Progress in the treatment of protein–energy malnutrition

By ANN ASHWORTH,* *Tropical Metabolism Research Unit, University of the West Indies, Kingston 7, Jamaica*

In some hospitals many children with protein–energy malnutrition (PEM) die within a few days of admission, and it is unfortunate that some of these hospital deaths are the result of inadequate or misguided medical treatment. In our Unit in Jamaica few children die and the mortality rate has rarely exceeded 5%. Elsewhere in Jamaica, although the severity of malnutrition is very uniform, mortality from PEM can vary from 5 to 50% depending on the hospital. Mortality rates of up to 50% have also been reported from hospitals in other countries, and it is therefore not surprising that some people question whether a hospital is the right place in which to treat PEM (Cook, 1971; Koppert, 1977). There are, however, hospitals with excellent records of low mortality and in each case the basic principles of treatment are similar and are based on a fundamental understanding of the physiological and biochemical changes which occur in PEM (Nichols *et al.* 1974; Suskind, 1975).

In addition to mortality being unnecessarily high it is also regrettable that recovery from PEM is often distressingly slow, and a better understanding of the nutritional requirements for 'catch-up' growth would greatly improve the efficiency of treatment in both hospitals and nutrition rehabilitation centres. We find in our Unit, for example, that the weight deficits of even the most-severely-malnourished children can be corrected in 4–6 weeks, which is in marked contrast to the prolonged periods sometimes reported (Bengoa, 1976).

The treatment of children with PEM can be divided as follows:

(1) acute phase (a) resuscitation, (b) initiation of cure;

(2) rehabilitation phase (a) catch-up growth, (b) transfer to 'family-type' diet.

Children are most at risk in the acute phase and therefore treatment during this period is best carried out in hospital. The second phase of rehabilitation carries little risk, and an alternative location for treatment could be a nutrition rehabilitation centre.

Acute phase

(a) *Resuscitation*

Malnourished children who are critically ill need urgent attention. Dehydration, infection and occasionally severe anaemia are the main conditions threatening life.

Severe dehydration. Diarrhoea or vomiting or both can lead to severe dehydration which is a serious condition best remedied by intravenous therapy.

*Present address: Dept of Human Nutrition, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

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Dehydration may be difficult to recognize because wasting can mask some of the usual signs and oedema may even be present as well. In PEM cardiac and renal function are impaired (Alleyne *et al.* 1977) and therefore the management of dehydration in malnourished children requires very special care and caution, because of the grave risks of cardiac failure and pulmonary oedema. In particular, malnourished children have a reduced capacity to excrete excess water and a marked inability to excrete sodium (Garrow *et al.* 1968; Klahr & Alleyne, 1973; Alleyne *et al.* 1977). Total body Na is increased even though serum Na levels may be low, and an excessive Na load increases the risk of death from cardiac failure (Wharton *et al.* 1967).

One must be very cautious as to both the amount and type of fluid administered. In the procedure suggested in Table 1 (Picou *et al.* 1975) the rapid initial

Table 1. *Schedule of intravenous therapy for severe dehydration*

Stage	Duration (h)	Fluid (ml/kg per h)	
Initial	Immediately	20 ml/kg	Hartmann's solution
	0–2	10	
Intermediate	2–12	10	4·3% dextrose in 0·18% saline*
Maintenance	12–24	3–4	

*Add KCl after urine has been passed (see p. 90).

infusion of Hartmann's solution (131 mmol Na/l) in the first 2 h is to expand the extracellular fluid volume and thereby improve the circulation and renal blood flow. In an emergency normal saline could be given (150 mmol Na/l), but hypertonic saline should never be used. During the remaining 24 h the fluid is changed to 4·3% dextrose in 0·18% saline which has a lower Na content (30 mmol/l and provides some energy. The aim is to restore and maintain fluid and electrolyte balance. The amounts of fluid suggested in Table 1 will vary depending on the extent of diarrhoea, vomiting, fever or respiratory infection as these conditions increase fluid requirements. In order to assess individual fluid requirements, the child must be carefully monitored throughout the period of intravenous therapy (*vide infra*).

In PEM there is potassium depletion (Alleyne, 1975; Alleyne *et al.* 1977) and the deficit is made more acute by diarrhoea. It is important to give additional K. K therapy should not be too vigorous because of its effect on the myocardium and K should not be given intravenously until a good urine flow has been established. Once this is achieved K should be added to the infusion fluid and the amount recommended is 7·5 ml sterile KCl (200 g/l)/l infusion fluid (Picou *et al.* 1975). This provides 20 mmol K/l intravenous fluid.

Assessing the adequacy of rehydration. The careful and continuous monitoring of children receiving intravenous therapy is very important and any error should be on the side of the underhydration. Initially dehydrated children may have raised pulse and respiratory rates because of volume depletion and acidosis, but the rates should fall as fluid is replaced. Clinical signs of too much fluid are an increase in

the pulse and respiratory rates, basal crepitations in the lungs, raised venous pressure and puffiness of the eyelids. Of these, the pulse and respiratory rates are the most practical and sensitive, but these rates will also rise if too little fluid is being given. Hence it is essential to monitor the child's weight at regular intervals to check whether it is increasing or not. Monitoring urine frequency, which should increase if treatment is succeeding, weighing napkins and measuring vomit are helpful, simple measures which enable fluid requirements to be assessed more accurately. If laboratory facilities exist, measurements of urinary and serum electrolytes are helpful. Interpretation of random measurements can be misleading, however, as discussed more fully by Waterlow *et al.* (1978). Fluid and electrolyte therapy in PEM has also been recently discussed by DeMaeyer (1976).

For mild or moderate dehydration, fluid should be replaced orally, or by nasogastric tube if the child is anorexic or has a very sore mouth. For these less-severe cases, 4·3% dextrose in 0·18% saline at a rate of 5–6 ml/kg per h would be a reasonable target, although the adequacy of therapy should be monitored as previously mentioned. Giving small volumes frequently is advantageous to the child but time-consuming for the nursing staff. It is a task, however, which can be competently performed by the mother or an auxiliary worker.

Infection. It is less easy to diagnose infection in the malnourished child as the usual responses of fever and increased pulse may be absent. Severe wasting leads to loss of thermal insulation (Brooke, 1973) and in PEM hypothermia may co-exist with severe infection. Where facilities exist, all severely-ill children should have a chest X-ray and blood, urine and throat cultures whether fever is present or not. To delay treatment until a specific diagnosis is made, however, can be fatal and therefore the early administration of a broad-spectrum antibiotic such as Ampicillin is often considered advisable. Once the diagnosis is known, the antibiotic therapy can be modified accordingly.

The commonest fatal infections are pneumonia and septicaemia, particularly gram-negative sepsis (Smythe & Campbell, 1959; Phillips & Wharton, 1968). Micro-organisms tend to colonize the intestinal tract in PEM and are a potential source of endotoxin production and gram-negative sepsis. It has been suggested that administration of Metronidazole (for anaerobic organisms) and Colistin (for aerobic organisms) reduces the risk of infection and facilitates the regeneration of an intact intestinal mucosa (Suskind, 1975). During the past 18 months, mortality at our Unit in Jamaica has fallen to zero and one of the new measures introduced has been the prophylactic administration of Metronidazole to children who are severely ill. We cannot say whether the association is causal or merely coincidental, but it would appear to merit investigation.

Anaemia. Opinion on the use of blood transfusions seems to vary. In Uganda, transfusions are not recommended in kwashiorkor unless the child is collapsed or in heart failure as a result of the anaemia (Alleyne *et al.* 1977). In Jamaica we recommend transfusion of whole fresh blood if the haemoglobin level is less than 40 g/l, the amount transfused being not more than 10 ml/kg given over 3 h (Picou *et al.* 1975). Such severe anaemia occurs only rarely in PEM. In recent years, we

have been giving transfusions to children who are not anaemic but are critically ill and whose condition is deteriorating. We find that these small amounts of whole fresh blood can be life-saving. The reason for this beneficial effect is not known, but it has been suggested that fresh blood provides important micronutrients (Waterlow *et al.* 1978).

Other conditions which can arise and require treatment are magnesium and vitamin A deficiencies, hypoglycaemia and hypothermia.

Mg deficiency may occur in malnourished children with chronic or severe diarrhoea (Montgomery, 1960; Caddell & Goddard, 1967; Alleyne *et al.* 1977). If signs of muscle twitching, hyperirritability or convulsions occur, and if they are not caused by hypoglycaemia or meningitis, Mg deficiency should be suspected and treated by intramuscular injection, for example by giving 0·5 ml $MgSO_4.7H_2O$ (250 g/l)/kg (Picou *et al.* 1975).

Vitamin A deficiency should be treated prophylactically in areas where the condition is prevalent by giving 30 mg vitamin A as retinyl palmitate for 3 d intramuscularly.

Hypoglycaemia is often associated with septicaemia, but can also occur if children (particularly those with marasmus) are not fed during the night. If signs of hypoglycaemia develop, such as twitching, convulsions or unconsciousness, it is recommended that the child should be given immediately 1 ml/kg of 50% dextrose intravenously.

Hypothermia can be fatal and is more common in marasmus where thermal insulation is reduced. Frequent feeding, especially at night, and a warm environment help in protecting against this condition (Brooke, 1972).

(b) *Initiation of cure*

This stage is usually completed within a week of admission and the aims are to introduce oral feeding and overcome any problems such as diarrhoea. Many children start directly at this point since it is only a few who need intravenous therapy. The basic principles of treatment remain the same and one must continue to be cautious of the amount of fluid given and the Na load. Since the mucosa is thinned and intestinal enzymes are reduced (Passmore, 1947; James, 1971; Alleyne *et al.* 1977) one must also be careful not to overload the gut. Small, frequent feeds are ideal as they reduce the risks of diarrhoea, vomiting, hypoglycaemia and hypothermia.

Two feeding schemes are shown in Table 2. Scheme no. 1 shows the gradual introduction of milk by progressively increasing its strength. It is a method which we found very effective and which we used for over 15 years. Scheme no. 2 is a new procedure which has also been very successful. It was introduced approximately 4 years ago to facilitate our clinical research studies and was designed to provide 0·6 g protein/kg per d which is the amount required to maintain nitrogen equilibrium (Chan & Waterlow, 1966) and 420 kJ/kg per d which is the energy required to maintain constant body-weight (Kerr *et al.* 1973; Spady *et al.* 1976). It is now part of our routine treatment. Both schemes have been successful even although they are quite different in certain respects. The important similarities are

Table 2. *Schedules for oral feeding in the acute phase* (week 1)*

	Day	Type of milk	No. of Feeds	Volume/feed (ml/kg)	Protein (g/kg per d)	Energy (kJ/kg per d)
Scheme no. 1	1	0·25 strength	12	10	1·0	84
	2–3	0·5 strength	8	15	2·0	168
	4	full strength	8	15	4·0	336
	5		6	20		
Scheme no. 2	1	Maintenance formula	24	5†	0·6	420
	2		12	10		
	3–5		8	15		
	6–7		6	20		

*For definition, see p. 89.

†Normally 120 ml/kg per d are given but the volume can be altered depending on the state of hydration and the formula adjusted accordingly so that the intakes of protein and energy remain as stated.

probably that initially very little protein is given and the feeds are small, but frequent. Careful attention to the feeding regimen during the first week is vital if mortality is to be kept low (a point also stressed by Nichols *et al.* (1974)). In their experience in Guatemala mortality was higher when whole cow's milk was given from the day of admission, whereas mortality was less than 5% when milk was introduced gradually. They suggest that for the first 2 d protein intakes should be approximately 1 g/kg per d with stepwise increments up to 3·5 g/kg per d by the sixth day. Too rapid an introduction to the rehabilitation diet may precipitate what has been termed the 'recovery syndrome' (a sudden rapid increase in pulse and respiration with distended abdomen and enlarged liver). Children with oedema are more vulnerable, and if these signs of cardiac failure occur it is suggested that a single dose of digoxin and frusemide be given (Waterlow *et al.* 1978).

All malnourished children should be given K supplements of 4–8 mmols/kg per d (Nichols *et al.* 1974; Picou *et al.* 1975; Suskind, 1975). Since it has been suggested that K depletion cannot be corrected if the child is also Mg depleted, it is advisable to give Mg supplements of 1–2 mmol/kg per d (Picou *et al.* 1975). In addition we recommend iron (150 mg/d), folic acid (1 mg/d) and a multi-vitamin preparation even though there may be no specific vitamin deficiencies.

Anorexia may be a problem during the first few days, especially in children with kwashiorkor, but it may be surmounted by tube-feeding. It is preferable to use a fine nasogastric tube (size 8 or 10 French) as this reduces the risk of aspiration into the lungs, and as a further precaution the gastric contents should be aspirated before each feed. Although many children with PEM have a history of vomiting, it invariably ceases when small, frequent feeds are given. If vomiting persists, gastric lavage can help. Rumination occasionally occurs in emotionally-disturbed infants. It may occur to such an extent that it seems impossible to make any progress. Our nursing staff, however, with much patience and dedication, have always succeeded in the end although it can take 2–3 weeks before rumination ceases.

Diarrhoea is commonly associated with PEM but it usually settles with oral administration of clear fluids such as 43% dextrose in 0·18% saline for 24 h, followed on subsequent days by small, frequent milk feeds as shown in Table 2. Malnourished children are occasionally lactose intolerant in which situation the diarrhoea becomes worse whenever 'full-strength' milk is introduced. For these patients it is best to change to a lactose-free milk. Chronic diarrhoea may result from trichuriasis, giardiasis, amoebiasis and rotaviruses, or from bacterial overgrowth in the small intestine (Viteri & Schneider, 1974). Where facilities exist, the stools should be examined for parasites. A negative result, however, may be recorded even in the presence of infestation, particularly in the instance of *Giardia lamblia* which is difficult to diagnose.

Rehabilitation phase

(a) *'Catch-up' growth*

By the end of the first week the acute problems have usually been overcome and the next aim is to restore wasted tissues and thereby correct the weight deficit. The theoretical protein and energy costs of tissue synthesis at different rates of growth are shown in Table 3. In practice most rehabilitation diets provide ample protein but many fail to provide the very high energy intakes which are necessary for rapid 'catch-up' growth. In our patients the key to successful 'catch-up' growth is the provision of a high-energy milk formula in which the energy density of milk is doubled by adding vegetable oil, thus providing 31 g protein and 5670 kJ/l (Ashworth *et al.* 1968). We transfer our patients to this high-energy formula as soon as the acute problems are overcome. For very rapid rates of 'catch-up' growth a protein:energy (P:E) ratio of approximately 0·1 is necessary (see Table 3). 'Humanized' milks such as SMA (John Wyeth Ltd) cannot be modified to provide a high-energy milk because the P:E ratio would be too low.

Table 3. *Theoretical protein and energy requirements for different rates of 'catch-up' growth*

Rate of growth	Protein* (g/kg per d)	Energy§ (kJ/kg per d)	Protein: energy	Period required for 5 kg child to gain 2 kg (d)
None (maintenance)	0·62†	420	0·025	∞
Normal:				
×1 (1g/kg per d)	0·78†	440	0·030	400
×2	0·94†	460	0·034	200
×10	2·73‡	620	0·074	40
×20	4·69‡	820	0·096	20

*Assumes maintenance requirement is 100 mg nitrogen/kg per d (Chan & Waterlow, 1966) and N retention for growth is 25 mg N/g weight gain (Waterlow, 1961).

†Assumes net protein utilization (NPU) 100.

‡Assumes NPU 80.

§Assumes maintenance plus activity is 420 kJ/kg per d and the energy cost of growth is 20 kJ/g weight gain (Kerr *et al.* 1973; Spady *et al.* 1976).

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Unless one increases energy density bulk becomes a constraint to 'catch-up' growth and we have shown in *ad lib.*-feeding studies that energy intakes are significantly less when ordinary milk is fed (Ashworth, 1974). With a high-energy milk formula given *ad lib.*, 4 hourly day and night, we achieve energy intakes of approximately 840 kJ/kg per d and growth rates twenty times faster than normal (Ashworth, 1975). Since a high-energy diet is the key to a rapid recovery, the diet should be prescribed in the same way as one would prescribe a medicine. Likewise, care should be taken in preparing and administering the diet, and in recording the intake. Feeding a ward of malnourished children is time-consuming but this vital task can be enjoyably shared by parents, auxiliaries or sympathetic volunteers.

At an intake of 820 kJ/kg per d, a 2 kg weight deficit in a 5 kg child can be corrected in 20 d or less. In contrast at an intake of 460 kJ/kg per d the time taken would be 200 d (see Table 3). In hospital a rapid recovery is vital, for in addition to economic considerations it lessens the risk of cross-infections and the emotional stresses of separation. Moreover, a child who is discharged in a good nutritional state is less likely to relapse at home. In nutrition rehabilitation centres very rapid rates of 'catch-up' growth may not be so vital, but in many centres energy intakes do not even reach 460 kJ/kg per d and 'catch-up' growth is exceedingly slow, if indeed there is any at all.

It is unrealistic to expect to correct a height deficit in hospital because skeletal growth occurs more slowly. We consider a child ready for discharge when he reaches a normal weight-for-height. At this point most children voluntarily reduce their energy intakes to approximately 500 kJ/kg per d and the rates of 'catch-up' growth dimish (Ashworth, 1969).

Other aspects of rehabilitation are currently being investigated at our Unit. One is the important question of whether mental performance of malnourished children can be improved by stimulation in hospital and after discharge. Another is the role of trace minerals, particularly zinc. Zn can limit 'catch-up' growth in children rehabilitated on soya-based preparations.

(b) *Transfer to 'family-type' diet*

When a child is ready for discharge we change to a 'family-type' diet based on the multi-mix principle (Jelliffe, 1967; Jelliffe, 1971), i.e. a nutritious mixture of low-cost foods. Making this transition to solid food ensures a more adequate diet at home and it is a very convenient way of demonstrating to parents that nutritious meals need not be expensive nor need food be specially purchased for children. Advice on infant feeding and child care can benefit the patient after discharge and also future siblings, but advice can only be effective if it is realistic and within the family's economic resources and capabilities. Encouragement and advice are also given at our 'follow-up' clinic where children are seen at regular intervals until they are 5 years-old, and we find that very few children relapse or die at home.

It can perhaps be argued that research units such as ours are sophisticated, with a high staff:patient ratio and thus do not reflect normal working conditions. We have, however, by working in rural hospitals in Jamaica, demonstrated that it is possible to apply these principles of treatment even where facilities are inadequate

and staffing is poor. It must be emphasized that high mortality is not necessarily related to the severity of PEM, but often is the result of inexperience or ignorance. It is therefore important that all those who are responsible for the care of severely-malnourished children are aware of the basic principles of treatment.

This paper has been largely based on experience in Jamaica and it reflects the work of present and past members of the Tropical Metabolism Research Unit. The author is indebted to them as colleagues and thanks them for their companionship and guidance during many memorable years.

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