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ncluded for each stage of the ablation procedure. A total of 175 fertilised eggs of White Leghorn Austral strain were used. The operative mortality was high: of 143 embryos submitted to diathermy ablation, 17 survived. 10 chicks were not deformed, and 7 others had leg deformities, 2 bilaterally. 5 had similar unilateral deficiencies of the lower leg on the side of the neural-crest ablation (fig. 4). Analysis of residual tissue showed no measurable reduction in spinal cord or mesodermal mass. However, dorsal-root ganglion mass was significantly reduced on the side of the ablation in the 5 chicks with unilateral deformities (fig. 5).

Discussion

This experiment produced deformities in 41% of survivors. Reduction of dorsal-root ganglion mass on the side of the deformity is interpreted as evidence of neural-crest damage. It should be emphasised that ablation of neural crest was carried out before limb buds had formed, and our results cannot be construed as neural-crest depletion secondary to limb-bud damage.[20] There was variable but minor damage to the unsegmented mesenchyme adjacent to the crest, the effect of which is being assessed at present. The ten chicks which survived diathermy ablation without limb deformity are thought to illustrate the known ability of neural crest to regulate and repair deficiencies. The two bilateral deformities may be due to diathermy current crossing the midline. Our results suggest that primary neural-crest injury contributes to the pathogenesis of congenital limb malformations.

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Details of both experiments are to be published in full elsewhere.

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Preliminary Communication

DIAGNOSIS OF PROTEIN-LOSING ENTEROPATHY BY GASTROINTESTINAL CLEARANCE OF ALPHA$_1$-ANTITRYPSIN

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Summary Alpha$_1$-antitrypsin was assessed, in 10 patients with protein-losing enteropathy and 13 control subjects, as an endogenous marker of plasma-protein loss into the gastrointestinal tract. Both fæcal α_1-A.T. concentrations and fæcal α_1-A.T. clearance were significantly higher in patients than in controls. With clearance there was no overlap between the groups. Over 10 days the normal gastrointestinal clearance of α_1-A.T. was $3{\cdot}07 \pm 2{\cdot}25$ (S.D.) ml/day. Measurement of α_1-A.T. clearance is easy and requires no radioisotopes.

INTRODUCTION

GASTROINTESTINAL loss of plasma-protein can be measured with ^{131}I-labelled serum-protein, ^{51}Cr-labelled albumin, ^{67}Cu-labelled cæruloplasmin, and other labelled macromolecules. These methods are expensive, imprecise, and cumbersome. Alpha$_1$-antitrypsin (α_1-A.T.), a protease inhibitor synthesised by the liver, is present in serum at a concentration of 2–5 g/l. This glycoprotein is not degraded by pancreatic enzymes and is readily detectable in the fæces of newborn infants, children, and adults.[1–3] We have tried α_1-A.T. as an endogenous marker of protein loss.

PATIENTS AND METHODS

23 adult inpatients were studied. 13 had no apparent digestive disease and acted as controls. 10 fulfilled the criteria of protein-losing enteropathy: either they had excessive loss of intravenously administered radiolabelled chromium chloride into the fæces or they had evidence of active chronic inflammatory bowel disease (see table). Blood-samples were taken on days 1, 5, and 10 and all stools were collected for 10 days. The clearance of serum α_1-A.T. by the gastrointestinal tract was determined for each day by the formula

$$C = \frac{F \times V}{P}$$

where F is fæcal α_1-A.T. concentration, V is daily fæcal volume,

PATIENTS WITH PROTEIN-LOSING ENTEROPATHY

Patients	Diagnosis	Serum-albumin (normal 40–45 g/l)	^{51}Cr loss (normal <50 ml/day)
1	Cœliac disease	25	408
2	Crohn's disease	30	N.D.
3	Ulcerative colitis	28	N.D.
4	Gastric ulcer; renal failure	20	102
5	Postgastrectomy syndrome	39·5	92
6	Crohn's disease	35·5	N.D.
7	Postgastrectomy syndrome	17	104
8	Lymphonodular hyperplasia of the gut	39·7	99
9	Ulcerative colitis	20·8	N.D.
10	Crohn's disease	35	N.D.

N.D.=not done.

and P is the mean of serum-α_1-A.T. concentrations on days 1, 5, and 10.

α_1-A.T. Determinations

α_1-A.T. was measured by radial immunodiffusion. The immunodiffusion plates contained a monospecific antiserum against α_1-A.T. (M or LC 'Partigen', kindly supplied by Behringwerke Laboratories). The precipitating ring was measured after 3 days. For each batch of plates a reference curve was established with a standard solution.

After centrifugation the sera were kept at −20°C until the day of assay. 5 µl of serum diluted/1/10 in NaCl (150 mmol/l) was put in wells of M partigen plates. Fæces were kept at −20°C until the day of assay. They were diluted in varying proportions (usually 1/4) in isotonic NaCl then agitated for 60 min. After centrifugation at 1500 *g* for 20 min, 20 µl of supernatant was put on partigen plates.

In addition, to test the stability of α_1-A.T. in fæces, 8 stools were kept at 37°C for 3 days and tested daily.

RESULTS

Fig. 1 shows fæcal concentrations of α_1-A.T. In control patients the mean (±S.D.) fæcal concentration was 80±93 mg/l, range 2-324 mg/l; in patients with protein-losing enteropathy the corresponding figures were 2210 mg/l and 174-13 740 mg/l ($P<0.01$).

Fig. 2 shows α_1-A.T. clearances in the two groups. In controls mean clearance (±S.D.) was 3·07±2·25 ml/day, range 0·5–7·0 ml/day; in patients with protein-losing enteropathy mean clearance was 91·7 ml/day, range 16·5–218·0 ml/day ($P<0.001$).

The α_1-A.T. concentration in stools kept at 37°C was 97·1±1·3% of the initial value at 24 h, 93·8± 1·5% at 48 h, and 92·6±2·8% after 72 h.

DISCUSSION

We have shown that gastrointestinal clearance of α_1-A.T. may prove an accurate and reliable method for diagnosis of protein-losing enteropathy. Gastrointestinal clearance was a more useful index than fæcal concentrations, which have been proposed for diagnosis of the condition in children. Why clearance of α_1-A.T. is lower than that of ^{51}Cr-labelled albumin we do not know. The difference does not adversely effect the sensitivity of our test. We are now determining the minimum number of days on which stools must be collected for diagnosis of protein-losing enteropathy: we expect that a 3-day collection will suffice.

The advantages of this test over previous methods are the use of an endogenous marker instead of radiolabelled molecules, the use of commercially available immunodiffusion plates, the feasibility of performing the test on outpatients, and the low cost. We expect the test to ease diagnosis of protein-losing enteropathy and to permit monitoring of response to treatment.

Requests for reprints should be addressed to Ch.L'H.

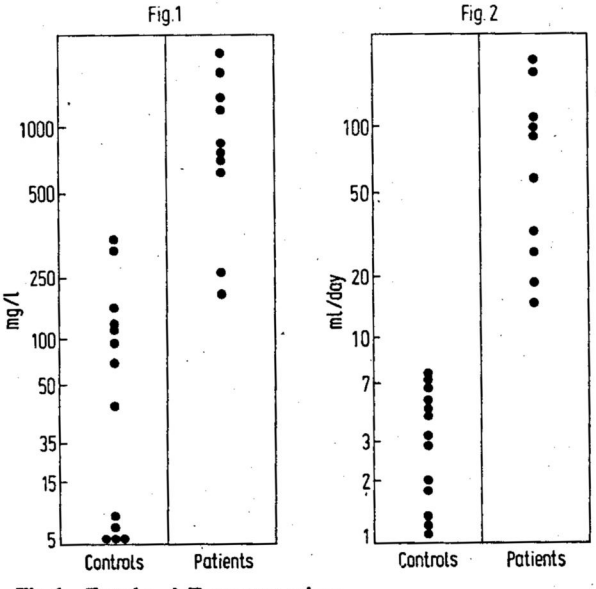

Fig. 1—Fæcal α_1-A.T. concentrations

Fig. 2—Gastrointestinal α_1-A.T. clearance.

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Hypothesis

THE HUMAN RUMEN

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Summary The cow is a ruminant, and cow's milk has evolved to promote bacterial growth in the upper small bowel; whereas human milk has evolved to discourage bacterial growth. Examination of the constituents of the two milks shows that their differences can be accounted for in terms of this difference in function. Children who are fed a calf's diet tend to develop a rumen. This may lead to chronic diarrhœa and malnutrition and may be a factor in diarrhœa ascribed to cow's-milk-protein allergy and lactose intolerance.

INTRODUCTION

THE term "weanling diarrhœa" appropriately describes one of the world's major child-health problems. In unhygienic conditions in poverty-stricken areas, weaning often heralds the start of a cycle of recurrent diarrhœa that leads to stunted growth and development. In better social conditions lactose intolerance and cow's-milk-protein allergy are the order of the day. The close association between the start of a diet based on cow's milk and the onset of diarrhœa is striking, whether the diarrhœa is ascribed to lactose intolerance, milk-protein allergy, or a bacterial or viral infection. A remarkable healing often occurs with a return to human milk.

The biochemical and physiological differences

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