AMINO ACIDS IN THE FEEDING OF INFANTS*

BY

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Introduction

Enzymic digests of protein, which only became available in this country during the later years of the war, had been made use of in the U.S.A. and Sweden for some time before then. The preparations which we have been using are digests of the casein of cows' milk. All such preparations have a bitter and unpleasant taste due to the presence of free amino acids, although this can be modified to some extent by dilution with milk. Fortunately this disadvantage does not constitute any serious drawback to their employment in infants up to three months of age, who do not appear to resent this taste, and this is the age group in which such pre-digested proteins have a great field of usefulness.

Indications for Amino Acid Feeds

There are obvious advantages in feeding pre-digested rather than raw protein to cases of cystic fibrosis of the pancreas whose duodenal secretions are deficient or completely lacking in trypsin. It has recently been demonstrated (West et al., 1946) that the level of plasma amino acid nitrogen rises in these cases after a meal of hydrolysed casein, indicating absorption from the gut, but not after a meal of unhydrolysed casein or gelatin. This difference is not shown by infants with a normal pancreas. Clearly, the absorption of protein by patients with pancreatic insufficiency is improved by feeding hydrolysed protein.

For those infants who manifest an allergic reaction to the proteins of cows' milk, it would seem reasonable to reduce the protein to its constituent amino acids before administration in an attempt to obviate the adverse effects of ingesting raw protein. This has, in fact, been tried with success (Hill, 1941).

There are two large groups of patients in whom oral fluids are contraindicated, namely those suffering from congenital or acquired obstruction of the alimentary tract, and those suffering from

gastro-enteritis of severe degree. In such cases the daily basal protein requirements must be administered parenterally. In these circumstances protein hydrolysates have proved invaluable, since, apart from the use of human plasma and blood, only protein in the form of amino acids may be given parenterally with safety.

The mixture of polypeptides and amino acids in these enzymic digests does not form a curd in the stomach, and is easily absorbed by the alimentary tract without need for much digestive activity. Hence hydrolysed casein is a valuable source of protein for any infant who cannot tolerate his full protein requirement as unmodified milk protein but who can take oral fluids. Such relative intolerance may be due to increased protein requirements or alimentary insufficiency. Often both factors occur together in the same individual.

In acute infections there is an increased need for protein but there is also a diminished tolerance for food by the gastro-intestinal tract, whether the infection is of enteral or parenteral origin. Here, too, pre-digested protein is a beneficial therapeutic adjunct.

Wasted infants require a high protein intake to make good their depletion of body protein. Whether this has come about as a result of pure starvation, as in pyloric stenosis, or as the result of infection, full milk feeds must be introduced with caution if vomiting and diarrhoea are to be avoided. In view of the diminished digestive powers of these infants (Andersen, 1942; Miller, 1941) protein digests fulfil a valuable function.

Premature infants at birth have a lower nitrogen content per kilo of body weight than full-term infants, and therefore require a high protein intake to make good this deficit and maintain growth. It has been shown that the enzymic activity of the stomach and bowel tends to be low (Miller, 1941), especially in the less mature and smaller infants, and therefore their protein must be supplied to them in a form that their digestive tracts can readily assimilate.

The indications for amino acid feeding may be

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FIG. 1.—A case of pyloric stenosis aged four weeks, 7 per cent. of the expected weight at operation.

listed as follows: (1) cystic fibrosis of the pancreas; (2) milk protein allergy; (3) parenteral feeding; (4) acute enteral or parenteral infection; (5) marasmus; (6) prematurity.

Investigation in Birmingham

At the time when British enzymic digests of casein were first made available by the Medical Research Council, Shohl and his co-workers (1939) had already published the results of feeding experiments with the American preparation, Amigen (Mead Johnson) and had shown by balance experiments that the nitrogen in this preparation is equal to that in evaporated milk in promoting nitrogen retention in normal infants. Furthermore, Magnusson (1944) had published a preliminary report on the value of a Swedish preparation, Aminosol, as a supplement to human milk for premature infants.

In view of these reports it was decided to embark on an investigation of the value of protein digests in certain groups of patients, particularly marasmic and premature infants.

A. Marasmic infants. During recent years, knowledge of the protein metabolism of man and animals has been greatly extended and the severe degree of protein depletion which exists in chronically wasted individuals appreciated. A high protein

as well as a high caloric intake is required if repair and recovery is to proceed smoothly and at a maximum rate. Limits to the achievement of this aim are often set by anorexia and intolerance of food, and it is in these circumstances that protein hydrolysates have proved advantageous.

The term 'marasmus' may be defined as indicating that an infant is under 80 per cent. of his expected weight, based on age and birth weight.

The feed used has been a dilute lactic acid milk with the addition of dextrimaltose and 2.2 per cent. of amino acids (Young et al., in the press). This contains 3.9 per cent. protein, a caloric value of 20 per oz. and provides about 6.5 g. of protein per kg. daily—or just under 3 g. per lb. It is well tolerated.

The accepted criteria for assessing protein nutrition in the infant are maintenance of: (1) normal weight gain; (2) positive nitrogen balance; and (3) normal amounts blood proteins especially serum albumin. Restoration of these values may be taken as an indication of successful treatment of protein depletion. We have been able to measure only (1) and (3) in the infants we have studied.

A comparison has been made of the postoperative average weekly weight gains in a small series of uncomplicated cases of pyloric stenosis and associated marasmus fed on breast milk with an equal number of similar cases fed on the above mentioned high-protein feeds. The weight gains were practically identical in the two series. Since the feeds are both equal to 20 calories per oz. the average caloric intake in the two groups is the same in each week. It is reasonable to presume, therefore, that the optimal weight gains in these artificially fed babies is due to the additional protein intake.

Changes in the amounts of haemoglobin and plasma proteins are liable, when estimated by the concentration of these proteins in the blood, to be masked by changes in blood volume. During the stage of regeneration after protein depletion, blood volume, haemoglobin, and plasma proteins are all increasing in amount; but the former regains its normal level at a more rapid rate, resulting in a temporary haemodilution with apparent increase in the anaemia and hypoproteinaemia. This has been proved by specially designed experimental investigations to occur in both man and animals (Walters et al., 1947; Weech et al., 1937).

Preliminary investigations show that the same mechanism is operative in the regenerative phase of infantile marasmus.

Fig. 1 shows the postoperative course of an uncomplicated case of pyloric stenosis who was 71 per cent. of his expected weight at the start of treatment.

B. Premature infants. A reasonable assumption is that the optimum weight gain for a premature infant in the first few months of life is the rate at which it would be gaining in utero had pregnancy continued to term. Table 1 is adapted from Huggett (1946), and shows the average daily deposition of protein by the foetus. Taken in

FIG. 2.—Total serum protein in forty premature infants.

TABLE 1
AVERAGE DAILY DEPOSITION OF PROTEIN BY
THE FOETUS (HUGGETT)

Stage of foetal life	Protein deposition
Throughout foetal life	1.4 g.
In last three lunar months	3.57 g.
In last month	6.4 g.

conjunction with the average weights of foetuses of various ages, these figures represent a deposition of about 1 g. per lb. body weight daily. Assuming a protein content of 1.5 per cent. in human milk and a utilization of 50 per cent., a daily intake of 4½ oz. of breast milk per lb. of body weight would be necessary to supply the quantity of protein required.

This rate of growth represents the optimum weight gain, but a slower rate seems to be compatible with good physical and mental development. Weight gains comparable to those in utero have, however, been achieved by Jorpes et al. (1946) who added 2.5 g. casein hydrolysate per kilo body weight per day to breast milk, and by Lind (1945) who added 1.5 g. protein as dried human plasma per kilo body weight per day to breast milk.

In our investigation (Young et al., in the press) we have used four feeds. Two of these are based on breast milk and two on an evaporated cow's milk mixture. The two breast milk feeds have the same caloric value, but in one the protein content is brought up to 3.5 per cent. by the addition of 2.2 per cent. amino acids, and in the other the protein content is only 1.5 per cent. Similarly, the evaporated milk mixtures are equicaloric, but the protein contents are 3.8 per cent. and 1.6 per cent. (table 2).

TABLE 2
COMPOSITION OF FEEDS

	Protein %	Fat %	Carbohydr. %	Cals. %
Evaporated milk mixture (control)	1.6	1.9	9.2	17.5
Evaporated milk mixture with casein hydrolysate	3.8 1.6 milk 2.2 cas. hyd.	1.9	7.0	17.5
Breast milk (control)	1.5	3.3-4.0	7.5	19-20
Breast milk with casein hydrolysate	3.5 1.3 milk 2.2 cas. hyd.	2.9	6.6	20

All observers agree that the total serum protein concentration in the premature infant at birth is lower than that in the full-term infant; the average value is under 5 g. per cent. Fig. 2 shows the average levels of serum protein, in two groups of premature infants fed on unmodified breast milk and breast milk with added protein, the daily protein intake being approximately 1.5 g. per lb. in the first and 2.5 g. per lb. in the second: and another two similar groups fed on evaporated milk with high and low protein content. The higher serum protein levels achieved with the additional hydrolysed protein is clearly shown in both groups.

C. Parenteral administration. Using a solution of hydrolysed casein; Shohl (1943) found that 2.2 g. of protein per kg. body weight (1 g. per lb.) daily is required to keep an infant in nitrogen balance. This may be accepted as the minimum daily requirement. Amounts in excess of this may be utilized as a source of energy and not of protein when the total caloric intake is low, as is inevitably so with parenteral alimentation alone.

We have favoured solutions of strengths of 1.7 per cent. and 2.5 per cent. casein hydrolysate, with 5 per cent. glucose. This is given by slow intravenous drip. No untoward reactions during

administration have been encountered. The flushing, pyrexia, and vomiting observed by earlier workers may have been due to impurities in the preparation, which have been eliminated by improved methods of manufacture.

Conclusion

Our observations on this mode of therapy are at the present stage limited to clinical impressions. Briefly, it has been demonstrated to be a valuable additional aid in the management of congenital abnormalities of the gut. A bolder policy is possible in the treatment of gastro-enteritis; and complete deprivation of oral feeds in young infants is a much less hazardous step. There is a noticeable diminution in the intractable anorexia (probably due to specific amino-acid deficiency) so often a major problem in the treatment of gastro-enteritis. Gross fatty changes in the liver are not so frequently seen in those who fail to survive.

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