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Total body water in malnutrition: the possible role of energy intake

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1. Total body water (TBW) was measured using tritiated water in sixty-five children. The measurements were distributed throughout rehabilitation in order to define the effect of changing energy intakes.

2. Oedematous children had a high TBW which decreased to the normal range during loss of oedema providing they were not receiving more than maintenance amounts of energy during this period.

3. Marasmic children who had not received greater than maintenance amounts of energy had a normal TBW.

4. Treatment with a high-energy diet was associated with an initial increase in TBW.

5. The possible mechanisms for this phenomenon are discussed.

Many studies have demonstrated that in severe protein-energy malnutrition (PEM) total body water (TBW) as a percentage of body-weight is increased (Schnieden, Hendrikse & Haigh, 1958; Smith, 1960; Brinkman, Bowie, Friis-Hansen & Hansen, 1965; Flynn, Hanna, Asfour & Lutz, 1967; Alleyne, 1968; Graham, Cordano, Blizzard & Cheek, 1969). Some of the highest values have been obtained in children with marasmus (Hansen, Brinkman & Bowie, 1965). This seeming paradox of a child with non-oedematous malnutrition, marasmus, having a higher TBW (% body-weight) than a child with obvious fluid retention manifest as oedema, kwashiorkor, has been attributed to a change in the reference measurement, body-weight. There is said to be a greater loss of body solids in marasmus. It has been shown that in this condition the extracellular fluid volume (ECF) tends to be preserved while body solids are decreasing (Kerpel-Fronius & Kovach, 1948), so that expressed as a percentage of body-weight the ECF is increased, and consequently the TBW (% body-weight) is also increased.

In kwashiorkor there is an increase in the ECF, estimated as the thiosulphate space, which decreases during the loss of oedema (Brinkman *et al.* 1965). For some time after the loss of oedema the bromide space (% TBW) is increased (Alleyne, 1968), and it then shows a progressive decrease throughout recovery.

During a study of body composition in severely-malnourished marasmic children we were unable to demonstrate an increase in TBW (% body-weight). All these patients were investigated within 4 d of admission, and they were all receiving a maintenance energy intake at the time of study (Reeds, Jackson, Picou & Poulter, 1978). In an independent study on leucocyte electrolytes (Patrick, unpublished results) there was evidence that as soon as malnourished children were given a high-energy diet, the intracellular water was increased in relation to dry solids. During the first few days of rehabilitation the leucocyte intracellular water increased significantly from a mean value of 2·12 l/kg dry solids (DS) – 2·49 l/kg DS (n 15, t 3·47, $P < 0·01$).

It seemed, therefore, that an important factor to consider in assessing the results of the TBW (% body-weight) measurements was the dietary experience of the child before the measurement was made, in particular the dietary intake of energy. We have taken further measurements of TBW (% body-weight) in malnourished children at different stages in their

Table 1. *Criteria for the classification of the severely-malnourished children admitted to the Tropical Metabolism Research Unit*

Maintenance energy intake (< 420 kJ (100 kcal)/kg body-wt per d)			Above maintenance energy intake (> 420 kJ (100 kcal)/kg body-wt per d)			
With oedema	After loss of oedema	No oedema	First phase of wt gain	Second phase of wt gain	Third phase of wt gain	Expected weight-for-height 100%

recovery. The TBW (% body-weight) has been related to the energy intake and the phase of recovery at the time of study, rather than to any classification based upon anthropometric measurements of the child. We have included in this analysis values for TBW previously reported from the Tropical Metabolism Research Unit (Smith, 1960; Alleyne, 1968).

METHODS

Patients

Measurements of TBW (149) were made in sixty-five severely-malnourished children admitted to the Tropical Metabolism Research Unit. The nature of the investigation and its purpose, particularly its lack of immediate therapeutic value, was explained to the parent or guardian and written consent for the investigation was obtained. The children were diagnosed initially as suffering from kwashiorkor, marasmus, marasmic-kwashiorkor or undernutrition as defined by the Wellcome criteria (Wellcome Classification of Malnutrition, 1970) and were considered to be recovered when they had reached their expected weight-for-length.

For the purposes of this analysis the TBW measurements were classified not into the usual categories of marasmus, marasmic-kwashiorkor and kwashiorkor but into two categories according to the energy intake of the child at the time of the measurement. The first category included measurements made on those children who were receiving 420 kJ/kg body-weight per d or less (maintenance diet). This energy intake corresponds with the value found at zero weight gain from a regression analysis of children growing at varying rates during recovery from malnutrition (Kerr, Ashworth, Picou, Poulter, Seakins, Spady & Wheeler, 1973). On average there was neither significant weight gain nor weight loss (in the absence of oedema) on this energy intake. The second category included those children who were receiving more than 420 kJ/body-weight per d and who were in the phase of rapid weight gain.

The children who were receiving maintenance amounts of energy were subdivided into three groups, those with oedema, those who had lost oedema and those who had never had oedema. Because extracellular volume is known to be increased even after loss of the clinical signs of oedema (Chobanian, Burrows & Hollander, 1961) children whose TBW was measured within 4 d of the loss of oedema were included in the group with oedema.

The period of weight gain up to expected weight-for-length in the children receiving above maintenance amounts of energy was divided into three phases for each child so that measurements made in the early, middle and late phases of weight gain could be compared.

Measurements made when the child had reached expected weight-for-length were grouped separately and were designated recovered.

The groups considered are shown in Table 1. The composition of the diets varied slightly in the different studies but when calculated from manufacturer's (The Nestlé Co Ltd, Croydon, Surrey, UK) specifications and Atwater factors (Atwater & Bryant, 1900), the maintenance diet contained 2900 kJ (690 kcal)/l and 6·5 g protein/l and the rehabilitation

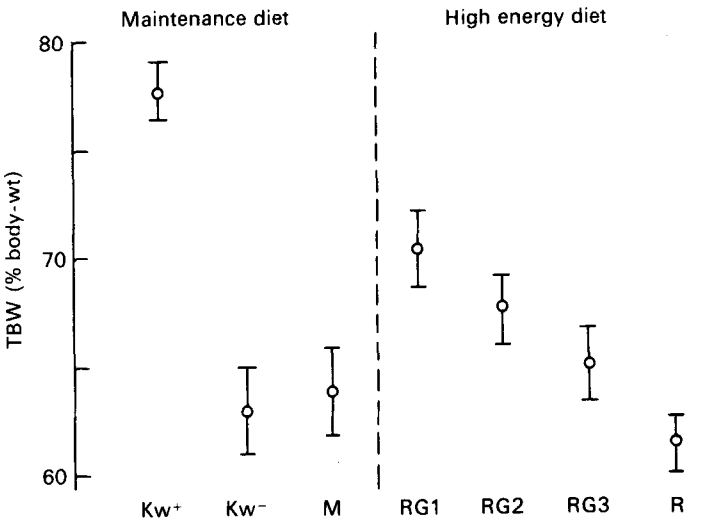

Fig. 1. The relationship between total body water (TBW) (% body-weight) and energy intake in groups of severely-malnourished Jamaican children (for details see Table 2) on a maintenance-energy intake (420 kJ/kg body-weight per d) and during recovery on a high-energy intake (> 420 kJ/kg body-weight per d). (For details of procedures and subjects, see p. 418 and Tables 1–4.) Vertical bars represent standard errors of the means.

diet 5670 kJ (1350 kcal)/l and 31 g protein/l. The sodium content of the diet was 1·0–2·0 mmol/l.

TBW (% body-weight) measurements

Three series of experiments were considered (Smith, 1960; Alleyne, 1968; Reeds *et al.* 1978). In each of these series of experiments tritiated water was used as the tracer and conventional isotope-dilution methods, which have been described in detail, were followed. More recently, the specific activity of tritiated water in plasma was measured. The dose used has been 0·2% of the recommended safe whole-body dose and this yields values of 50–100 disintegrations/min above background values.

The children were weighed daily. Their lengths were taken at weekly intervals. The results were analysed by the unpaired *t* test unless it is specifically stated that the paired *t* test is used.

RESULTS

Most of the children described in this paper were studied one to three times during their recovery. Because the importance of energy intake was recognized retrospectively only on a few occasions was the transition from one level of energy intake to the next studied in the same child. The results are therefore reported as separate groups and where possible paired values are also presented. Statistical summaries of the results in each group and the anthropometric details at the time of the study are given in Tables 2–4. The changes in TBW are shown in Fig. 1.

1. *Results obtained during the period when maintenance amounts of energy were consumed*

Seventy measurements were made during this period; forty-eight measurements were obtained from thirty-seven children with oedema, eleven in children who had lost oedema and eleven in marasmic children. Five children were studied before and after loss of oedema on the maintenance diet. The duration of the maintenance diet was determined by the child's clinical condition. TBW (% body-weight) was highest in the children with oedema

Table 2. *Age (months), weight-for-age, height-for-age and weight-for-height (% normal value (Wellcome classification of Malnutrition, 1970)) for severely-malnourished Jamaican children*

(Mean values and standard deviations)

	Group	*n*	Age (months) Mean	Age (months) SD	Weight-for-age Mean	Weight-for-age SD	Height-for-age Mean	Height-for-age SD	Weight-for-height Mean	Weight-for-height SD
Kw+	Kwashiorkor with oedema on the maintenance diet†	48	12·5	4·3	60·9	14·5	90·4	6·8	75·9	9·8
Kw−	Kwashiorkor after loss of oedema on the maintenance diet	11	13·1	5·7	64·1	10·4	91·2	7·6	75·9	6·5
M	Marasmus on the maintenance diet	11	10·3	3·9	48·6	6·7	88·3	4·9	67·8	6·3
RG1	Rapidly-growing phase 1	24	12·4	3·2	61·1	9·3	90·1	5·1	76·1	7·4
RG2	Rapidly-growing phase 2	17	13·5	4·2	68·0	8·9	90·2	5·5	82·6	5·5
RG3	Rapidly-growing phase 3	23	15·5	4·4	72·6	10·4	88·2	5·6	93·2	5·6
R	Recovered at expected weight-for-height	15	15·6	4·7	83·1	11·4	90·9	4·9	99·4	3·9

† For details, see p. 418.

Table 3. *Subdivision of the groups of severely-malnourished Jamaican children in terms of the original diagnosis based on Wellcome* (1970)

Group†	Kwashiorkor	Marasmic-kwashiorkor	Marasmus
Kw+	19	29	—
Kw−	8	3	—
M	—	—	11
RG1	9	9	6
RG2	10	5	2
RG3	10	6	7
R	7	3	5

† For details, see Table 2.

with a mean (±SEM) value of 77·8 ± 1·3. This value becomes 77·7 ± 1·5 (% body-weight) if duplicate measurements in the same child are included as a single average value. All subsequent conclusions are the same whichever value is used.

Eleven children were studied after loss of oedema on the maintenance-energy diet. Five of these children had been studied with oedema. The TBW (% body-weight) after loss of oedema was 62·9 ± 2·0 (mean ± SEM). This was a highly significant ($P < 0·01$) reduction compared with the value found in children with oedema. In the five children for whom measurements were made before and after loss of oedema the average TBW (% body-weight) decreased from 77·3 to 63·2 ($P < 0·05$).

Eleven marasmic children who had never had oedema were also studied during the maintenance period. The TBW (% body-weight) in this group was 63·8 ± 2·2 (mean ± SEM) which is not significantly different from the value found in children who lost oedema on the

Table 4. *Statistical comparison of values for total body water in severely-malnourished Jamaican children*

Group†	*n*	Mean	SD	SE	Significance of differences between groups:
Kw+	48	77·8	9·3	1·3	All groups**
Kw−	11	62·9	6·5	2·0	Kw+ and RG1**, RG2**
M	11	63·8	7·3	2·2	Kw+ and RG1**, RG2*
RG1	24	70·8	8·2	1·6	All groups**
RG2	17	66·8	7·6	1·8	Kw+ and R**, Kw−*
RG3	23	65·0	8·9	1·8	Kw+ and RG1**
R	15	61·2	4·9	1·3	Kw+, RG1 and RG2**

* $P<0.05$, ** $P<0.01$.
† For details, see Table 2.

maintenance diet. In subsequent comparisons these groups were therefore combined. However, other reported values for TBW in marasmic children are rather larger, for example 76·9% body-weight (Hansen *et al.* 1965) and 73·1% body-weight (Smith, 1960), but this latter group was defined as within 35 d of being oedema-free and included many children classified in group RG1 (see Table 1) in this study. Those marasmic children in Smith's (1960) study who had not received more than maintenance energy intakes had a mean TBW of 64·2% body-weight. The discrepancies with other studies were further resolved by considering the values measured after feeding the rehabilitation diet had been commenced.

2. *Results obtained after the commencement of refeeding with high energy intakes*

This period was arbitrarily divided into three phases for each child but the most important results were obtained during the first 3 weeks of refeeding. The average period of time to reach expected weight-for-length was 64 ± 27 d (mean ± SD).

The twenty-four children studied during early weight gain had been gaining weight for 3–24 d. The average TBW (% body-weight) for this group was $70{\cdot}8 \pm 1{\cdot}6$ (mean ± SEM) which was a highly significant increase compared to the value obtained from malnourished children without oedema who were still consuming maintenance amounts of energy. Moreover, this average value concealed the true extent of the increase because, as Fig. 2 shows, during the first 14 d of refeeding there was a positive correlation between TBW (% body-weight) and period of refeeding (r 0·71, $P<0.01$). The equation for the regression line was TBW (% body-weight) = 1·67 (period of high-energy feeding (d)) + 56·7. The intercept on TBW (y) axis was quite close to the value found at the end of the maintenance period. Paired studies for the increase in TBW which occurred with weight gain on a high-energy diet were available in fourteen children. The average change was from 63·3 to 68·1% body-weight (t 2·48, $P < 0.05$).

Compared to the period of refeeding and the requirement for above maintenance energy intakes other factors were relatively unimportant, for example the initial diagnostic category had no effect on the increase in TBW with refeeding neither was there any correlation between TBW and energy intake above maintenance requirements.

More importantly for the resolution of the discrepancies in the literature, ten of the twenty-four children in this group were still marasmic, i.e. less than 60% weight-for-age and not less than seventeen children were below 65% weight-for-age. Thus although we have shown that marasmic children on a maintenance diet had a normal TBW (% body-weight) marasmic children who were being given above maintenance amounts of energy had an increased TBW.

After the initial increase in TBW (% body-weight) with the onset of weight gain there was a slow progressive return to normal values on recovery as shown in Fig. 1.

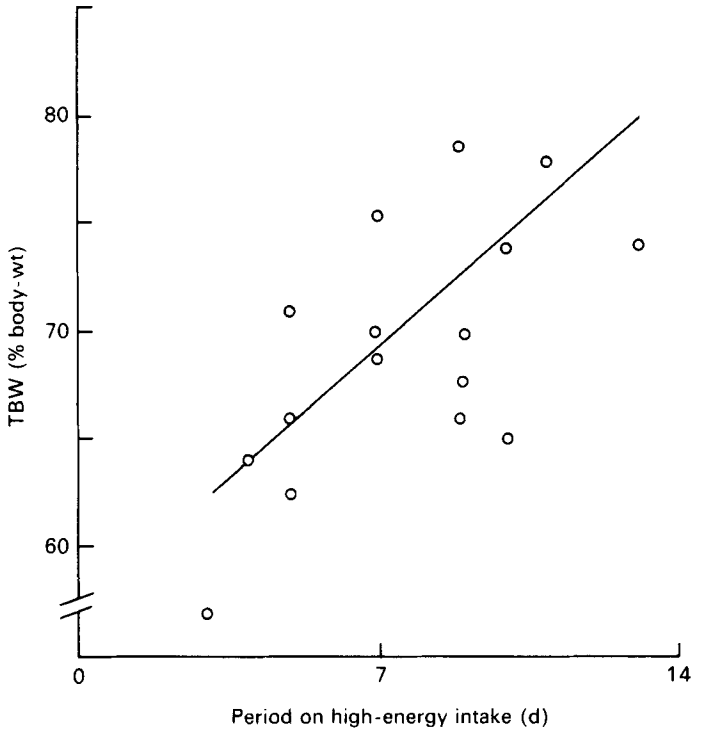

Fig. 2. The relationship between total body water (TBW) (% body-weight) and the period (d) of high-energy feeding (> 420 kJ/kg body-weight per d) in severely-malnourished Jamaican children (r 0·72, $P < 0·01$). After 14 d increasing numbers of lower values destroy the correlation. All the values illustrated are derived from the group in phase 1 of rapid growth. (For details of procedures and subjects, see p. 418 and Tables 1–4.)

DISCUSSION

In previous studies of TBW in malnutrition the emphasis was placed either on the reduction occurring during the loss of oedema, or on the difference between the malnourished and recovered state. The information available has been summarized in reviews as demonstrating that malnutrition leads to overhydration, and the excess water is predominantly in the extracellular space (Waterlow & Alleyne, 1971). Values for the size of the extracellular space were based on measurements of the thiosulphate and bromide spaces. These tend to have a greater volume of distribution than most other markers (Swales, 1975), and therefore tend to over-estimate the extracellular space. In addition there is a considerable body of evidence that in disease states the distribution volume of many ECF markers may increase dramatically (Overman, 1946). Thus the exact distribution of the increase in TBW found in severe PEM, must at present be considered to be unresolved.

Alterations in TBW in malnutrition have not previously been related to energy intake. Two points have emerged from a consideration of this factor. First, oedema may be lost and a normal TBW (% body-weight) attained without provision of more than maintenance amounts of energy. Secondly, refeeding is associated with an initial increase in TBW which subsequently decreases to normal values; because this initial increase occurs early in rehabilitation many of these children were still marasmic by the criteria of the Wellcome Classification of Malnutrition (1970). It is perhaps important to emphasize that major metabolic changes occur in malnourished children before significant weight gain has occurred.

The time-course of the increase in TBW (% body-weight) during rehabilitation with high-energy feeding is of interest. It was surprising that it should be linear over the first 2 weeks (Fig. 2). During this period total body potassium (TBK) is being repleted (Garrow, 1965). It seems likely that the temporal similarity of the two processes is more than coincidental. TBK and total body Na are closely correlated with TBW (Edelman, Liebman, O'Meara & Birkenfeld, 1958) so that any increase in TBK will be associated with an increase in TBW which must be intracellular. However, there is also other evidence which suggests that there is an initial large increase in intracellular water during the first 2 weeks of refeeding. One child studied had a TBW after loss of oedema of 64·2% body-weight (5·06 kg). During early rapid weight gain TBW increased to 74·1% body-weight. Body-weight increased by 0·69 kg and the bromide space by only 42 ml. If bromide measured the ECF space it follows that intracellular water had increased by 968 ml. Flynn *et al.* (1967) studied one marasmic child five times and their results show that during the first 4 weeks of refeeding the ECF increased by 60 ml whilst the intracellular fluid increased by 500 ml. On the other hand, Graham *et al.* (1969) studied nine children after this initial phase and found roughly parallel increases in extracellular water and intracellular water but a decreasing TBW (% body-weight) which reflected the increasing body solids, particularly body fat, which is a relatively anhydrous tissue.

Therefore as a working hypothesis we propose that the increase in TBW (% body-weight) seen during early rapid weight gain is largely intracellular and that the subsequent decrease in TBW (% body-weight) is due to increasing body solids.

Several potential mechanisms exist to explain this pattern. One of the determinants of cell volume and hence intracellular water is the Na pump (Leaf, 1970). Metcoff (1973) has suggested that the Na pump may be impaired in malnutrition because this would explain the increase in total body Na and decrease in TBK found in malnourished children even in the absence of oedema (Halliday, 1967). It has recently been demonstrated that the Na pump is impaired in leucocytes obtained from malnourished children (Patrick, 1977); moreover, the time-course for the correction of this defect is approximately 2–3 weeks of refeeding.

Most of the children in the present series had a diet in which 60% of the total energy was derived from fat, in the form of added peanut (*Arachis hypogaea*) oil. Many membrane-bound enzymes including ($Na^+ + K^+$) ATPase (ATP phosphohydrolase; *EC* 3.6.1.3) have a specific requirement for lipids (Tanaka & Sakamoto, 1969; Wheeler, Walker & Barker, 1975). Alterations in the fatty acid composition of membrane lipids have been shown to alter the fluidity of the membrane and the activities of the lipid-requiring enzymes in bacterial and reconstituted membrane vesicles (Coleman, 1973). Recent studies in animals have provided evidence that dietary-induced changes in the composition of the structural lipids of different tissues can also alter the characteristics of these enzymes. Changes in the ($Na^+ + K^+$) ATPase activity, specifically, have been described in rats deficient in essential fatty acids (Brivio-Haughland, Louis, Musch, Waldeck & Williams, 1976) and in rats given diets supplemented with different types of fat (Farias, Bloj, Morero, Sineriz & Trucco, 1975). It is possible therefore that the dietary manipulations which we use in the treatment of malnutrition could induce changes in membrane function. The specific role of the high-fat diet has not been studied but it has been suggested that lipid abnormalities, especially of essential fatty acids, may play a role in the genesis of kwashiorkor (MacDonald, Hansen & Bronte-Stewart, 1963; Taylor, 1971; Naismith, 1973).

Glycogen deposition is another potential cause for an increase in intracellular water because a greater than normal concentration of glycogen was found in the skeletal muscle of malnourished children during rapid growth (Alleyne & Scullard, 1969). Since glycogen is a hydrated molecule it is at least partially responsible for the increase in intracellular water. The major causes of increased extracellular water, renal and cardiac disfunction, although a

feature of malnutrition are usually corrected within a few days (Alleyne, 1966, 1967; Klahr & Alleyne, 1975). We would suggest therefore that in early rapid weight gain there is an increase in TBW which is probably intracellular and dependent upon at least three factors; K repletion, glycogen synthesis and alterations in membrane handling of Na and K secondary to alterations in membrane Na transport and probably determined in part by the nature of the diet.

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