clinical gastroenterologists.

Abstracts of the papers contributed during the rest of the meeting follow.

Influence of Immediately Preceding Insulin Test on Response to Pentagastrin after Highly Selective Vagotomy

D. Johnston, A. R. Wilkinson, C. S. Humphrey, and R. B. Smith (University Department of Surgery, The General Infirmary at Leeds) Acid outputs (AOs) in response to (a) intramuscular pentagastrin (10 μg/kg) alone (PGT) and (b) the PGT immediately after an insulin test (IT + PGT) were compared in 17 men, more than one year after highly selective vagotomy without a drainage procedure (HSV) for duodenal ulcer. We thought that patients with a positive response to insulin might have higher AOs in the IT + PGT than in the PGT.

The opposite was found. In the 17 paired tests, mean peak AO in the PGT was 20.63 ± 0.65 m-equiv per hour, and in the IT + PGT, 18.38 ± 1.60 m-equiv per hour. Although this difference was not significant (p > 0.01), when the period five to 20 minutes was considered, the difference was significant (p < 0.05). AO was significantly higher in the PGT alone in six patients with negative insulin tests (p < 0.05). In six patients whose insulin tests were early positive, AO in the PGT alone was the greater in five, and averaged 25% higher than in the IT + PGT. The difference was not significant (p just > 0.05).

These preliminary results suggest that stimulation of the vagi after HSV may inhibit, not enhance, the response of the parietal cell mass (PCM) to exogenous or endogenous gastrin. The vagi both stimulate and inhibit gastric secretion and with most of the vagal fibres to the PCM cut after HSV, the inhibitory influence of the
The Metabolism of Pentagastrin

BRIAN H. STAGG, JOHN M. TEMPERLEY, AND JOHN H. WILLIE (Department of Surgery, University College Hospital, London). We have studied the inactivation of pentagastrin in vitro using homogenates of rat, dog, and human liver. Bioassay (Smith, Lawrence, Colin-Jones, and Schild, 1970) allowed the rapid progress of inactivation to be followed. It was accompanied by conversion of pentagastrin to a more acidic derivative. Although pentagastrin was not degraded by carboxypeptidase the derivative was, showing that it contained a free carboxyl group. The derivative was isolated, hydrolysed and analysed; it contained all the amino acids in pentagastrin. We conclude that pentagastrin is inactivated by deamination to pentagastrin acid:

\[
\text{t-BOC-}_{2}\text{Ala-Try-Met-Asp-PheNH}_{2} \rightarrow \text{t-BOC-}_{2}\text{Ala-Try-Met-Asp-PheOH}
\]

Pentagastrin acid (inactive)

When $^{14}$C-labelled pentagastrin was infused intravenously in dogs up to 80% of the radioactivity reappeared in the bile. Of this, 40% represented unchanged pentagastrin, 36% pentagastrin acid, and the rest products of further metabolism. Thus, similar reactions occurred in vivo and in vitro.

Pentagastrin and gastrin both possess the tetrapeptide in the rectangle. To it they owe all their acid-secretagogue activity. It is therefore important to know the fate of this moiety in the body; defective inactivation would cause gastric hypersecretion and vice versa.

Reference


Reaction of Human Smooth Muscle Antigen with Liver Cells

L. J. FARROW, E. J. HOLBOROW, AND W. D. BRIGHTON (Department of Medicine, St Mary's Hospital, London, M.R.C. Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow, and National Institute for Medical Research, Hampstead Laboratories, London) A report that rabbit antibody against smooth muscle actomyosin binds to cell surfaces in an immunologically specific manner (Groschel-Stewart, Jones, and Kemp, 1970) suggests that human smooth muscle autoantibodies (SMA), found in acute infective (Farrow, Holborow, Johnson, Lamb, Stewart, Taylor, and Zuckerman, 1970) and chronic active hepatitis (Johnson, Holborow, and Glynn, 1966), may be directed at antigens in liver cells.

Monolayer cell cultures from chick embryo livers were treated with cold isopentane. After drying, the monolayers were incubated with various human sera. The cells were then washed and stained with sheep antihuman globulin fluorescein conjugates. Cells treated with sera containing smooth muscle antibody showed a microfilamentous pattern of immunofluorescent staining which was not given by normal sera or sera containing other autoantibodies. Similar results were obtained with cultures of human foetal lung cells. Prior absorption of the SMA positive sera with human myometrial homogenate abolished the staining. Conversely, absorption with isopentane-treated foetal lung cells diminished the titre of smooth muscle staining in cryostat sections of rat stomach from 1:80 to less than 1:10. Cells not treated with isopentane or treated with cold acetone did not give any staining.

Thus, smooth muscle autoantibodies found in human hepatitis are reactive with a component of liver and other cells. In acute infective hepatitis this component might be rendered autoantigenic by the presumed viral infection of the liver cells.

References


Secretory Antibodies to Food Proteins

Coeliac and Non-coeliac Children

ANNE PERFOSON AND FLEETING CARSWELL (Departments of Bacteriology and Immunology and Child Health, University of Glasgow) Tests for antibodies to food proteins have been carried out in serum and upper intestinal secretions of children investigated for suspected gastrointestinal disease. The purpose of the study was two-fold: (1) to determine whether the presence of secretory antibody to wheat or gluten was pathognomonic of coeliac disease and (2) to detect children with secretory antibodies to non-wheat proteins possibly suffering from allergy to food. Antibodies, principally to sheep serum, gluten, wheat, and oats, were present in secretions of all the coeliac children, but also in more than half of the non-coeliac children. For

References


children had secretory antibodies to milk, although most had circulating milk antibodies.

We conclude that (1) coeliac disease is not due simply to the presence of antibodies to cereal proteins (studies of the immunoglobulin classes of these antibodies are in progress); (2) the presence of jejunal secretory antibody to a food protein should not be considered as diagnostic of food allergy.

Small Bowel Mucosal Changes in Psoriasis

R. M. BARRY, P. R. SALMON, AND A. E. READ (Department of Medicine, University of Bristol) The concept of dermatogenic enteropathy was introduced by Shuster and Marks (1965) following their observation that steatorrhoea occurring in nine out of 10 consecutive patients with widespread skin disease, including psoriasis and eczema, improved following treatment of the skin alone. Their initial observations demonstrated a structural abnormality of the jejunal mucosa in psoriasis. Recently, however, they have reassessed their data (Marks and Shuster, 1970) and now find no difference between the jejunal mucosa from patients with psoriasis and that from a control population. The current status of dermatogenic enteropathy seems, therefore, to be in doubt.

We have studied the mucosal architecture in 22 cases of extensive psoriasis and compared the findings with control populations in the Bristol area. Fresh peroral biopsies and postmortem preparations using the method of Loehry and Creamer (1966) have been used. Biopsies were allocated to one of four grades defined so as to eliminate subjective assessment of mucosal features. A difference from normal has been demonstrated. This finding was further confirmed using the lactose utilization test as a measure of small intestinal surface area.

An attempt has been made to elucidate the mechanisms by which the mucosal changes are produced by measuring the loss rate of deoxyribonucleic acid by the method of Croft, Loehry, Taylor, and Cole (1968).

The findings suggest that mucosal changes do occur in psoriasis and that, unlike the lesion in the skin, may be caused by a decreased rate of epithelial cell turnover. The findings are discussed in the light of similar studies in other wasting diseases.

References


Differences in the Colonic Motor Response during Meals in Patients with Constipation or Diarrhoea

SHEILA L. WALLER AND J. J. MISIEWICZ (MRC Gastroenterology Unit, Central Middlesex Hospital, London) It has been suggested that diarrhoea and constipation are respectively associated with low and high levels of colonic segmenting pressure activity, but it has proved difficult to separate the two groups satisfactorily on the basis of manometric observations (Connell, 1962). Ingestion of food is probably the most important stimulus of colonic motility, and we have shown that increased activity occurs during, as well as after, the meal (Holdstock and Misiewicz, 1970). The response during the meal, however, has not been analysed previously in patients with a disturbed bowel habit.

In 26 patients (12 with diarrhoea and 14 with constipation) who had no organic disease of the bowel, the segmenting pressure activity of the left colon was measured with intraluminal manometry before, during, and after a meal. The technique has been described elsewhere (Misiewicz, Waller, and Eisner, 1966).

The average level of colonic activity in the basal period was lower in diarrhoeal than in the constipated subjects (p < 0.01), but the overlap between the two groups was considerable. On the other hand, during the meal the increase of activity in diarrhoeal patients was marked, but present only during the time food was taken. The response to meals of constipated subjects was less striking, but more sustained, and the level of segmenting pressure activity remained high in the postprandial period.

These observations suggest that the brief segmenting response in diarrhoea may fail to prevent the propulsion of faeces into the rectum, with consequent initiation of defaecation. The motor response of the left colon during meals appears to be a promising experimental discriminant between patients with constipation or diarrhoea.

A Simple Method for Measuring Protein Turnover in the Liver: The Effects of Starvation and Low Protein Feeding on Liver Protein Metabolism in the Rat

D. J. MILLWARD (London School of Hygiene and Tropical Medicine) Protein turnover rates in rat liver were measured with three different labels: 14C (guanidine) arginine (Ag14C), 14C Na2CO3, and 35Se selenomethionine (SM). The standard use of Ag14C for protein turnover measurements (Schimke, 1970) was shown to underestimate turnover rates. This resulted from the uptake of the Ag14C by peripheral tissues and its subsequent release and recycling in the liver. SM was unsatisfactory because of pronounced reutilization.

Injecting 14C Na2CO3 produced labelling of liver protein-bound arginine and the carboxyl groups of aspartate and glutamate and other non-essential amino acids. These labelled amino acids rapidly exchange carbon with the tissue H CO3- pool and are not reutilized significantly (Millward, 1970). The half lives of liver and plasma proteins labelled by 14CNa2CO3 injection was shorter than with Ag14C and was similar to that obtained by the constant infusion method.

Starvation and a protein-free diet produced the same loss of liver protein but by different mechanisms. In the starved liver synthesis fell from 0.51 to 0.40 days-1 with little change in catabolism. In contrast the protein-free diet increased catabolism from 0.45 to 0.56 days-1 with little change in synthesis.

References


ing turnover of enzyme proteins during epithelial cell migration.

The interpretation of measurements after the single injection of 14C leucine was complicated by reutilization of the label. Therefore a constant infusion of 14C tyrosine was given to permit measurements of fractional synthetic rates (K in days⁻¹) of total proteins under cyclical feeding conditions (Waterlow and Stephen, 1968). Six-hour infusions with fasted rats showed a K of 1.9 days⁻¹ with a drop to 1.3 days⁻¹ on feeding. Fasted rats infused for 10 hours had a K of 3-7 days⁻¹. These results suggest: (a) a small selective precursor pool for intestinal protein synthesis; (b) considerable recycling, i.e., protein catabolism; (c) an inability to measure true synthetic rates in the intestine by this technique.

The extent of recycling of leucine was demonstrated with a double labelling technique using 3H leucine and 14C carbonate. This permitted calculations of protein catabolic rates without the problem of recycling of labelled amino acids (Millward, 1970).

References


Effect of Sarcoid Spleen Suspension on In Vitro Leucocyte Migration in Crohn’s Disease

J. M. T. WILLOUGHBY AND D. MITCHELL

(Received for publication, 11 October 1970)

In the present study the migration of leucocytes from 18 patients with Crohn’s disease and from four patients with probable Crohn’s disease has been measured after overnight culture with sarcoid (K19) and normal spleen suspensions. Specific inhibition of migration by sarcoid spleen suspension occurred in 12 (67%) of the patients with a definite diagnosis and in three of those with probable Crohn’s disease. Parallel testing of nine patients with ulcerative colitis and nine with various other diagnoses yielded no instance of significant inhibition. The implications of these findings are discussed.

References


Portal Hypertension in Primary Biliary Cirrhosis

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(Royal Free Hospital, London)

The prevalence of portal hypertension and the stage at which it develops in the course of the disease was studied in 117 unscreened patients with primary biliary cirrhosis. Clinical and radiological evidence of portal hypertension was found in 56 patients (47-9%) and 33 bled from oesophageal varices. In five patients, bleeding from varices was the initial presentation and a further 20 developed portal hypertension within two years of the first symptom of primary biliary cirrhosis. The mortality rate in those with portal hypertension was 53-6% compared with 16-4% in the control group; death was due to bleeding in the majority of cases. Portal decompression operations improved the immediate prognosis in individual cases but probably did not alter the progress of the disease. In 47 patients the histological findings in wedge biopsy or necropsy material was correlated with the presence or absence of portal hypertension. Nodular regeneration, marked or moderate fibrosis, and consistent twin-hepatoocyte plates were slightly more common in patients with portal hypertension, but there was no difference in cellular infiltration, lymphoid aggregates and number of thin-walled vessels or arterioles in portal tracts, number and size of effenter veins, or size of sinusoids. Possible mechanisms for the obstruction to portal venous flow in primary biliary cirrhosis are discussed.

Absorption of Dipeptides in Normal and Cystinuric Subjects

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It had been widely assumed until recently that protein is completely hydrolysed to free amino acids before being absorbed but there is now increasing evidence that dipeptides can leave the intestinal lumen intact. This may be nutritionally significant especially in patients with an inherited defect of amino acid transport. Patients with Hartnup disease have been shown to absorb certain neutral amino acids as dipeptides but not as free amino acids (Navab and Asatourian, 1970: Asatourian, Cheng, Edwards, Lane, Matthews, Milne, and Richardson, 1970).

The purpose of this study has been to quantify absorption of dibasic amino acids and their dipeptides in normal and cystinuric subjects using a jejunal perfusion method.

In five normal subjects lysine was absorbed significantly better as glycyll-lysine than as free lysine. In two cystinuric patients, lysine was extremely poorly absorbed in its free form but was absorbed normally as the dipeptide. These results indicate that this dipeptide is being transported from the lumen intact.

When a second dipeptide, L-lysyl-L-lysine, was perfused in a normal subject, and a cystinuric patient, lysine was once again absorbed faster as the dipeptide than as free lysine. However, the dipeptide was poorly absorbed by contrast with glycyl-L-lysine and in the cystinuric patient lysine absorption remained abnormally low even when lysine was given as the dipeptide. In addition, although little free lysine was measured in the lumen during glycyll-lysine perfusion, a considerable quantity was present during the perfusion of L-lysyl-L-lysine.
A Study by Perfusion Techniques of the Absorption Abnormalities in the Jejunum in Adult Coeliac Disease

R. I. Russell, J. G. Allan, V. P. Gerskowitch, and J. W. K. Robertson (Department of Gastroenterology, Royal Infirmary, Glasgow) Little is known of the basic abnormalities in absorption which occur in coeliac disease. Evidence is presented that in many patients with adult coeliac disease there is not only impairment of absorption but also of secretion of water, sodium, and chloride.

The transport of water and electrolytes across the mucosa of the proximal jejenum has been studied in 14 patients with untreated adult coeliac disease by means of a triple-lumen tube perfusion system (Cooper, Levitan, Fordtran, and Ingelfinger, 1966). The results were compared with data obtained by identical methods in 15 normal control volunteers. The perfusate consisted of 2.822 ml of isotonic saline, containing 154 m-equiv/l of sodium and chloride, and 778 ml of 5 g/100 ml glucose. This gave an isotonic solution (56 mM with respect to glucose), whose osmotic pressure was 301 milliosmosls. $^{31}$Cr EDTA and phenol red were used as non-absorbable water-soluble markers.

Mean water absorption in the adult coeliac disease patients was $-26 \pm 4.7$ (SE) m-equiv/hour/30 cm segment compared with $+226 \pm 8.2$ ml per hour in the control group. Mean sodium absorption in the coeliac disease group was $-6.2 \pm 1.3$ (SE) m-equiv/hour/30 cm segment compared with $+25.3 \pm 1.8$ m-equiv/hour in the controls, and for chloride was $-6.1 \pm 0.9$ m-equiv/hour compared with $+22.9 \pm 1.5$ m-equiv/hour in the control group. In patients with adult coeliac disease there was thus a highly significant reduction ($p < 0.001$) in the absorption of water, sodium, and chloride compared with normal.

In a number of patients the study was repeated two to four months after a gluten-free diet was commenced. In all these patients clinical and histological improvement had occurred but in none was there a statistically significant im-

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Poisoning Misadventures by Lloyd Bryan Jensen, published by Charles C. Thomas, Springfield, Ill. (Pp. x + 202, price $10.50) An unusual and often very interesting account of poisoning throughout the ages, full of historical references but also with much present day information on food-borne illnesses.

Amyloidosis. Cause and Manifestation of Senile Deterioration by Philip Schwartz (395 pages. Charles C. Thomas, Springfield, Ill. 1970. $31.00). Amyloidosis is an important component of the aging process and involves many parts of the body, particularly the cardiovascular, cerebral, and alimentary systems. This extensive monograph brings together a vast literature and much experimental animal work.

Gastrointestinal Motility edited by Ludwig Demling and Rudolf Ottenjann (Pp. vi + 219. Georg Thieme Verlag, Stuttgart; Academic Press, New York and London. 1971. DM 27.50). This is a report of an international symposium on motility of the gastrointestinal tract held in Erlangen in July 1969. It was attended by 19 of the leading research workers in this field and provides an admirable record of the progress of our knowledge of order and disorder of motility in the oesophagus, stomach, small intestine, and colon.

Notes on books

Hirschsprung’s Disease by Theodor Ehrenpreis. (175 pages, Year Book Medical Publishers, Inc., Chicago. John Wiley & Sons Ltd, Chichester, £6 30) This valuable monograph reviews the development of present concepts of Hirschsprung’s disease and includes historical notes and a full account of surgical techniques and results.

Intestinal Transport of Electrolytes, Amino Acids and Sugars edited by W. McD. Armstrong and A. S. Nunn, Jr., published by Charles C. Thomas, Springfield, Ill. (Pp. x + 352, price $21.50) This book is based on an international symposium held in 1968, which was concerned mainly with the transport of electrolytes, sugars, and amino acids across the small intestine. The morphology and ultrastructure of the intestinal epithelium is discussed in detail and the basic mechanisms of intestinal transport are described in depth. In addition some of the broader implications of coupled transport in systems other than the intestine are also discussed.

Pathology of Civilization Diseases by J. Sós, T. Gáti, L. Csalay and I. Dési, published by Akadémiai Kiado, the Publishing House of the Hungarian Academy of Sciences, Budapest. (174 pages, price £2.50) This Hungarian book written in English brings together environmental factors in the aetiology of the so-called diseases of civilization—hypertension, coronary artery disease, peptic ulcer, and cancer. The problems arising from chemical contamination of the environment are discussed in detail. This book is a mine of unusual and important information.

Surgical Treatment of the Dumping Syndrome Experience with Gastro-jejunal Fixation by Kristian Stray (56 pages. Universitetsforlaget, Bergen—Oslo. 1970. N.Kr. 30). This short monograph reports a very simple and apparently effective method of dealing with severe cases of dumping after partial gastrectomy, and the same principle can be used to prevent it at the primary operation. By simply attaching 6-8 cm of the efferent loop to the greater curve precipitate emptying ceases.

Pathology of Civilization Diseases by J. Sós, T. Gáti, L. Csalay and I. Dési, published by Akadémiai Kiado, the Publishing House of the Hungarian Academy of Sciences, Budapest. (174 pages, price £2.50) This Hungarian book written in English brings together environmental factors in the aetiology of the so-called diseases of civilization—hypertension, coronary artery disease, peptic ulcer, and cancer. The problems arising from chemical contamination of the environment are discussed in detail. This book is a mine of unusual and important information.