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Studies on total body potassium in malnourished infants
Factors affecting potassium repletion

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1. Serial measurements of total body potassium were made in children while they were malnourished and as they recovered. Initially, there was a low total body potassium which rose slowly and reached the normal levels of 45 m-equiv./kg at 3–4 weeks after admission to hospital.

2. The early stages of recovery were divided into three phases. In the first 5 days of treatment, retention of potassium served to correct a true potassium deficiency and the amount of potassium retained during this phase was related to the initial level of total body potassium. There was no relationship between serum potassium and total body potassium. There was indirect evidence that antecedent diarrhoea was an important factor in the production of potassium depletion.

3. In the next phase—the lag phase—potassium was retained in relation to deposition of new body tissue.

4. In the phase of rapid growth, potassium was also retained in the amount appropriate for deposition of new tissue.

5. After the repair of the acute potassium depletion, potassium retention was always correlated with the protein intake.

The occurrence of severe potassium depletion in malnourished Jamaican children has now been conclusively established (Waterlow & Mendes, 1957; Smith & Waterlow, 1960; Garrow, 1965*a*; Alleyne, 1968; Nichols, Alleyne, Barnes & Hazlewood, 1969) and confirmed in other parts of the world (Hansen, 1956; Pretorius & Wehmeyer 1964; Metcoff, Frenk, Antonowicz, Gordillo & Lopez, 1960). Very little attention has been paid, however, to the factors which cause the depletion or to those circumstances which alter the rates and efficacy of repletion. It has always been assumed that the potassium defficiency was caused by gastro-intestinal loss, and all of the subjects studied by Hansen (1956) had had diarrhoea in the recent past. Hansen (1956) in balance studies on seven children with kwashiorkor showed that initially there was a high degree of retention of potassium compared with nitrogen, and after the 1st week, this fell to approximately 3 m-equiv. of potassium retained per g nitrogen. This has been interpreted to mean (Garrow, Smith & Ward, 1968) that potassium deficiency still existed even after 1 week of therapy, since the ratio of potassium to nitrogen retained was higher than could be accounted for by the deposition of normal body tissue. Workers in the Belgian Congo (Vis, Dubois, Vanderborght & de Mayer, 1965) could not substantiate this retention of potassium in excess of nitrogen in children recovering from malnutrition.

More recently we have re-emphasized the concept originally proposed by Scribner & Burnell (1956) that there are two important factors to be considered in the assessment of potassium 'deficiency' in these children (Alleyne, Millward & Scullard,

1969). The total capacity of the body for potassium is important. Muscle is probably the most important of the potassium-containing tissues, and here it is the cellular protein and glycogen which are the major determinants of the muscle's ability to store potassium. Smith & Waterlow (1960) considered that low levels of body potassium could be caused by a reduction in muscle mass. The other factor to be considered is the concentration of potassium in the tissues, and a true potassium deficiency exists only when, irrespective of the amount of the potassium-containing tissues, the concentration of potassium in these tissues is reduced. In effect a person can only be said to be potassium-deficient when the body's potassium content is inappropriately low for its potassium capacity. It has frequently been observed that in spite of high potassium supplements, total body potassium in cases of potassium deficiency does not return to normal for some weeks. In the present investigation an analysis is made of the factors which affect the repletion of the body with potassium.

EXPERIMENTAL

Clinical material

Investigations were carried out on thirty-eight malnourished Jamaican infants whose mean age on admission to hospital was 12 months. They all had the clinical stigmata of moderate or severe protein-calorie malnutrition (Waterlow, Cravioto & Stephen, 1960) and for the purpose of this study, no attempt has been made to separate them into different clinical groups. They were all admitted to the metabolic ward of the Medical Research Council's Tropical Metabolism Research Unit, and treated with graduated milk feeds, iron and vitamin supplements, and in most instances antibiotics were given. Potassium supplements (4–8 m-equiv. per kg per day) were given after the first measurements of total body potassium. It was the practice here to continue these supplements until the [TBK] was above 40 m-equiv./kg, but the current schedule is outlined below. Throughout this paper total body potassium is referred to in two ways. [TBK] refers to the concentrations of body potassium in m-equiv./kg body-weight while TBK refers to the total amount of potassium present in m-equiv.

METHODS

Total body potassium was estimated by measuring the naturally occurring ^{40}K in a whole body counter (Garrow, 1965*b*). Children were weighed daily and their heights recorded after every measurement of TBK. After admission most children who had very low levels of [TBK], i.e. less than 35 m-equiv/kg, were re-counted on alternate days or every 3rd day for the first 2 weeks. From the 3rd week, TBK was usually measured weekly. Since some children were the subjects of other metabolic studies it was not always possible to follow each child through to recovery. The TBK values were plotted for each child, and a curve was fitted to the points by eye. Special attention was paid to three early periods after admission to hospital: (*a*) the acute repletion phase which was arbitrarily taken as the first 5 days after admission; (*b*) the 'lag phase' which represents the period from day 6 until the child started to gain weight

rapidly (the average length of this period was 11·5 days); (*c*) the rapid growth phase, the onset of which was clearly marked by a distinct change in slope of the weight curve. The first 14 days of this rapid growth phase were used for analysis. If TBK measurements were not made on the exact days which marked the ends of these periods, a value for TBK was obtained by interpolation on the potassium curve. Some children were excluded from this analysis because there were not enough measurements made in the early period after admission. Since the children initially were all on a liquid diet, the protein and calorie intakes were easily determined. As an index of the severity of diarrhoea before admission, a record was made of the number of stools passed in the first 5 days after admission. This measurement is of course open to several inaccuracies, since with profuse diarrhoea, two or three stools may be measured as one. It is appreciated that stool weight or volume might have been more appropriate.

Serum potassium was measured by internal standard flame photometry.

RESULTS

Fig. 1 shows a summary of all the total body potassium [TBK] measurements divided into weekly periods. The [TBK] was low initially and rose gradually with recovery. After the 3rd or 4th week, there was no significant variation in the levels of [TBK].

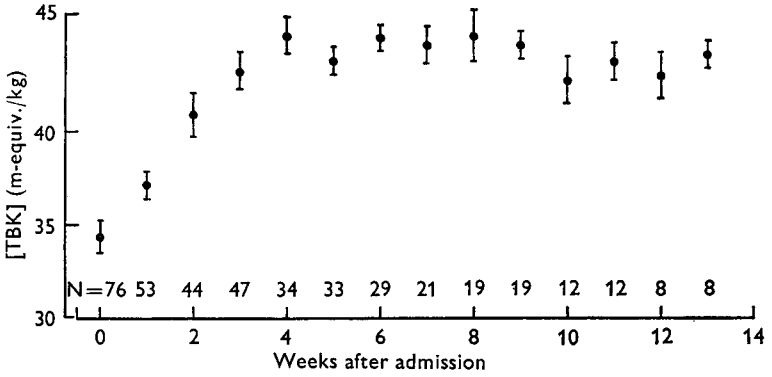

Fig. 1. Total body potassium concentration [TBK] in children as they recovered from severe malnutrition. The standard errors of the mean values are indicated by the vertical bars.

Fig. 2 shows a chart of TBK measurements for an illustrative case from admission through to recovery. This child, an 11-month-old girl, retained 40 m-equiv. of potassium in the first 4 days when her [TBK] rose from 22·8 to 31·1 m-equiv./kg. Then there was a period of approximately 12 days when the TBK did not increase significantly. Thereafter there was a steady rise.

Initial phase. There was a statistically significant correlation between TBK (y) and the child's weight expressed as a percentage of the median weight for a normal child of the same height (x) ($r = -0{\cdot}35, y = -0{\cdot}28x + 51{\cdot}9, P < 0{\cdot}05$). The median weight for height is derived from the Boston figures (Nelson, 1959). This indicates that the

[TBK] was rather lower in those children who were less underweight. In oedematous children, the minimum weight after loss of oedema was the value used.

In Fig. 3 the potassium retained in the first 5 days after admission is plotted against the initial [TBK]. This demonstrates that those children with the lowest [TBK] retained the most potassium.

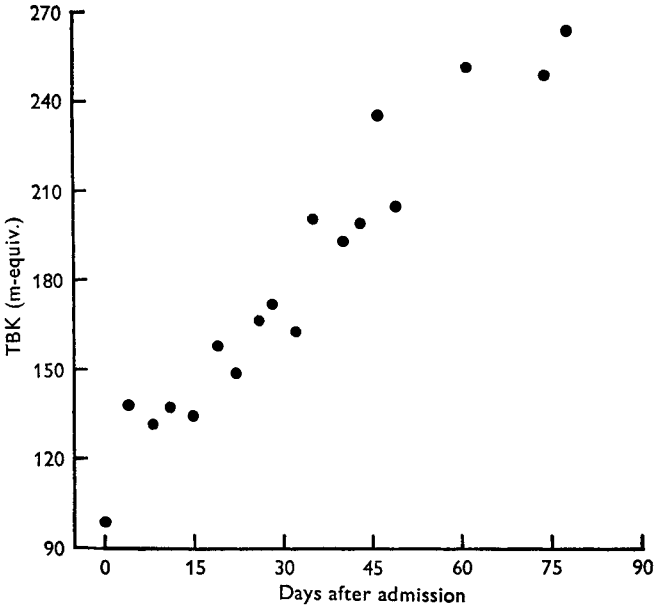

Fig. 2. Increase in total body potassium (TBK) in one child as she recovered from malnutrition.

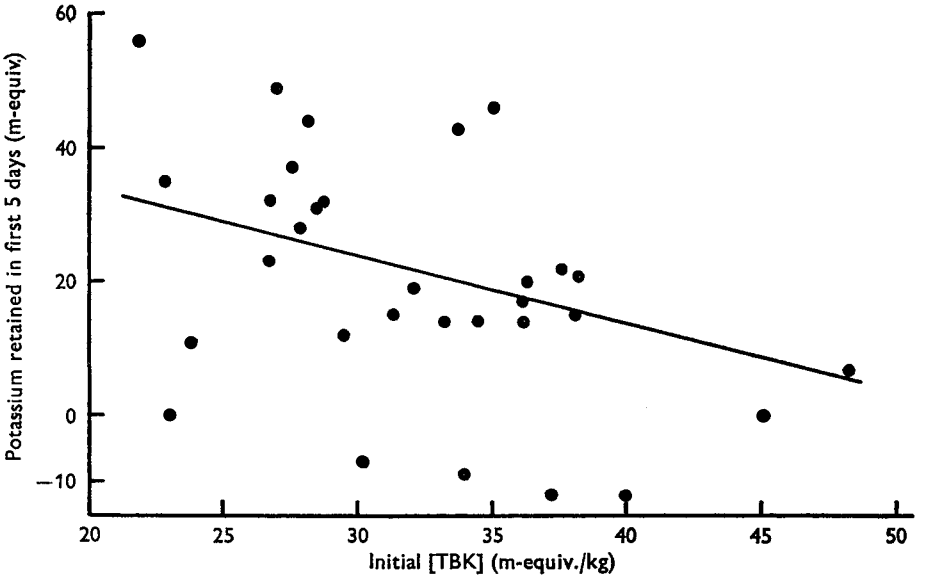

Fig. 3. The relationship in malnourished children between the retention of potassium in the first 5 days after admission to hospital and the initial total body potassium concentration ([TBK]) ($y = -1{\cdot}2x + 59{\cdot}0$; $P < 0{\cdot}02$).

Serum potassium was measured in twenty-three of these children before any potassium supplements had been given, and the mean value was 4·0 ± 0·3 m-equiv./l. (mean ± standard deviation). There was no correlation between serum potassium and [TBK] ($r = 0{\cdot}215$, $P = 0{\cdot}3$). The number of stools passed in the first 5 days after admission was related to the initial [TBK] ($r = -0{\cdot}366$, $P < 0{\cdot}025$) i.e. those children who were passing more stools had lower levels of [TBK].

The statistical relationships between the potassium retained in this early period and other measured variables are shown in Table 1. There was no correlation between the amount of potassium retained and protein or calorie intake during this period.

Table 1. *Correlations in malnourished children of potassium retained, in the first 5 days, with protein intake, calorie intake and initial concentration of body potassium* ([*TBK*])

(Dependent variable (y) is potassium retained in first 5 days of therapy)

Independent variable	r	P
Protein intake (g)	+0·085	> 0·7
Calorie intake (kcal)	+0·273	> 0·1
Initial [TBK](m-equiv./kg)	−0·422	< 0·02

Table 2. *Correlations in malnourished children of potassium retained in lag phase* with protein intake and calorie intake*

(Dependent variable (y) potassium retained in lag phase)

Independent variable	r	P	Regression equation
Protein intake (g)	+0·852	< 0·001	$y = 0{\cdot}186x + 4{\cdot}9$
Calorie intake (kcal)	+0·884	< 0·001	$y = 0{\cdot}045x - 236{\cdot}5$

* For definition of lag phase, see p. 206.

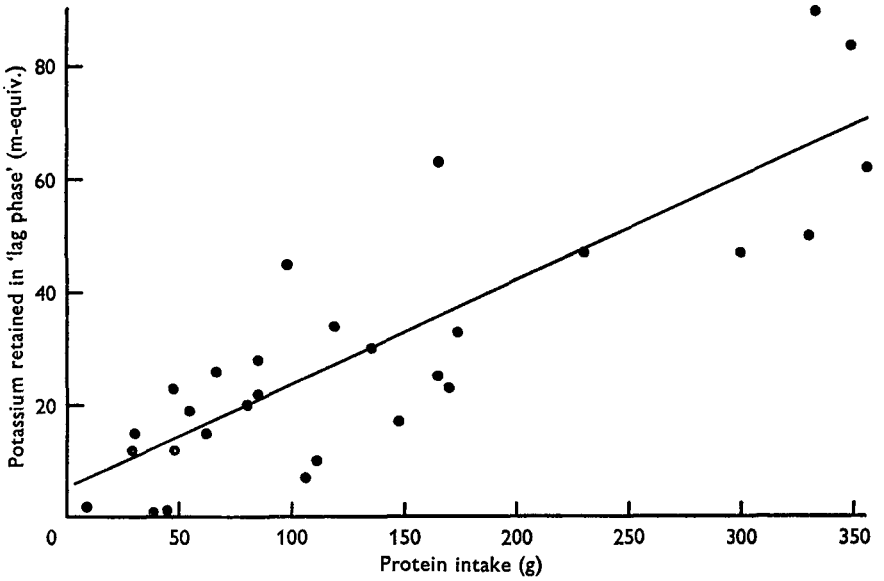

Fig. 4. The relationship in malnourished children between potassium retained in the 'lag phase' and the protein intake during this period. (For regression equation see Table 2.)

'*Lag phase*'. Similar correlations were derived for the 'lag phase' which has been defined on p. 206 (Table 2). There were highly significant correlations between the potassium retained in this phase and the protein and calorie intakes. The relationship between potassium retention and protein intake is shown in Fig. 4. For the whole series, the mean protein intake during this period was 133·3 g and the mean retention of potassium was 29·7 m-equiv. This protein intake corresponds to 21·3 g of nitrogen. The results of Waterlow & Wills (1960) show that, in children at this stage of recovery and receiving the same range of intakes, on the average 48·5% of the nitrogen intake was retained during this period. If a calculation is based on these values, 10·33 g N would be retained with 29·7 m-equiv. potassium, which gives a value of 2·9 m-equiv. potassium per g nitrogen.

Table 3. *Correlations in malnourished children of potassium retained in rapid growth phase with weight gain, protein intake and calorie intake*

(Dependent variable (y) is potassium retained in rapid growth phase)

Independent variable	r	P	Regression equation
Weight gain (g)	0·457	$< 0·01$	$y = 57x + 1·6$
Protein intake (g)	0·348	$< 0·05$	$y = 0·18x + 0·9$
Calorie intake (kcal)	0·197	$> 0·3$	—

Rapid growth phase. The relationships between potassium retention, weight gain, calorie and protein intakes during the phase of rapid weight gain are shown in Table 3. Protein intake was significantly correlated with the potassium retention but there was no correlation between potassium retention and calorie intake during this phase of recovery.

DISCUSSION

The results of this study show that total body potassium is low in malnourished children.

It has been shown that the more oedematous children of the kwashiorkor type have lower levels of [TBK] than the marasmic children who have no oedema (Garrow, 1965*a*; Alleyne, 1968). Indeed there is a good correlation between decrease in [TBK] and expansion of the extracellular fluid volume in malnutrition (Alleyne, 1968). Also it has been observed that the more oedematous children when assessed after they have lost their oedema are less underweight and less stunted in height than those children who never had oedema (Alleyne, 1965). The demonstration of a negative correlation between [TBK] and weight as a percentage of normal weight is in agreement with those observations. It is likely that the children with oedema were relatively well nourished, and then became acutely malnourished with perhaps more diarrhoea than those children without oedema. Thus while they were more potassium-deficient they would be less underweight than the more chronically malnourished children who had no oedema.

It has been shown that when [TBK] was lower than 30 m-equiv./kg there was a markedly reduced potassium concentration in muscle (Alleyne *et al.* 1969). In the thirty-one children in whom the acute repletion phase could be followed, the mean

initial [TBK] was 32·3 m-equiv./kg. We would thus expect that at these levels of [TBK] there would be a genuine and severe depletion of potassium. In terms of the previously expressed concept of potassium capacity and content (Alleyne *et al.* 1969) at these low levels of [TBK], although there is a reduction in amount of potassium-containing tissues, there is also reduction in potassium concentration in these tissues. There is a fall not only in potassium capacity but also in potassium content, hence there is a genuine depletion, so we would expect there to be an initial rapid retention of potassium which, as we have shown, is related to the [TBK]. The results here do not allow us to determine if a renal leak of potassium existed, since balances were not done: but in only three of the thirty-one children studied was there a net loss of potassium during this early phase. On the single occasion on which a severe fall in TBK occurred during the early period, the child had developed massive diarrhoea after admission to hospital.

The lack of correlation between serum potassium and [TBK] indicates once more that serum potassium is an unreliable guide to the body's potassium status. The serum potassium, since it is only about 1% of the total body potassium, reflects mainly acute losses of potassium from the extracellular fluid. There are other factors such as acid–base status, which might also affect the levels of serum potassium.

The correlation of the number of stools with the initial [TBK] is a very crude guide to the possibility that gastro-intestinal loss contributed significantly to this reduction in TBK.

In the lag phase, the assumption is that any depletion of potassium has been repaired and a low [TBK] is now a reflection of a reduced potassium capacity—the body is still short of those tissues which are richest in potassium. Muscle is the most important of these; thus it is not surprising that potassium retention is now correlated with the protein and calorie intakes. As the child is fed more protein and calories and more tissue is laid down, TBK increases. Previous work from this Unit shows that muscle is being laid down during this phase, since creatinine excretion rises (Standard, Wills & Waterlow, 1959; Picou, Alleyne & Seakins, 1965; Alleyne *et al.* 1969). The average retention of 2·9 m-equiv. potassium per g nitrogen is in keeping with the value of about 3·0 reported by Hansen (1956). The normal ratio of potassium to nitrogen in the whole body in children of this age is approximately 2·2 (Garrow, Fletcher & Halliday, 1965). The value of 2·9 for these children most likely indicates that they were laying down new tissue which is rich in potassium, e.g. muscle. The normal ratio of potassium to non-collagen nitrogen intracellularly is 3·3 for muscle (Frenk, Metcoff, Gómez, Ramos-Galván, Cravioto & Antonowicz, 1957).

During the phase of rapid growth in these children the growth rates were between 7 and 18 g/kg per day. The significant correlation between weight gain and potassium retention was to be expected, since from Fig. 1 it is clear that levels of [TBK] remained fairly constant once the plateau had been reached. The fact that [TBK] remained constant after the 3rd week indicates that the children were in general laying down tissue of normal composition and were not becoming obese. There were, however, occasional individual children in whom, although total potassium increased, [TBK] reached a plateau and then fell, suggesting accumulation of fat. The lack of correla-

tion between potassium retention and calorie intake is surprising in view of the findings of Ashworth, Bell, James & Waterlow (1968) that calorie intake was significantly correlated with weight gain in recovering children. In that study children were assessed at a later stage in the recovery phase, 3–6 weeks after admission, and this may in part account for the difference.

The clear picture which emerges from these studies complements previous work from this Unit and other centres. In severely malnourished children there is a genuine potassium depletion superimposed on a reduction in potassium-containing tissue mass. If adequate potassium supplements are given this depletion is rapidly repaired—and thereafter the rise in TBK and further potassium retention reflect mainly increase in tissue mass. A practical point emerging from these studies relates to potassium therapy. Contrary to previous recommendations (Garrow, 1965*a*), it is useless and perhaps dangerous to continue with large potassium supplements after the 1st week of treatment unless the child has severe diarrhoea. For the 1st week, daily potassium supplements of the order of 6–8 m-equiv./kg body-weight are necessary. Thereafter 1–2 m-equiv./kg per day is enough for normal needs, and the danger of marked hyperkalaemia in the recovery phase is thus avoided.

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