Protein malnutrition in gastro-intestinal disease

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Loss of weight with loss of body protein is not uncommon in malabsorption syndromes although severe hypoproteinaemia is rare. This paper briefly reviews the causes of protein malnutrition due to gastro-intestinal disease, describes the clinical features and discusses methods of treatment. The features of protein-losing enteropathy will not be described as this subject was fully discussed at a similar conference last year (Munro, 1966).

Protein malnutrition is due to inadequate intake of protein by the body either: (1) because of inadequate diet, or (2) because of inadequate digestion and absorption. These causes may co-exist in gastro-intestinal disease.

Clinical features

Protein-deficiency syndromes have been most extensively studied in children living in areas of the world where malnutrition is endemic. Two major conditions have been recognized: marasmus and kwashiorkor. In pure marasmus there is very severe wasting and failure of growth but little or no oedema and the skin and hair remain normal. This condition appears to be primarily due to a deficient intake of calories; it is the end-result of simple starvation.

In contrast, in kwashiorkor, there is severe hypoproteinaemic oedema, the skin breaks down and the hair becomes fine and loses its colour. Children with this condition are miserable and apathetic, and laboratory tests show marked biochemical abnormalities. The cause seems to be severe prolonged protein-deficiency associated with little or no reduction in dietary carbohydrate.

1. Total calorie-deficiency

In this country a high partial gastrectomy is the commonest gastro-intestinal condition causing severe wasting in an adult (Fig. 1). The loss of weight is usually due to inadequate food intake, often because of fear of abdominal discomfort after meals (Johnston, Welbourn & Acheson, 1958). Severe malabsorption associated with such conditions as idiopathic steatorrhoea, massive intestinal resection, the blind-loop syndrome and

chronic pancreatitis may also lead to a clinical state resembling marasmus in which there is marked wasting but no oedema.

Fig. 1. Severe caloric undernutrition in a patient with a Polya partial gastrectomy and dumping syndrome. There is no oedema and serum proteins are normal.

In children long-continued undernutrition may lead to a failure of growth and delayed maturation, but again without hypoproteinaemia. A similar picture is seen in the experimental animal given restricted quantities of a normal diet (McCance, 1960).

2. Protein calorie malnutrition resembling kwashiorkor

More rarely patients with gastro-intestinal

disease present a clinical picture reminiscent of children with kwashiorkor (Fig. 2). Malabsorption has been recognized as a cause of the kwashiorkor syndrome on only rare occasions (Krikler & Schrire, 1958; Leitner, 1958; Silverblatt & Brown, 1960; Brain, Anstall & Jeejeebhoy, 1965; Neale *et al.*, 1967). There are, however, many descriptions by earlier workers of severe malnutrition of a similar kind in infants with gastroenteritis fed solely on a cereal diet for several weeks (Czerny & Keller, 1906) and in patients with malabsorption following gastro-intestinal surgery (e.g. Lambling & Conte, 1949; Binet, Bour & Dejours, 1950; Naish & Capper, 1953). Frequently an intercurrent illness such as an infection seems to precipitate the development of this condition in a patient who is already severely malnourished.

FIG. 2. Kwashiorkor syndrome in a patient with a Billroth I gastrectomy and pancreatic insufficiency. She recovered after feeding her a liquid diet together with pancreatic enzymes via a gastrostomy tube for 2 months. In this picture taken 1 month after starting treatment the ankle oedema has nearly resolved and her hair is growing again.

In obvious cases the patients develop severe oedema and skin dystrophy, their hair loses its

colour and becomes lifeless, and they become miserably apathetic just like the children with kwashiorkor. There may be EEG and ECG abnormalities. The most striking biochemical feature is a severe reduction in serum proteins (particularly serum albumin) and this may be associated with a reduction in essential amino acids in the serum taken from the fasting patient (Whitehead & Dean, 1964). The main cause for the hypoproteinaemia appears to be a reduced synthesis of albumin by the liver (Jeejeebhoy, 1964; Jones *et al.*, 1966). Other signs of liver dysfunction are increased bromsulphthalein retention, very low levels of circulating cholesterol and a high excretion of urocanic acid after an oral dose of L-histidine (Whitehead & Arnstein, 1961). None of the liver-function tests however, are specific for protein-calorie malnutrition.

Aetiology. This condition has been recognized in eight patients admitted to Hammersmith Hospital during the past 4 years. Six had had partial gastrectomies but in all cases there was an additional cause for malabsorption; four patients had stagnant-loop syndromes and two had severe pancreatic insufficiency. Two other patients had severe idiopathic steatorrhoea and in one case this was associated with Crohn's disease.

Pathogenesis. In all cases the major cause for the malnutrition was severe malabsorption which was investigated in detail in seven of the eight patients (Table 1). On a 70 g fat diet they excreted from 28 to 52 g fat/day. Faecal nitrogen was also markedly elevated. Two patients excreted almost as much nitrogen in the faeces as they ingested. Their net absorption of protein was less than 15 g/day and like children with kwashiorkor, their blood ureas were very low (less than 5 mg/100 ml). They both had chronic pancreatic insufficiency associated with high partial gastrectomies, and thus secreted virtually no proteolytic enzymes.

The other five patients had a net nitrogen absorption of 5–6 g which is equivalent to 30–36 g protein and they had blood urea levels in the low normal range (18–28 mg/100 ml). Clearly nitrogen was passing into the urea cycle of these patients but it is probable that a considerable proportion of this nitrogen was in the form of bacterial metabolites, some of which would not be available for body-protein synthesis. For example, bacteria proliferating in the lumen of the gut produce indole from the essential amino acid L-tryptophan. This metabolite is absorbed from both the small and large bowel, is not used by the body and is excreted in the urine as indoxyl

TABLE 1
Details of fat absorption and nitrogen metabolism in seven patients with the kwashiorkor syndrome due to malabsorption

Patient	Diagnosis	Faecal excretion		Urinary indican (mg/day)	Blood urea (mg/100 ml)
		Fat (g/day)	Nitrogen (g/day)		
	Normal:	5	2	23-92	15-40
1	Billroth I gastrectomy, pancreatic insufficiency	35	8.5	35	< 5
2	Polya gastrectomy, pancreatic insufficiency	45	9.5	5	< 5
3	Polya gastrectomy, afferent loop stasis	30	5.5	Very high	18
4	Polya gastrectomy, afferent loop stasis	32	—	220	20
5	Polya gastrectomy, jejunal diverticulosis	52	6.2	250	28
6	Polya gastrectomy, duodenal obstruction	28	5.0	150	25
7	Idiopathic steatorrhea, Crohn's disease	47	5.3	350	22

The patients were eating a diet containing 70 g fat and 70 g protein (11.2 g nitrogen) when the measurements were made.

sulphate (indican). In the five patients who were absorbing moderate quantities of nitrogen, urinary indican excretion was much higher than usual clearly indicating enhanced bacterial degradation of protein. Four of these patients had a stagnant loop syndrome associated with a partial gastrectomy and the fifth had both idiopathic steatorrhea and Crohn's disease. Jones *et al.* (1966) have made a detailed study of one patient with a blind-loop syndrome and hypoproteinaemic malnutrition. They demonstrated a marked reduction of the rate of albumin synthesis which returned to normal on the administration of antibiotics. They suggested that the intestinal bacterial flora interfered with the use of dietary protein. It is interesting to contrast the biochemical features of patients showing evidence of excess degradation of protein by bacteria with that of patients unable to digest protein because of a deficiency of proteolytic enzymes (Table 1). The two patients we have seen with the latter condition excreted much larger amounts of nitrogen in the faeces and very little indican in the urine. The very poor absorption of nitrogen by these patients is reflected in the very low levels of blood urea.

Thus in patients with severe malabsorption protein may be wasted by direct loss into the faeces or by bacterial conversion to nutritionally useless nitrogen products.

Treatment. Intravenous protein feeding may correct the clinical features of protein calorie malnutrition within a week or two. In addition absorption is sometimes improved by this treatment alone. In one patient with a partial gastrectomy and jejunal diverticulosis faecal fat excretion

fell from 40 to 15 g/day following the administration of 25 g albumin intravenously daily for 6 days (Fig. 3). This dramatic improvement in absorption may have been due to an enhanced synthesis of the pancreatic and intestinal enzymes necessary for digestion and absorption. Pancreatic enzyme secretion is reduced in children with kwashiorkor (Thompson &

FIG. 3. Response of one patient (G.L.) to intravenous albumin. He had severe malabsorption due to jejunal diverticulosis associated with a Polya partial gastrectomy.

Trowell, 1952) and small intestinal mucosal abnormalities have also been described (Stanfield, Hutt & Tunnicliffe, 1965). Bile-salt deficiency may also occur in severe malnutrition (McLeod & Wiggins, 1967 personal communication) and this would be particularly serious in a patient with a blind-loop syndrome, a condition in which bacterial deconjugation of bile salts is a potent cause of steatorrhoea (Tabaqchali & Booth, 1966).

Sometimes patients with protein-calorie malnutrition are so apathetic and miserable that they cannot eat. In one of the patients we have studied good health was finally restored by feeding a liquid diet with added pancreatic enzymes through a gastrostomy tube day and night for 2 months (Fig. 2).

In all cases, however, it is necessary to determine and treat the underlying cause of the malabsorption. Of the eight patients described in this communication five are alive and well. The two patients with partial gastrectomies and chronic pancreatic disease are maintained on pancreatic enzymes fed with meals; and the three patients with the stagnant-loop syndrome have done well following surgery to remove the blind loop.

One further patient with a partial gastrectomy and a blind-loop syndrome responded to repeated courses of antibiotics and finally died of carcinoma of the lung. The two patients with idiopathic steatorrhoea did poorly. One died of peritonitis following perforation of the small intestine, and the other, who had an associated Crohn's disease, died of a *Pseudomonas* septicaemia.

Conclusion

Protein malnutrition may be simple under-nutrition which causes wasting in the adult and can delay maturation in children; or it may be sufficiently severe to cause major biochemical disturbances similar to those seen in children with kwashiorkor. When this happens there is probably a reduction in hepatic, pancreatic and intestinal enzymes which in turn enhance the degree of malabsorption. This vicious circle can be broken by intravenous protein feeding but the underlying disease needs treatment to restore the patient to good health.

Acknowledgments

I wish to thank Professor C. C. Booth for his help, advice and encouragement and the Smith, Kline and French Foundation for financial support. The patients with protein malnutrition after partial gastrectomy have been fully reported elsewhere (Neale *et al.*, 1967), and the case of Crohn's disease complicating idiopathic steatorrhoea was the subject of a clinico-pathological conference at the Royal Postgraduate Medical School (Booth, 1967).

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