was collected over 6 hours and an aliquot was analysed by gas liquid chromatography.

Crohn's patients absorbed significantly more lactulose (p<0.01; Wilcoxon rank sum test) and less mannitol (p<0.01) than normals or ulcerative colitics. Patients with ileal disease had significantly higher lactulose/mannitol excretion ratios than normals (p<0.01) or ulcerative colitics (p<0.01). Furthermore the 6 patients with Crohn's disease limited to the colon also had significantly higher excretion ratios than normals (p<0.01) or ulcerative colitics (p<0.01).

We conclude that small intestinal permeability to lactulose may be increased in patients with ileal and/or colonic Crohn's disease. Mannitol absorption is decreased perhaps reflecting reduction of intestinal surface area. Lactulose/ mannitol excretion ratios may help to separate Crohn's colitis from ulcerative colitis and provide a useful adjunct to the diagnosis of Crohn's disease. Our results provide support for the concept of Crohn's disease as a diffuse intestinal disorder.

63 THE SECRETION OF INDIVIDUAL PEPISINS IN NORMAL SUBJECTS

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The time-course of pepsin 1 secretion has been previously communicated (Roberts, Sheers and Taylor, Clinical Science, 61, 37P). Pepsin 5 has now been determined as the pepstatin-resistant pepsin activity of gastric juice (Walker and Taylor, Gut, 20, 977-982) and also from electrophorograms of gastric juice, standardised against the pepstatin-resistant activity of basal gastric secretions. Pepsin 3 is determined by subtracting the pepsin 1 and 5 values from the total pepsin concentration.

The basal secretion of pepsin 5 (pepstatin-resistant activity) ranged from 41 to 140 ug/min mean 335 ug/min, accounting for 29.0% of the total pepsin. During continuous pentagastrin stimuli gastric juice (50 ug/min) the value rose to 547 ug/min, 35.0% of the total, at 50 to 60 min. Pepsin 1 secretion was also highest after 50-60 min, but peak pepsin 3 secretion occurred earlier at 30-40 min.

Following intravenous insulin in 10 normal subjects pepsin 5 secretion peaked at 60-70 min with a mean value of 548 ug/min, 13.2% of the total pepsin. Pepsin 3 secretion also peaked at 60-70 min but pepsin 1 peaked at 50-60 min. The proportion of total activity accounted for by pepsin 5 fell as low as 8.7% at 50-60 min.

The secretory mechanisms for individual pepsins thus differ. The proportions of the individually secreted pepsins also differ appreciably with the two types of stimulation. Pentagastrin thus increased the secretion rate of pepsin 1 over the basal rate by a factor of 4.5, pepsin 3 by 2.0 and pepsin 5 by 1.6. For insulin hypoglycaemia the comparable data are pepsin 1, 10.6; pepsin 3, 3.4; pepsin 5, 1.6. Insulin hypoglycaemia is very effective at releasing pepsins 1 and 3.

Pepsin 5 secretion, when measured electrophoretically, ranged from 42% to 90% of the pepstatin-resistant activity. Some electrophorograms showed the appearance of pepsin 4 as stimulation proceeded. Pepsin 4 may be pepstatin-resistant. We have not observed such a change in patients with peptic ulcer.

64 MECHANISMS OF PROTEIN LOSS IN INTESTINAL LYMPHANGIECTASIA


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Enteric protein loss in primary intestinal lymphangiectasia (I.L.) is believed to occur either by direct leakage of lymph from abnormal lymphatic vessels or by cellular disruption caused by interstitial oedema. We have investigated a patient with typical features of I.L. with results which suggest that protein loss is due to an enteroocyte abnormality.

Jejunal biopsies obtained before, and after 9 months treatment with a 10 g/day long-chain triglyceride diet were maintained in organ culture. (L'Hirondel, C., Doe, W.F. and Peters, T.J. Clin. Sci. and Mol. Med. (1976), 50, 425-429). After 3 hours in culture, the pre-treatment biopsies showed increased protein loss from tissue into the mucus layer. (Tissue: mucus ratio 1:1.9, 2.2 and 2.7 for 3 biopsies, compared to 15 controls 1:0.761 ± 0.09 (Mean ± 1S.E.)). Total specific activities of 5 brush border enzymes and 3 intracellular enzymes were no different from controls before or after 3 hours in culture; but after culture, only 20-40% of total activity remained within the tissue (55-70% in controls), the remainder being predominantly in the mucus layer. The loss of activity from the tissue compartment was greater for brush border enzymes (60-70%) than for intracellular enzymes (40-55%). In the post-treatment biopsies these changes had reverted towards normal.

Our data is consistent with decreased viability of enterocytes in culture. Since light microscopy pre-culture showed no interstitial oedema, and only minimal dilatation of occasional lymphatics it is likely that enterocytes were the source of protein loss in vitro. Thus, reversible enterocyte abnormalities can occur in I.L. without evidence of histological damage. This may be an additional mechanism for the protein loss seen in this disease.

65 SUBCELLULAR EVENTS IN THE RAT LIVER DURING THE DEVELOPMENT OF COPPER TOLERANCE

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Copper overloading in the rat causes hepatocellular disruption followed by regeneration and subsequent tolerance to copper (Haywood, 1980, J.comp.Path. 90: 217). A sequential study of the subcellular events was undertaken in order to explore the relationships between copper accumulation and liver damage.

Male rats fed a high copper diet were killed at intervals and compared to appropriate controls. Livers were examined histologically and marker enzymes for the principal organelles were assayed.