Malnutrition and Electrolyte Metabolism

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Abnormal total body and serum electrolyte concentrations are common in protein-energy malnutrition (PEM). The subject of electrolyte metabolism in PEM was studied in depth in the 1960s and early 1970s but has seldom been investigated in the past decade. Electrolyte status has been assessed by a variety of methods, including electrolyte concentrations in serum, urine, or muscle tissue; external electrolyte balances during recovery; and isotopic techniques. Although there is general agreement that total body water and sodium are increased and total body potassium and magnesium are decreased (1), many uncertainties persist about the importance, prognostic significance, or therapeutic implications of such findings, especially with regard to potassium depletion. Some of the discrepancies may derive from methodologic differences but also from variations in the type or degree of malnutrition, severity of the associated diarrhea, or differing electrolyte composition of the deficient diet in various parts of the world.

WATER

Body water content, distribution, and turnover may all vary with nutritional status. In malnutrition, adipose tissue is absent, and muscle tissue mass is markedly diminished in relation to the mass of the visceral organs. Since muscle tissue has less water than viscera, the total body water, expressed as percent of body weight, increases from a normal value of 60% of lean body mass to values approaching 75% or more in marasmus and clearly in excess of 80% in kwashiorkor (2). There is a direct relationship between weight loss and proportional increase in body water.

Muscle biopsies have shown that the increased water content corresponds mainly to an increase in extracellular water (3–10) (Table 1). Normally, the extracellular fluid volume in healthy infants is about 25% of lean body mass, distributed in plasma (6%) and interstitial fluid (19%). In PEM, the drop in plasma albumin leads to a marked shift of water to the interstitial space, resulting in low plasma volume and appearance of edema. There is no apparent correlation between total muscle
TABLE 1. Muscle electrolyte composition in various investigations (mean ± SEM)

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<td>FFDW²</td>
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<tr>
<td>H₂O (liters/kg)</td>
<td>4.9</td>
<td>5.1</td>
<td>4.8</td>
<td>4.0</td>
<td>4.5</td>
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<td>± 0.4</td>
<td>± 0.2</td>
<td>± 0.2</td>
<td>± 0.3</td>
<td>± 0.70</td>
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<tr>
<td>K (mmol/kg)</td>
<td>268 ± 31</td>
<td>296 ± 21</td>
<td>365 ± 18</td>
<td>287 ± 20</td>
<td>313 ± 16</td>
<td>334 ± 26</td>
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<td>Na (mmol/kg)</td>
<td></td>
<td>449 ± 31</td>
<td>417 ± 18</td>
<td>295 ± 20</td>
<td>303 ± 16</td>
<td>408 ± 26</td>
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<tr>
<td>Cl (mmol/kg)</td>
<td>237 ± 26</td>
<td>322 ± 37</td>
<td>228 ± 18</td>
<td>199 ± 14</td>
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<td>304 ± 17</td>
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<td>Normal</td>
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<tr>
<td>H₂O (liters/kg)</td>
<td>3.8</td>
<td>3.9</td>
<td>3.4</td>
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<td>± 0.1</td>
<td>± 0.06</td>
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<td>± 0.2</td>
<td>± 0.23</td>
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<tr>
<td>K (mmol/kg)</td>
<td>328 ± 12</td>
<td>345 ± 8</td>
<td>422 ± 10</td>
<td>335 ± 8</td>
<td>334 ± 23</td>
<td>309 ± 23</td>
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<td>Na (mmol/kg)</td>
<td>300 ± 14</td>
<td>258 ± 10</td>
<td>202 ± 6</td>
<td>189 ± 6</td>
<td>199 ± 6</td>
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<td>Cl (mmol/kg)</td>
<td>138 ± 10</td>
<td>154 ± 11</td>
<td>155 ± 5</td>
<td>163 ± 5</td>
<td>196 ± 5</td>
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*FFDW, fat free dry weight.

Numbers in parentheses are refs.

Data taken from ref. 10.

Water and either the degree of edema or the plasma concentration of albumin (6). The intracellular water content is normal (6) or increased (7) in relative terms, depending on the tonicity of the extracellular compartment. However, intracellular water volume per total body weight always decreases, as a consequence of the diminished body cell mass (11).

A multiple isotope dilution technique, measuring body distribution of tritiated water and ²²Na, permits the quantitative assessment of water compartments, as well as the indirect measurement of total exchangeable potassium. Investigation of adults with a moderate degree of malnutrition has shown results similar to those reported in children (11). The expansion of the extracellular mass is reflected in an elevated exchangeable sodium and extracellular water volume per unit of total body weight, which are both measures of the extracellular mass corrected for body size. The loss of body cell mass is reflected in a decreased exchangeable potassium per unit of total body water and decreased intracellular water volume per unit of total body weight, which are both measures of the body cell mass. The ratio of exchangeable sodium to exchangeable potassium is a measure of the extracellular volume as a function of the body cell mass and is significantly raised in malnourished individuals in relation to controls: 1.95 ± 0.08 versus 0.98 ± 0.02, respectively (11). According to Shizgal (11), this ratio is a sensitive index of nutritional status, and malnutrition in adults...
should be suspected in the presence of an exchangeable sodium/potassium ratio in excess of 1.22. Similar data are not available in malnourished children.

The expansion of the extracellular fluid volume obscures the loss of body cell mass, and, therefore, the actual weight of a malnourished child does not accurately reflect the true degree of malnutrition. Although the proportional increase in body water could be an indication of water restriction during the early realimentation period, the presence of an inability to concentrate the urine (12,13), the increased urine volume resulting from higher protein intake (14), and the increased dermal losses that occur with catch-up growth (14,15) should all be taken into consideration when prescribing an adequate fluid intake. At least 150 ml/kg per day should be administered initially with the necessary adjustments if profuse vomiting or diarrhea is present (14). In children with profound hypoalbuminemia, rapid restoration of plasma volume by protein administration may lead to relative hypervolemia and pulmonary edema, and careful reintroduction of protein intake should be recommended.

**SODIUM**

Extracellular sodium concentration is reduced in children with PEM, despite a significant increase in total body and cellular sodium content. The fall of serum sodium is generally moderate and is caused by the expansion of the extracellular fluid volume. In most patients, the mean serum sodium concentration is between 130 and 135 mmol/liter (6,9,16,17), but occasional cases may show marked hyponatremia. Osmolality is also diminished, in the range of 250 to 270 mOsm/kg. Some authors have related the prognosis of PEM to values of serum sodium. In Jamaica (1), seven of nine children with a serum sodium concentration less than 121 mmol/liter died, while only 12 deaths occurred in a series of 98 children who had a serum sodium concentration higher than 121 mmol/liter. In Mexico (7), sodium concentration in extracellular water in muscle tissue was also lower in nonsurviving children. As pointed out by Finberg and co-workers (18), the concept of hypernatremia (serum sodium >150 mmol/liter) and hyponatremia (serum sodium <130 mmol/liter) should be redefined in children with PEM. The low serum sodium observed in these patients represents the result of an adaptive steady state, and any rapid elevation or fall in their particular serum sodium concentration may produce marked neurologic damage no matter what the initial levels.

The study of muscle biopsies consistently shows a marked increase in cellular sodium, which is accompanied by a parallel decrease in cellular potassium (Table 1). A reduction in cytoplasmic protein content and a lack of energy for active ion transport across the cell membrane could bring about this result. Normally, the concentration of sodium inside the cells is kept low and potassium high by an energy-dependent, ouabain-inhibited process governed by the Na\(^+\),K\(^+\)-ATPase pump (19). Other ion transport systems present in mammalian cell membranes are bumetanide-inhibited Cl\(^-\)/Na\(^+\)/K\(^+\) cotransport, Na\(^+\)/Li\(^+\) countertransport, and ouabain- and
bumetanide-resistant passive Na\(^+\) efflux (20). The study of these different transport systems would be of great interest. Kaplay (21) found no alterations in Na\(^+\),K\(^+\)-ATPase in erythrocytes of children with PEM, but this result should be confirmed in other tissues, such as leukocytes, liver, or muscle, since red cells are not appropriate for investigating changes in sodium and potassium transport following nutritional perturbations (22).

Balance studies have shown that children with PEM put on a low-protein diet maintain a negative sodium balance due both to fecal and urinary losses (14,23). The fecal losses are mainly related to diarrhea, which is an associated feature in more than 90% of cases. The persistence of sodium loss in these moderately hyponatremic children may be the result of the adaptive steady state, with maintenance of the homeostatic mechanisms at a different regulatory level (18). However, if sodium intake exceeds the renal excretory capacity, renal retention results in the formation of edema.

It is known that subjects with PEM have an impaired ability to handle sodium loads when compared with their capacity to handle the same loads after protein repletion (24). Gordillo et al. (25) infused hypertonic saline in three children with malnutrition and showed that they retained all the infused sodium. Thus, the presence or absence of edema in PEM could correlate with the dietary history of sodium intake. The possible mechanisms responsible for the incapacity to handle sodium loads are related to hypoalbuminemia and decreased plasma volume. The fall of cardiac output and glomerular filtration rate causes a reduction in the filtered load of sodium and water. At the same time, renal tubular sodium reabsorption is increased as a result of the decreased plasma volume and the increased circulating levels of aldosterone (26). The study of other regulatory factors in sodium homeostasis, such as atrial natriuretic peptide (27), would be of great interest.

During the initial period of increased protein intake, there is, generally, a marked elevation in fecal and urinary sodium excretion (6,14,23,28,29). The disparities observed in different studies may depend on the severity of the associated diarrhea or on the amount of sodium provided by the deficient and repletion diets. The negative sodium balance is rapidly reverted, and, after a period of 10 to 15 days, a positive sodium balance accompanies the progressive weight gain of recovery. The sodium requirements during treatment have been estimated by Nichols et al. (14) to be of about 4 mmol/kg per day, with a range between 2.2 and 6.4 mmol/kg per day.

**CHLORIDE**

Chloride status in PEM is similar to that of sodium. In general, there is an increase in total body and cellular chloride content (Table 1), with normal or slightly decreased serum values (9,17,30). Vis et al. (6) found a significant increase in serum chloride concentration in the Congo, a feature also observed in Jamaica (31). This hyperchloremia would indicate that metabolic acidosis was also present, probably as a consequence of associated gastroenteritis. It is known that malnourished
children present a certain incapacity to excrete an acid load (12), which is partly compensated by an increased ammonia production driven by the stimulatory effect of potassium deficiency on the renal glutaminase system (24). If severe diarrhea is not present, the renal incapacity for acid excretion does not lead to metabolic acidosis, because the endogenous acid production, coming from catabolism of ingested proteins, is also markedly reduced (32).

An elevated sweat chloride concentration has been also reported in malnutrition. Beck et al. (33) found that of 33 children with high sweat chloride (>50 mmol/liter) who did not have cystic fibrosis, 14 (44%) had some degree of malnutrition or suffered from growth failure. With improvement in nutritional state, the sweat chloride levels reverted toward normal. However, Senecal and Dan (34) have reported lower than normal sweat chloride values in 41 children with severe PEM, so that finding should not be considered as obligatory.

POTASSIUM

Potassium depletion is an almost universal feature of severe malnutrition, even though not always manifested by a low serum concentration of potassium, which is normal in most studies (4,6,9,17,30) but may also be moderately diminished (16). Since potassium is mainly situated in the intracellular compartment, the body content of this electrolyte must be judged by special techniques, either isotopic or by direct measurement of potassium concentration in muscle tissue.

Smith and Waterlow (35) and Nichols et al. (14) demonstrated the existence of intracellular potassium depletion using the dilution of the isotope $^{42}$K, and similar results have been obtained by total body counting of a naturally occurring isotope, $^{40}$K (8,17,36–39). Total body potassium in children is directly related to weight, and there are no sex-related differences below 30 kg (40). In South Africa, Mann et al. (17) found that only seven of 56 malnourished children had a total body potassium above 37.5 mmol/kg, which represents the lower limit of normality. Four of six children who died had a total body potassium of less than 30 mmol/kg on admission.

Whole body analysis in adult humans has shown that approximately 60% of total body potassium is present in skeletal muscle; thus, the muscle biopsy constitutes an important tool for the estimation of total body potassium. The use of the Baylor muscle biopsy needle has permitted the wide application of this technique (41). In children with PEM, muscle potassium content, expressed on a dry weight basis, is clearly diminished (3,6,8,9,38,39), although in some studies, the values are close to normal (7,10). Even in the latter cases, however, when potassium concentration is expressed on a wet weight basis, a low value is found due to the simultaneous increase of the intracellular water content (7).

These discrepancies in muscle potassium content may depend not only on the severity of the associated diarrhea but also on the potassium content of the deficient diet and on the type or severity of malnutrition. As pointed out by Vis et al. (6), when the basic food is made of beans with bananas, as was the case in the Congo,
the diet is rich in potassium, while if corn or manioc is the basic nutrient, the diet is rather poor in potassium. It is also accepted that electrolyte body composition is more altered in kwashiorkor than in marasmus. Frenk et al. (3) found that electrolyte composition of muscle from marasmic children was nearer normal than that of children with kwashiorkor. Alleyne et al. (8,39) found that total body potassium was 20% lower in children with kwashiorkor than in children with marasmus. Recently, Nichols et al. (10) compared muscle electrolyte composition in 10 infants with marasmus and eight children with kwashiorkor and confirmed these data with regard to water and sodium content. However, muscle potassium content, on a dry weight basis, was not statistically different from controls in either group of children. This finding raises the question of the value of muscle potassium determinations in assessing the body content of this electrolyte in children with a diminished muscle mass. Total body potassium may be decreased as a direct consequence of the reduced muscle mass, without there necessarily being any alteration in muscle potassium concentrations. In this regard, Alleyne at al. (37,38) have introduced the concept of potassium capacity. This is defined by the sum total of anions and other chemical groups outside the extracellular space capable of holding or binding potassium ions. If a reduced muscle potassium concentration is present, it may be due either to incomplete filling or desaturation of the cellular capacity for the ion or to true reduction in tissue capacity for the ion. In the first circumstance, potassium therapy may be lifesaving, while in the second one, the depletion would be significant only when there is a superimposed loss of total body potassium.

In a study of 52 Jamaican children with PEM, Alleyne et al. (38) found a curvilinear correlation between total body potassium and muscle potassium concentration. Muscle magnesium was also reduced, but the depression of the potassium/magnesium ratio implied a major loss of muscle potassium. When total body potassium was between 30 and 40 mmol/kg, there was a very modest reduction in muscle potassium concentration, which mainly reflected a reduction of potassium capacity. When total body potassium fell below 30 mmol/kg, there was a marked and rapid decrease in muscle potassium concentration, which represented not only the fall in potassium capacity but also the decreased saturation of that capacity; this was interpreted as true potassium depletion (Fig. 1). The important finding of the existence of a reduced tissue capacity for potassium in malnutrition has been partly confirmed by Nichols et al. (9), who found a slow increase in muscle potassium concentration when repeat muscle biopsies were performed following potassium supplementation. Alleyne et al. (42) have shown that brain and liver share with muscle the intracellular loss of potassium, so it is also possible that the potassium retained in the early period of recovery was mainly accumulated in the brain (43). The above finding may have important prognostic and therapeutic significance. When true potassium depletion occurs, survival may be jeopardized if high doses of potassium supplements are not given. Conversely, in children with moderate deficiency, who mainly have a reduction in potassium capacity, administration of high doses of potassium salts may lead to hyperkalemia.

The mechanism by which the capacity of cells for potassium is restricted in PEM has not been definitely established. Nichols et al. (9) have stressed the close inverse
correlation between muscle concentrations of sodium and potassium: approximately two sodium ions are gained for each three potassium ions lost. The altered cell electrolyte composition probably represents a consequence of an abnormality in the Na\(^+\),K\(^+\)-ATPase pump, caused by a reduction in energy metabolism. Muscle potassium concentration is linearly related to muscle glycogen (38), and enzymatic studies of muscle tissue have shown that intracellular concentrations of phosphoenolpyruvate, pyruvate, \(\alpha\)-ketoglutarate, and oxaloacetate are significantly related to intracellular concentrations of sodium and potassium (7).

Balance data from children recovering from PEM show a parallel retention of potassium and nitrogen (6,14,23,28,29). In some studies, potassium retention corresponds exactly to that expected from nitrogen retention: 3 to 4 mmol of potassium for each g of nitrogen (6). In others, retention of potassium is greater than would be expected for the growth of normal tissue, indicating the coexistence of true potassium depletion (23). When computing potassium retention during balance studies, it is important to take into account not only the fecal and urinary losses but also the dermal loss, which may be markedly increased during the recovery period (14). Potassium requirements during treatment have been estimated to be about 8 mmol/kg per day, with a range between 5.7 and 9.7 mmol/kg (14). It must be remembered, however, that true potassium depletion is not always present and that in some geographic areas, potassium chloride supplements may not be required (6).

MAGNESIUM

Magnesium is the second most abundant cation of the intracellular compartment and, as cofactor of numerous enzymatic reactions, is essential for a large number of
metabolic steps, including most of those concerned with transfer or utilization of energy, protein synthesis, and normal activity of the nervous system (44).

In PEM, plasma magnesium concentration is usually normal or slightly decreased on admission (16,45), but low magnesium reserves are present because significant hypomagnesemia rapidly develops during the recovery period if magnesium salts are not provided (16,45). Hypomagnesemia may manifest clinically by the appearance of neuromuscular hyperirritability and electrocardiographic changes (16). Magnesium content in muscle is diminished (16,38,46), but a lower than normal potassium/magnesium ratio implies a greater potassium loss (38). This may be partly explained by the fact that a major proportion of potassium is stored in muscle, whereas bone is the main reservoir for magnesium.

Urinary magnesium excretion is markedly diminished on admission, and urinary values are at or below 0.5 mmol/liter (16,28,30,45,47). The low magnesium excretion reflects the presence of body magnesium depletion, despite normal or only slightly decreased values of magnesium. Caddell et al. (48) have proposed that a parenteral magnesium load should be given children with PEM to evaluate the body reserves. This test was initially proposed in children with magnesium deficiency by Harris and Wilkinson (49). In 32 malnourished Thai children, an intramuscular load of magnesium, 0.25 mmol/kg, was administered, and retention was calculated by subtracting the amount lost in the urine following the load. Retention of more than 40% of the load should be interpreted as indicative of magnesium depletion. In children with PEM, high values of retention were found. Some children also had low serum magnesium values, but other patients with high retention had normal serum values, a fact also found by us when applying this test to infants recovering from acute gastroenteritis (50). The role of gastroenteritis in the development of magnesium depletion has also been stressed by Caddell et al. (48). Fifteen children with little or no recent gastroenteritis retained 27% of the load, whereas 15 children with more severe gastroenteritis retained 73%.

Large amounts of magnesium must be administered to children with PEM during recovery, both for tissue repletion and to sustain new growth. Magnesium requirements in healthy children decrease from 1 mmol per day during the first months after birth to 0.75 mmol per day beyond the second year of life (51). In malnourished children with evidence of magnesium depletion, the amount should be increased to 0.50 to 0.75 mmol/kg per day, administered orally in the form of magnesium chloride or as a combination of magnesium chloride and magnesium citrate (52).

**CALCIUM**

Little information is available on the alterations of mineral metabolism in children with PEM. Both hypocalcemia and hypocalciuria are present before therapy (1,30). Hypocalcemia is exclusively related to the low plasma proteins, and no abnormalities in neuromuscular excitability should be expected, given the normality of the ionized fraction. Serum inorganic phosphate concentration and alkaline phosphatase are also moderately decreased.
Therapeutic diets used for the rehabilitation of children with PEM are not only protein-rich but also calcium-rich. Caballero et al. (53) performed balance studies in 20 children with edematous PEM during the first 45 days of recovery. All children received 4 g/kg per day of protein and 150 kcal/kg per day of energy from a milk-based formula providing 130 to 140 mg/kg per day of calcium. The average calcium retention was 50 mg/kg per day, which represented 8.3 mg/g body weight gain per day. As pointed out by Harrison (54), this high retention of calcium is identical to that observed in healthy infants between 4 and 7 months of age fed a high-protein and high-calcium diet and thus should not be attributed to a special avidity for calcium retention related to malnutrition. An interesting finding of the study by Caballero et al. (53) was that the presence or absence of lactose in the diet did not affect intestinal calcium absorption, even though the children fed a lactose-free diet had lower stool output than those fed lactose. Although many studies indicate that dietary lactose promotes calcium absorption (55,56), this advantage does not appear to be present when high dietary calcium levels are provided. An important conclusion should be that there is no contraindication to using lactose-free milk if gastrointestinal intolerance to complete cow's milk is present (57).

In the study of Caballero et al. (53), urinary calcium excretion during the recovery period was rather high, ranging from values of 2.6 ± 2.1 mg/kg per day on days 2 to 5 of hospital admission to 4.6 ± 2.9 mg/kg per day on days 42 to 44. These high rates of calcium excretion may lead to stone formation or renal calcinosis if urine volume is not adequate, so strict monitoring of these possible complications is indicated (54).

The high calcium retention reported by Caballero et al. (53) is similar to that observed during fetal life (58) and parallels the rapid weight gain observed during the recovery period of PEM. A calcium-rich diet should be provided for a long period of time and always beyond the period of normalization of body weight and lean body mass. The actual calcium requirements for each geographic area will depend on the relative deficiencies of calcium and protein in the deficient diet prior to diagnosis, on the rapidity of weight gain, and on the vitamin D status of the child. In general, vitamin D deficiency, as judged by circulating levels of 25-hydroxyvitamin D₃, is not an obligatory part of the malnutrition picture if there is effective skin biosynthesis through sunlight exposure (59). However, cases of rickets have been reported in tropical countries where the exposure to sunlight would be expected to be high (60). This may be the result of social customs or taboos, which prevent adequate sunshine exposure, or of alterations of bone structure, more related to malnutrition itself than to dietary deficiency in vitamin D (61,62).

**RESEARCH TRENDS FOR THE FUTURE**

More studies are needed concerning ion transport systems in cell membranes. In particular, the investigation of $\text{Na}^+,\text{K}^+\text{-ATPase}$ in leukocytes, liver, and muscle cells could contribute to a more complete understanding of the cause of the altered electrolyte composition in the cell.
Recent years have brought about many advances in the possible role of new hormones or circulating factors in the regulation of sodium homeostasis. The study of the circulating levels of atrial natriuretic peptide or digoxin-like immunoreactive substances could be of interest in developing our understanding of the pathogenesis of edema in PEM. In addition, easy and noninvasive tests are required for the better diagnosis of potassium or magnesium depletion and to enable us to judge the correct level of supplementation in the malnourished child.

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**DISCUSSION**

*Dr. Haschke:* The increased calcium excretion in urine is not surprising. We have learned, from premature infants with hypophosphatemic rickets, that high calcium excretion in urine is related to low phosphorus supply in the diet. Of the body’s calcium, 98% is within the osseous minerals. Of phosphorus, 70 to 80% is within the osseous minerals, and 20% is in the intracellular compartment. Calcium and phosphorus can only be incorporated as hydroxyapatite into the growing bone at a ratio of 2/1 (mg/mg). During nutritional therapy in the premature infant, and probably also in the malnourished infant, 2 mg calcium has to be given together with 1 mg phosphorus. If the phosphorus supply is inadequate, calcium wasting occurs, and calcium is excreted in the urine.

*Dr. Rodriguez-Soriano:* I think you are correct. A diet providing 4 g/kg of protein may seem as though it is also supplying adequate phosphorus, but this may not be the case. Children retain only part of the calcium, while the rest is excreted in the urine. It is important to recognize, therefore, that when the necessarily high calcium supplement is provided, urinary calcium excretion should be monitored, because of the risk of developing nephrolithiasis.

*Dr. Jackson:* Patrick (1) and Kaplay (2) have measured the activity of the Na\(^+\), K\(^+\)-ATPase and membrane permeability. Patrick has been able to show differences between edematous and nonedematous children. Furthermore, the activity of the Na\(^+\), K\(^+\)-ATPase appears to be sensitive to zinc status (3). In a small group of edematous children, there appeared to be a defect in the down-regulation of the pump. When these children were presented with a generous supply of energy, they rapidly developed a syndrome characterized by cardiac failure and circulatory overload, with subsequent loss of the circulating volume into the gastrointestinal tract, leading to death from circulatory collapse (4). This demonstrates the importance of controlling energy intake.

I should like to emphasize the important role that potassium deficiency has in the genesis of edema. This cannot be identified by measurements on plasma, but generous potassium supplementation is vital if edema is to be effectively mobilized.

*Dr. Rodriguez-Soriano:* Your comment is logical because of the need to provide potassium to replace intracellular sodium in order to mobilize the edema.

*Dr. Suskind:* Studies of malnourished children in India demonstrated an elevated, inappropriate antidiuretic hormone (ADH) in children with protein-energy malnutrition (PEM), which reverted to normal with the initiation of feeding and the mobilization of fluid.

*Dr. Okeahialam:* The children who come to our hospital have low potassium levels. Their state of hypokalemia may be due to recurrent diarrhea, which is a common clinical feature, and low levels of potassium in their maize gruel diet. We routinely treat with oral potassium in conjunction with a high-protein diet. As the edema disappears, potassium levels return to normal within 7 to 10 days.

*Dr. Rodríguez-Soriano:* I agree that it is important to relate the potassium levels to the pre-
disease dietary intake and to the severity of diarrhea, both of which have a great impact on
the severity of the potassium deficiency.

Dr. Guesry: In developing countries, PEM is almost always associated with acute or se-
vere chronic diarrhea. This is important in relation to electrolyte status.

Second, the importance of phosphorus is not just for the fixation of calcium on hydroxyap-
atite, but because of increasing evidence that phosphorus deficiency impairs muscle function,
especially respiratory muscle function.

Dr. Suskind: Dr. Caddell has demonstrated the effects of magnesium deficiency on cardiac
function where electrocardiogram (EKG) changes, similar to those in potassium deficiency,
are found. There are reports of children in severe cardiac failure who respond to magnesium
supplementation.

Dr. Rodríguez-Soriano: Dr. Caddell made the point that magnesium deficiency became
especially apparent when realimentation was started. Hypomagnesemia is not present at ad-
mission. However, when food is provided without magnesium supplementation, serum mag-
nesium may drop, and the child may develop the electrocardiographic functional changes
associated with magnesium deficiency.

Dr. Suskind: Magnesium deficiency was often apparent in our children at the time of ad-
mission, even before therapy. We routinely gave them intramuscular and oral magnesium.

Dr. Rodríguez-Soriano: I have seen a few children with severe hypomagnesemia of renal
origin, and they never had cardiac dysfunction.

Dr. Suskind: Were they functionally and electrocardiographically normal?

Dr. Rodríguez-Soriano: Perhaps in malnutrition something combines with hypomagnese-
mia to worsen the child's cardiac status. We have seen children with hypomagnesemia be-
come symptomatic following an episode of intercurrent infection, for example. They develop
tetany or have characteristic changes in the electromyogram, although no cardiac abnormali-
ties are present. Future studies are needed on sodium and potassium transport across cell
membranes. These should be done in cells having active protein synthesis, such as leukocytes
or muscle cells. Also, I am not aware of studies in malnutrition of atrial natriuretic peptide or
digoxin-like substances, both involved in renal sodium hemostasis. It would be important to
develop easy, noninvasive tests to assess intracellular potassium and magnesium deficiency
without the need of performing a muscle biopsy. This would help guide potassium and mag-
nesium supplementation.

Dr. Walker: Most malnourished children with diarrhea have significant potassium deple-
tion as well as low serum potassium levels. The EKG is a simple tool for recognizing this and
for controlling replacement therapy. It is possible to treat potassium depletion aggressively if
you have some EKG control over the amount you administer.

Dr. Gordillo: We had problems with marasmic children who had severe potassium deple-
tion after diarrhea. I wonder if this were related to simultaneous magnesium deficiency. I was
able to control the urinary potassium losses, in some cases, by giving magnesium supplemen-
tation. This is the advantage of becoming aware of supplemental relationships.

Dr. Rodríguez-Soriano: A status of severe magnesium deficiency is essentially accompa-
nied by a secondary state of potassium deficiency. To correct potassium deficiency, magne-
sium must be given first; otherwise, all administered potassium is lost in the urine. This is
important, since both deficiencies are simultaneously present in malnutrition.

Dr. Monckeberg: We have observed that the intracellular content of potassium in under-
nourished, dehydrated children may be decreased up to 60% of normal. Interestingly, this
may not be correlated to plasma potassium levels, which may be high.

Electrocardiograms have not been useful in quantifying potassium deficits. We found, in-
stead, a significant correlation between potassium deficits and clinical symptoms such as hypotonia, hyporeflexia, and psychic compromise. When the symptomatology was marked, there was a coincidental greater deficit in potassium, as determined by muscle biopsy.

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