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# THERAPEUTIC IMPLICATIONS OF ELECTROLYTE, WATER, AND NITROGEN LOSSES DURING RECOVERY FROM PROTEIN-CALORIE MALNUTRITION

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# *Therapeutic implications of electrolyte, water, and nitrogen losses during recovery from protein-calorie malnutrition*

*The importance of recognizing the altered physiologic status of the child with protein-calcium malnutrition at admission and during rehabilitation is emphasized by the difference in continuing losses and in growth requirements in these periods. Features of great significance are the inability to concentrate urine at admission and during early rehabilitation, the increased urine volume resulting from higher protein intakes, and the increased dermal losses which occur with early and late catch-up growth. For the child at admission, it is suggested that whole cow's milk diluted two parts with one part of a solution of 15 per cent dextrimaltose and 1.5 per cent potassium chloride will meet the water and electrolyte requirements when fed at the rate of at least 150 ml. per kilogram per day. If the child is committed to the catabolic state by gastrointestinal disturbances, an oral or intravenous infusion of a solution containing 55 mEq. of K and 25 mEq. of Na at an average rate of 120 ml. per kilogram per day will provide for the average continuing losses or maintenance requirements of water and electrolytes.*

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IN A REVIEW of the altered electrolyte metabolism in the child with protein-calorie malnutrition (PCM), Garrow and co-authors[1] concluded that total body water is increased, total body potassium is decreased, and sodium concentration is reduced. Quantitative therapeutic recommendations were not possible because the continuing losses of water, nitrogen, and potassium during recovery were not clearly documented. This article reports balance observations made on these continuing losses in children suffering from PCM in the catabolic state at admission (A period) and the state of rapid growth during therapy (T period). These losses reflect a malabsorption of water, electrolyte, and nitrogen and a reduction in renal function at admission; they are also influenced by a changing metabolic rate which increases dermal losses during recovery. The total requirements reflect the actual changes in body composition during recovery and include the retention related to growth and biochemical recovery.

| Abbreviations used | |
|---|---|
| PCM: | protein-calorie malnutrition |
| IWL: | insensible weight loss |

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**Table I.** Total balance of nitrogen, sodium, and potassium (mean ± S.D.) (number of observations)

| Period | Admission (A) | | Therapy (T) | | | Recovery (R) | |
|---|---|---|---|---|---|---|---|
| | $A_1$ | $A_{2-3}$ | $T_1$ | $T_2$ | $T_{3-5}$ | R | F* |
| Days of study | 0-5 | 6-10 | 0-15 | 16-45 | 46-95 | 96-120 | — |
| Weight (Kg.) | 9 ± 2 (26) | 9 ± 2 (19) | 9 ± 2 (54) | 10 ± 3 (56) | 11 ± 3 (34) | 13 ± 3 (47) | 13 ± 3 (14) |
| Insensible weight loss per day (IWL) (Gm.) | 396 ±71 (49) | 396 ±71 (49) | 576 ±94 (20) | 598 ±102 (16) | 778 ±97 (25) | 849 ±115 (26) | — |
| Potassium (mEq./3 da.) | | | | | | | |
| Ingestion | 188 ±52 (26) | 189 ±60 (19) | 205 ±55 (54) | 247 ± 46 (56) | 235 ±96 (34) | 233 ±131 (47) | 174 ±100 (14) |
| Fecal | 35 ±28 (26) | 33 ±34 (19) | 18 ±15 (54) | 13 ± 11 (56) | 18 ±13 (34) | 16 ± 13 (47) | 9 ± 4 (14) |
| Urinary | 111 ±44 (26) | 122 ±62 (19) | 129 ±39 (54) | 162 ± 41 (56) | 150 ±81 (34) | 139 ± 74 (47) | 101 ± 61 (14) |
| "Retention" | 42 ±29 (26) | 34 ±30 (19) | 58 ±40 (54) | 72 ± 37 (56) | 67 ±42 (34) | 78 ± 72 (47) | 64 ± 41 (14) |
| Sodium (mEq./3 da.) | | | | | | | |
| Ingestion | 84 ±44 (26) | 90 ±53 (19) | 106 ±58 (54) | 129 ± 63 (56) | 150 ±43 (34) | 164 ± 52 (47) | 165 ± 39 (14) |
| Fecal | 28 ±31 (26) | 20 ±25 (19) | 10 ±12 (54) | 8 ± 15 (56) | 8 ± 9 (34) | 7 ± 5 (47) | 6 ± 3 (14) |
| Urinary | 66 ±44 (26) | 72 ±43 (19) | 77 ±45 (54) | 73 ± 54 (56) | 102 ±50 (34) | 107 ± 63 (47) | 91 ± 51 (14) |
| "Retention" | −10 ±43 (26) | −2 ±53 (19) | 19 ±63 (54) | 48 ± 31 (56) | 40 ±37 (34) | 50 ± 39 (47) | 69 ± 21 (14) |
| Nitrogen (Gm./3 da.) | | | | | | | |
| Ingestion | 3.2± 0.9(26) | 3.3± 1.1(19) | 14.2± 4.1(54) | 16.5± 5 (56) | 16.0± 6.9(34) | 12.1± 5.8(47) | 3.5± 0.8(14) |
| Fecal | 1.4± 0.9(26) | 1.3± 0.8(19) | 1.8± 0.4(54) | 1.8± 0.7(56) | 2.2± 1.0(34) | 1.9± 1.0(47) | 1.1± 0.2(14) |
| Urinary | 2.2± 0.8(26) | 2.3± 1.4(19) | 6.7± 2.7(54) | 9.7± 3.5(56) | 8.9± 5.6(34) | 7.2± 4.3(47) | 2.3± 0.6(14) |
| "Retention" | −0.4± 1.8(26) | −0.3± 1.0(19) | 5.7± 2 (54) | 5.0± 2 (56) | 4.9± 2 (34) | 3 ± 2 (47) | 0.1± 0.5(14) |

*During F period, children who had recovered completely were placed on a low protein intake for the purpose of a separate study on minimal protein requirements.

## METHODS

Children with edematous protein-calorie malnutrition were studied at the Biomedical Division of the Institute of Nutrition of Central America and Panama.* The clinical characteristics of these children have been described previously.[2] Patients with significant complications during hospitalization were excluded from this series.

The subjects of this study were also included in a previous report[3] on muscle electrolyte composition, where their individual clinical findings and dietary management were detailed. All of the patients were edematous. The average age was 40 months; the average admission weight was 9 kilograms. The mean per cent of normal weight for height was 79 per cent. Total serum proteins and albumin concentrations averaged 3.9 and 1.6 Gm. per 100 ml., respectively. The mean creatinine-height index was 44 per cent.

The clinical management of the children admitted to the study was divided into two periods in order to separate the effects of therapy from the adaptations in metabolic function preceding admission.[3] During the initial admission (A) period, the diet provided 0.7 Gm. per kilogram per day of protein and 80 calories per kilogram per day. During the therapeutic (T) period, the diet was increased to 3 Gm. per kilogram per day of protein and 120 calories per kilogram per day. The diet in these periods consisted of casein, supplemented with 0.2 per cent methionine, sucrose, corn starch, and corn oil. A supplementary vitamin and electrolyte mix was given throughout the two periods, and an oral potassium supplement of 4 mEq. per kilogram per day was given as a KCl solution separate from the diet. The length of the A period was determined by general clinical considerations; however, the patient was kept on the low protein diet for two weeks, if possible.

The children were also studied at the time of complete recovery, R period.[3] On the average, the duration of the therapeutic diet was 117 days. At the R period, the average weight was 13 kilograms, and the per cent of normal weight for height was 101 per cent. The A and T periods were subdivided, and the data grouped as indicated by subscripts. The duration of study of each subgroup is indicated in Table I.

An additional series (F) was studied when children who had completely recovered were placed on a low pro-

*Informed consent was obtained from parents according to the usual National Institutes of Health guidelines. The protocol was approved by the Human Investigation Committees of both institutions.

tein diet as part of a separate investigation of protein utilization rates. This series is included in the present report to allow a differentiation between the effects of the low protein diet and the preceding metabolic adaptations in these subjects at admission.

The balance studies were conducted in periods of three days. The sample collection and analytical techniques have been fully described previously.[3,4] The apparent water balance was computed by the difference of the volume of measured intake and that of the combined urinary and fecal output. Insensible weight loss (IWL) is that portion of the apparent water balance not appearing as actual change in body weight. The portion of insensible weight loss due to the difference between $O_2$ utilization and $CO_2$ production is computed by the method of Newberg and associates.[6] Respiratory water loss is computed from average figures for respiratory rate, tidal volume (unpublished data), and an estimated average difference of 40% saturation between ambient and expired air at body temperature. Daily body weights were determined on a scale sensitive to 1 Gm. The ambient temperature during these studies ranged from a mean minimum of 20.3 ± 2.2° C. to a mean maximum of 26.0 ± 2.7° C. The subjects were at bed rest during the periods of observations.

Total body potassium was determined by the $^{42}K$ isotope dilution method of Smith and Waterlow.[5] The exchangeable pool was determined from the specific activity of urine K at approximately four-hour intervals from 24 to 48 hours after intramuscular injection of 1 $\mu c$ per kilogram of body weight. The total exchangeable K values reported are a mean of five to six estimates of pool size in each study. In order to test the reliability of indirectly computed concentrations of insensible potassium loss, direct estimates of the concentration of dermal potassium losses were made. Potassium-free filter papers, 20.8 cm.$^2$ in area, were placed on the forehead, chest, back, arm, thigh, and foot. A total area of 125 cm.$^2$ was covered. The skin was cleansed with deionized water and air dried before the filter was secured in place with a mineral-free plastic barrier. After eight hours the filter paper was removed. Dermal losses were estimated by changes in filter paper weight. Potassium was extracted from the paper with deionized water and estimated by flame photometry.[3]

## RESULTS

The data on diet, fecal, and urine analyses for nitrogen, potassium, and sodium are given in Table I. "Retention" expresses the difference between ingestion and fecal plus urinary output. The data from balances have also been computed in relationship to body weight of the

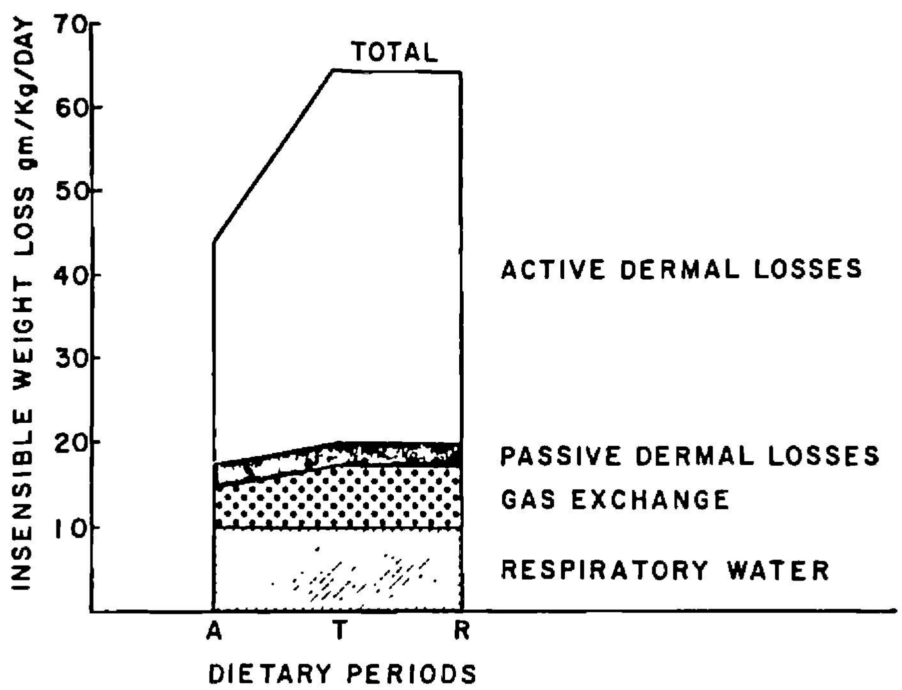


Fig. 1. Analyses of the nature of insensible weight loss. The derivations of estimates of respiratory water loss, passive dermal loss, and weight loss due to gas exchange are given in the text. The active dermal loss accounts for most of the total insensible water loss and virtually all of the changes in insensible weight loss at admission (*A*), during therapy (*T*), and at recovery (*R*).

individual subjects (Table II). In this table "growth" expresses the estimated change of body composition. During the admission period (A) the children were in negative sodium and nitrogen balance and in positive potassium balance. During the therapeutic (T) period sodium and nitrogen "retention" was evident. Potassium "retention" did not vary significantly during the study. Total body exchangeable potassium was found to increase by 5 mEq. per kilogram during the observation of the A period. The values for exchangeable K are given in Table III.

Insensible weight loss (IWL) is recorded in Table I. This was less than 400 Gm. per day in the catabolic (A) period and had doubled by the end of the therapeutic period (T). The subdivisions of insensible weight loss are indicated in Fig. 1.

There was an average respiratory water loss of 10 ml. per kilogram per day. Values for the passive diffusion of water through skin are those published by Berenson and Burch[7] (75 ml. per square meter per day). The remaining dermal loss is classified as insensible although at times perspiration was visible. Insensible dermal water loss is 59 per cent of insensible weight loss in A and 67 per cent in T and R periods. The direct estimate of dermal loss under plastic barriers demonstrated rates of 0.38 ± 0.07 and 1.02 ± 0.34 Gm. per 125 cm.$^2$ per 8 hours (M. ± S.E.) in periods A and R, respectively. The potassium concentration varied with the rate of collected dermal losses (Fig. 2).

Fecal weights averaged 205 ± 34, 117 ± 9, and 89 ± 7

**Table II.** Corrected balance for dermal losses and growth retention of potassium, sodium, and nitrogen

| | *Admission (A)* | | *Therapy (T)* | | | *Recovery* |
|---|---|---|---|---|---|---|
| | $A_1$ (26)* | $A_{2\text{-}3}$ (19) | $T_1$ (54) | $T_2$ (56) | $T_{3\text{-}5}$ (34) | R (47) |
| Potassium (mEq./day) | | | | | | |
| Ingestion | 6.96 | 7.00 | 7.59 | 8.23 | 7.12 | 5.97 |
| "Retention" | 1.56 | 1.26 | 2.14 | 2.40 | 2.03 | 2.00 |
| Fecal | 1.29 | 1.22 | 0.67 | 0.43 | 0.54 | 0.41 |
| Urinary | 4.11 | 4.52 | 4.78 | 5.40 | 4.55 | 3.56 |
| Insensible† | 0.73 | 0.73 | 1.69 | 1.85 | 1.64 | 1.72 |
| Total continuing losses | 6.13 | 6.47 | 7.14 | 7.68 | 6.73 | 5.69 |
| Growth | 0.83 | 0.53 | 0.45 | 0.55 | 0.39 | 0.28 |
| Sodium (mEq./Kg./day) | | | | | | |
| Ingestion | 3.11 | 3.33 | 3.92 | 4.30 | 4.54 | 4.20 |
| "Retention" | −0.37 | −0.07 | 0.70 | 1.60 | 1.21 | 1.28 |
| Fecal | 1.04 | 0.74 | 0.37 | 0.27 | 0.24 | 0.18 |
| Urinary | 2.44 | 2.66 | 2.85 | 2.43 | 3.09 | 2.74 |
| Insensible‡ | 0.86 | 0.86 | 1.26 | 1.37 | 1.22 | 1.27 |
| Total continuing losses | 4.34 | 4.26 | 4.48 | 4.07 | 4.55 | 4.19 |
| Growth | −1.23 | −0.93 | −0.56 | 0.23 | −0.01 | 0.01 |
| Nitrogen (gm./Kg./day) | | | | | | |
| Ingestion | 0.12 | 0.12 | 0.53 | 0.55 | 0.48 | 0.31 |
| "Retention" | −0.01 | 0.01 | 0.21 | 0.17 | 0.15 | 0.08 |
| Fecal | 0.05 | 0.05 | 0.07 | 0.06 | 0.06 | 0.05 |
| Urinary | 0.08 | 0.08 | 0.25 | 0.32 | 0.27 | 0.18 |
| Insensible§ | 0.04 | 0.04 | 0.05 | 0.06 | 0.05 | 0.05 |
| Total continuing losses | 0.17 | 0.17 | 0.37 | 0.44 | 0.38 | 0.28 |
| Growth | −0.05 | −0.05 | 0.16 | 0.11 | 0.10 | 0.03 |

*Number of observations.
†K: 16.7 and 26.4 mEq./Kg. IWL in *A* and *T*, respectively.
‡Na: 19.6 mEq./Kg. IWL.
§N: 0.84 Gm./Kg. IWL.

Gm. per day ( ± S.E.) in the A, T, and R periods, respectively. The mean daily fecal weight in period A is significantly greater than that of the T or R periods. Fecal potassium loss averaged ( ± S.E.) 11.6 ± 1.5, 6.0 ± 0.5, and 5.2 ± 0.7 mEq. per day in the A, T, and R periods. A significant correlation exists between fecal potassium loss and daily fecal mass. The computed slope is not different in the three periods and a mean potassium concentration of 36 to 42 mEq. of K per kilogram of feces was indicated by these observations. Fecal sodium concentration was much more variable, averaging 46 ± 5 mEq. per kilogram in the A period and 8 ± 8 mEq. per kilogram in the R period (M. ± S.D.).

Urine volumes varied according to the dietary periods. Mean daily volumes were 602 ± 242, 792 ± 261, and 469 ± 135, (ml. ± S.D.) in the A, T, and R periods, respectively. Each of these mean values is significantly different from the others.

## DISCUSSION

**Insensible losses and growth requirements.** McCance and co-workers[8] have summarized the previous reports on the balance of nitrogen and potassium in children during treatment of PCM. The universal finding has been an avid "retention" of potassium and nitrogen. We are in quantitative agreement with the previous observations (Table I) except for the reduction of N "retention" in the R period, a period much later in the course of rehabilitation than those reported from previous studies. All of these "retentions" are in excess of the reasonable increase in body composition expected during recovery. As an example, the "retention" of potassium was between 1.8 and 2.2 mEq. per kilogram per day during the therapeutic period. At 100 days of recuperation, this would mean that total body K exceeded 200 mEq. per kilogram. This is physiologically impossible. Gamble[9] believed that the excess retentions

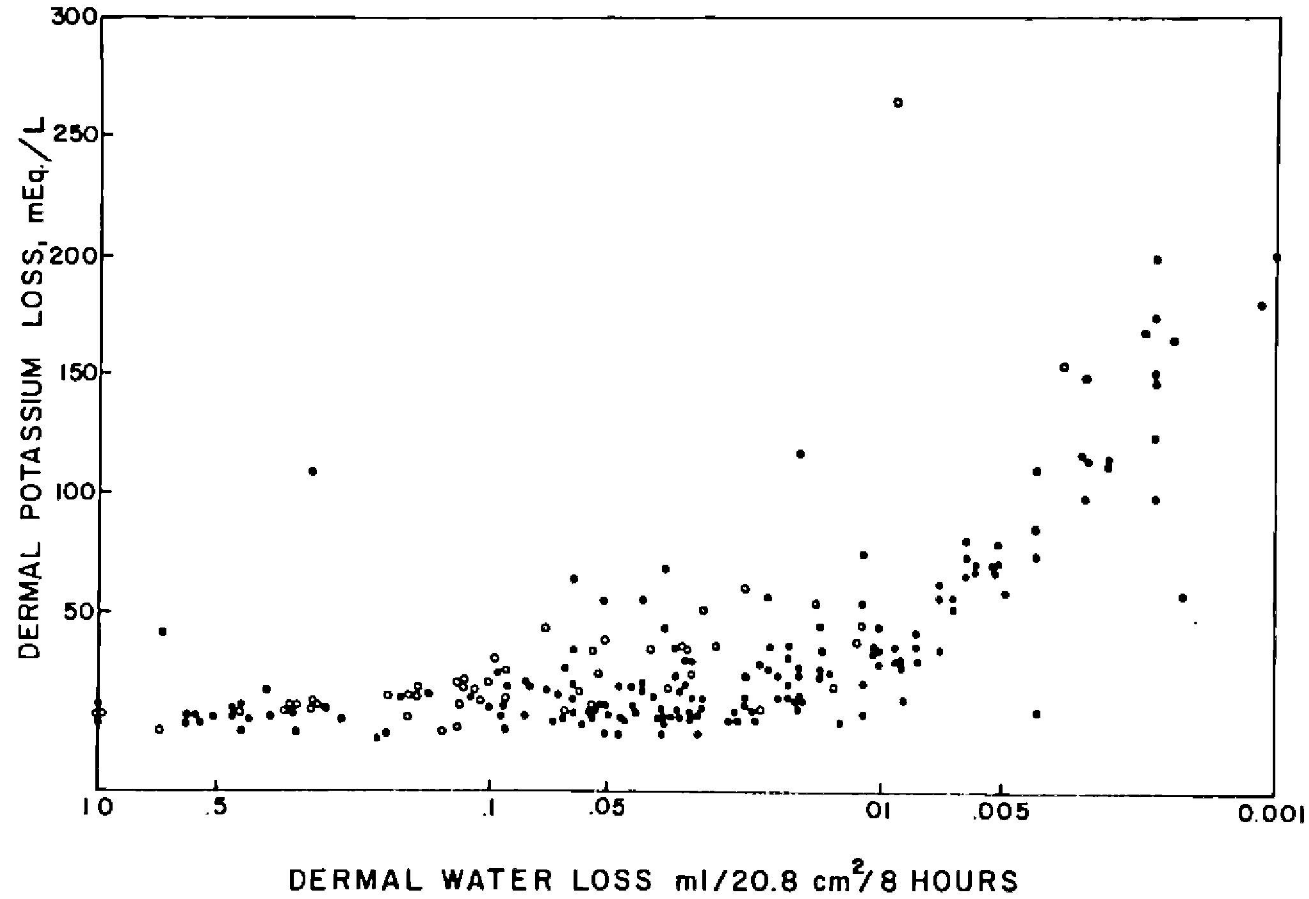


**Fig. 2.** Direct estimate of potassium concentration in dermal water losses. Determinations during the *A* diet period are in closed circles, those during the *R* period are in open circles. The insensible water loss is plotted against potassium concentration.

**Table III.** Total body composition of potassium, sodium, and nitrogen

| | *Patient* | *Days* | $A_1$ | $A_{2\text{-}3}$ | *R* |
|---|---|---|---|---|---|
| Potassium (mEq./Kg.) | | | | | |
| (determined by $K^{42}$ exchange) | 226 | 9 | 11.5 | 22.0 | |
| | 225 | 9 | 12.5 | 16.4 | |
| | 221 | 7 | 17.1 | 21.0 | |
| | 220 | 6 | 22.2 | 28.6 | |
| | 227 | 7 | 19.1 | 19.2 | |
| | Mean | 7.6 | 16.4 | 21.5 | 46.0[11] |
| Sodium (mEq./Kg.) | | | 110[13] | | 60[14] |
| Nitrogen (Gm./Kg.) | | | 10[12] | | 15.3 |

beyond reasonable changes in body composition were dermal losses and introduced a correction based upon estimated changes in body composition. Isaksson and fellow investigators,[10] using isotope dilution techniques to define actual changes in body composition, have shown that the difference between "retention" and change in body composition is due to the dermal loss of electrolyte and N.

We have computed the average daily dermal losses of potassium, nitrogen, and sodium by the difference between total "retention" and the change in body composition (growth) during the same period (Table III). Body composition of potassium was estimated experimentally at admission and in the $A_{2\text{-}3}$ period. The normal value of 46 mEq. per kilogram was used for total body K at recovery.[11] Calculation of initial total body N is based upon the K:N ratio of 1.6 observed by Garrow and associates[12]; the final total body N is based upon the normal K:N ratio of 3 present at recovery. In order to estimate total body Na at the time of admission we have used the value of 110 mEq. per kilogram observed by Halliday[13] in the child who died of PCM. Normal total body Na is estimated as 60 mEq. per kilogram, based upon children of the same size, as reviewed by Widdowson and Dicker-

**Table IV.** Water balance (ml./Kg./day)

| Period | Admission (A) | | Therapy (T) | | Recovery (R) | |
|---|---|---|---|---|---|---|
| | Mean | Range[(a)] | Mean | Range | Mean | Range |
| Fecal | 23 | ( 0-50) | 12 | ( 0-24) | 7 | ( 4-10) |
| Insensible (uncorrected) | 44 | (36-52) | 65 | (55-75) | 65 | (56-74) |
| Urine | 67 | (40-94) | 79 | (53-105) | 36 | (26-46) |
| Total continuing losses | 134 | (72-196) | 156 | (108-204) | 108 | (86-130) |
| Water of oxidation | | | | | | |
| (mean ± 1 S.D.) | −10 | | −15 | | −13 | |
| Growth retention* | 0 | | +2 | | +1 | |
| Total water requirement | 124 | (62-186) | 143 | (95-191) | 96 | (74-118) |

*Based on average daily weight changes.

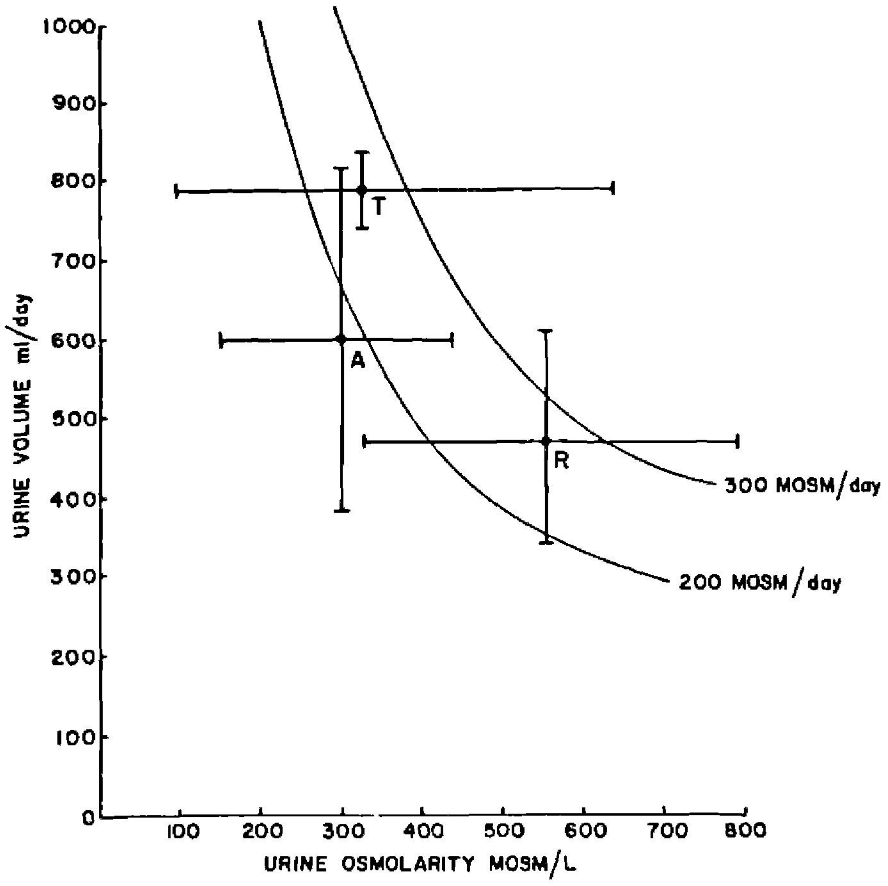


Fig. 3. The relationship between urine osmolar concentration and volume in three different dietary periods, admission (*A*), therapy (*T*), and at recovery (*R*). The osmolar relationship with urine volume as predicted by Gamble and Butler[25] is indicated as a basis for comparison.

son.[14] Because insensible weight loss (IWL) can be measured in clinical practice, we have related dermal losses of Na, K, and N to it. There is a technical error inherent in such a denominator because of the presence of respiratory water loss, passive dermal water loss, and weight loss due to gas exchange within the total IWL (see Fig. 1). These components, however, are relatively fixed and the major changes in insensible weight loss are those associated with active dermal water loss. Therefore, the IWL is a reasonable basis for predicting dermal nutrient loss at the clinical level.

The relationship between dermal loss and IWL reveals that a mean excretion of 16.7 and 26.4 mEq. per kilogram of potassium occurred during the A and T periods, respectively. Mean nitrogen loss was 1 Gm. per kilogram of IWL, and sodium loss averaged 19.6 mEq. per kilogram of IWL. The insensible losses can be identified by the use of these factors and the observed IWL in order to identify growth requirements (Table II).

The results of direct determinations of dermal potassium loss are presented for comparison in Fig. 2. At a moderate rate of dermal water loss, 0.01 to 0.1 Gm. per 20.8 $cm^2$ per 8 hours of sweat, the average K concentration is 23 ± 2 mEq. per liter (M ± S.E.). By using the data of Swanson and Iob[15] on dermal electrolyte loss in infants and the measurements of insensible weight loss by Levine and associates,[16] values comparable to those of our study are obtained: K, 23 mEq. per kilogram of IWL; Na, 10 mEq. per kilogram of IWL.

Gomez and associates[17] first described the increased postprandial perspiration of the child recovering from edematous malnutrition as a characteristic of the "nutritional recovery syndrome." The causes for this increased dermal water loss such as fever, exercise, and a hot environment can be excluded. Ashworth[18] and Brooke and Ashworth[19] have studied an alternative mechanism for the postprandial increase in heat loss in children recovering from edematous malnutrition. They documented that during recovery an excessive increase in oxygen consumption occurs following meals.

**Fecal losses.** Gomez and associates[17] indicated that diarrhea was present in more than 90 per cent of the children with PCM studied by their group. In our study, fecal losses are increased at admission (A) period (Tables I and IV). Diarrhea did not occur in the F period when recovered children were in a nonedematous catabolic state. The fecal losses must, therefore, reflect an adapta-

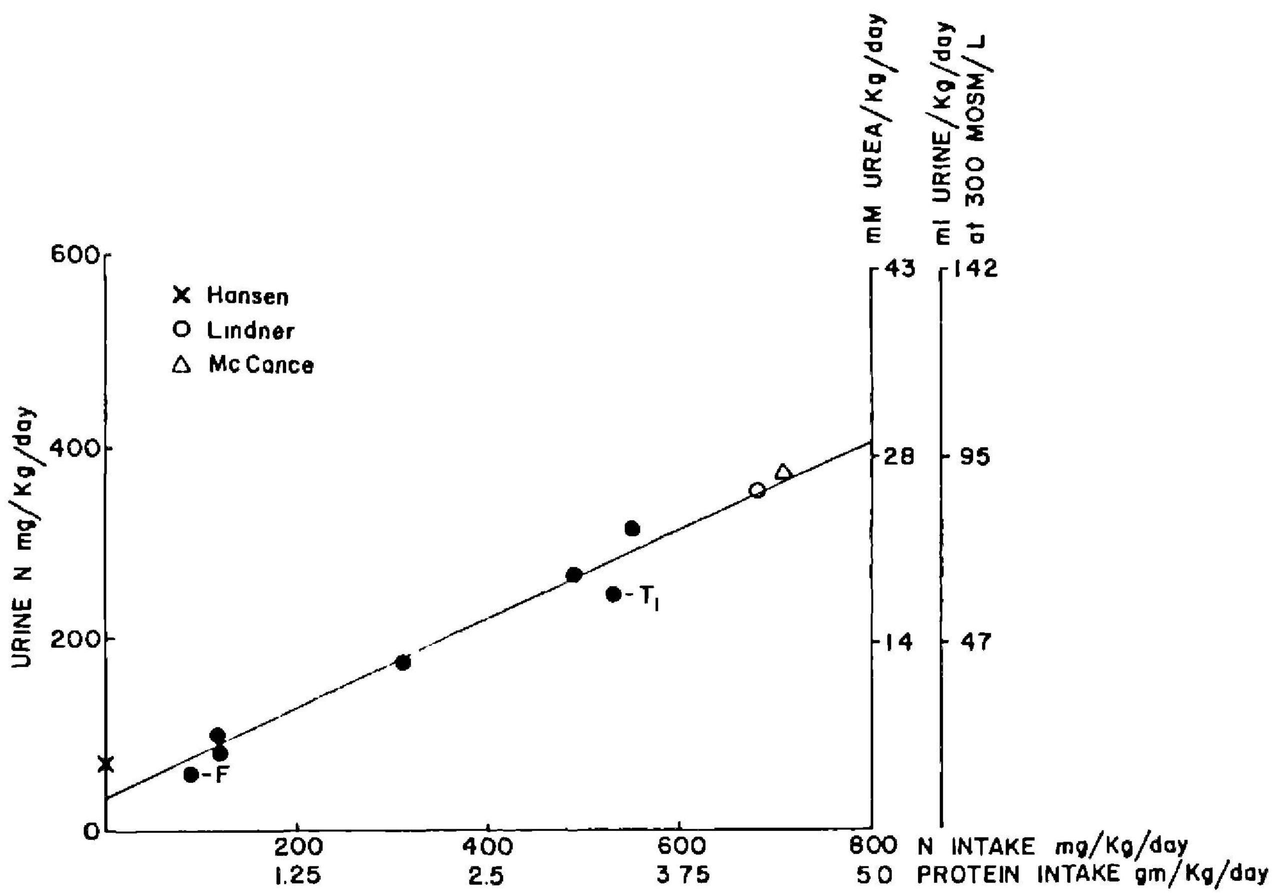


**Fig. 4.** The relationship between nitrogen and protein nitrogen intake and excretion of urinary nitrogen. The data from three studies and the obligatory volume are indicated. The relationship is described by the following equation: Urine N (mg./Kg./day) = 36 + dietary N (mg./Kg./day) × 0.47 (±0.03) R = 0.99.

**Table V.** Renal solute load

| | *Admission (A)* | | *Therapy (T)* | | *Recovery (R)* | |
|---|---|---|---|---|---|---|
| | *Mean* | *Range** | *Mean* | *Range* | *Mean* | *Range* |
| Inorganic cation (mOsm./L.) | 135 | (69-199) | 95 | (0-225) | 195 | (107-283) |
| Inorganic anion, est. | 135 | (69-199) | 95 | (0-226) | 195 | (107-283) |
| Urea nitrogen (mOsm./L., est.) | 29 | (19-39) | 140 | (98-182) | 175 | (124-226) |
| Total (mOsm./L.) | 299 | (157-437) | 330 | (98-632) | 565 | (338-792) |
| Urine volume (ml./day) | 602 | (360-844) | 792 | (531-1053) | 469 | (334-604) |
| Total (mOsm./day) | 180 | | 260 | | 325 | |
| Total (mOsm./Kg./day) | 20 | | 26 | | 25 | |

*The range is described by mean ± S.D.

tion present in the edematous state which is unrelated to the catabolic state *per se*.

**Renal losses.** Alterations in renal function have been documented in the malnourished child.[20-24] Reductions in glomerular filtration rate, renal blood flow, and maximum concentrating ability are present. In our investigation, evidences of the last are reflected in the increased urine volumes of the A and T periods. To explore this alteration in renal water loss, we have computed the renal solute excretion of our patients (Table V). The total osmolar excretion averaged 180, 260, and 325 mOsm. per day in the A, T, and R periods (300, 325, and 690 mOsm. per liter of urine, respectively). We have visualized the relationship between urine volume and osmolar excretion according to the coordinates of Gamble and Butler[25] in Fig. 3. Because of the loss of concentrating ability in PCM, urine volume becomes a function of solute load. This is clear in Fig. 3; urine volume increased by 20 ml. per kilogram per day after the protein intake was advanced to 3 Gm. per kilogram per day in the T period. The resulting threefold increase in urinary nitrogen, the Folin[26] effect (Table V), is associated with increased renal water loss in the form of a solute diuresis (free water clearance: −0.04, −0.11, and −0.49 c.c. per minute in periods A, T and R). The child with PCM is in the same position as the infant with immature renal function subjected to a high solute load.[23] To emphasize this relationship we have presented diagrammatically the data on protein intake, nitrogen excretion, and obligatory renal water losses (Fig. 4).

**Table VI.** Summary of average total requirements during recovery from PCM with a review of comparable published data

| | Admission (A) | | | Therapy (T) | | | | At full recovery (R) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | Range | Hansen and Jenkinson[29] | Mean | Range | Linder and group[30] | McCance and group[8] | Mean | Range | F | Macy[35] |
| Water (ml./Kg./day) | 124 | ( 62-186) | — | 143 | ( 95-191) | — | — | 96 | ( 74-118) | — | 70 |
| Potassium (mEq./Kg./day) | 7.0 | (5.0-9.0) | 6.8 | 7.7 | (5.7-9.7) | 5.7* | 10* | 6.0 | (2.7-9.3) | 4.4 | 5.9 |
| Sodium (mEq./Kg./day) | 3.2* | (1.4-5.0) | 4.5 | 4.2 | (2.2-6.4) | 3.5* | 2.2* | 4.2 | (2.9-5.5) | 4.2 | 4.3 |
| Protein (Gm./Kg./day) | 0.8* | (0.6-1.0) | 1.0* | 3.3 | (1.3-4.3) | 4.3 | 4.5 | 2.0* | (1.1-2.9) | 0.8* | 2.7 |

*At these levels of intake there was no significant growth retention, hence these values do not include the growth requirements.

Urinary sodium excretion exceeded the gastrointestinal absorption of the ion in the A period. The paradox of reduced renal Na retention when serum Na concentrations are reduced (serum Na, 132 ± 1 mEq. per liter in A vs. 136 ± 1 mEq. per liter in R) is difficult to explain. Evidence that this is a renal adaptation of the edematous state is offered by the observation on sodium excretion in the F period when recovered children who were receiving the same low level of protein retained sodium.

It is now common practice to supply oral potassium supplements during PCM therapy.[1] Urinary K excretion was high through all three dietary periods. The resulting increased urinary K must be recognized as another contributor to the solute diuresis.

**Deficit retentions.** Alleyne and fellow workers[27] have investigated the anatomic distribution of potassium deficits in PCM. Muscle, liver, and brain share in the loss of potassium. In a previous report[3] we demonstrated that, despite correction of serum K concentrations, no increase in muscle K concentrations occurred in these subjects during the A period. In unpublished observations, we found that liver K concentrations were also unchanged by the K supplements given during the A period. Garrow[28] has studied brain K content in PCM and recorded that brain K concentration increased from 50 to 120 mEq. per kilogram at complete recovery. It is logical to believe that the change in total body K observed in the A period (Table III) occurred in brain. The accumulation of potassium by brain during the A period emphasizes the necessity for including this deficit requirement in the calculation of dietary recommendations.

**Therapeutic implications.** At admission, the child with PCM is in a catabolic state which impairs the physician's attempts at rehabilitation. This is not an adaptation secondary to low protein intake, as evidenced by the normal physiologic response of recovered children in the F period when they are fed the identical A period diet. Diarrhea is an almost universal feature of PCM and contributes to salt and water losses during refeeding. The same physiologic considerations concerning limits of renal solute load for the newborn infant apply to these patients in the A and T periods. The circulatory system is labile in these children; Wharton and co-workers[31] have clearly indicated the danger of high salt loads which cause expansion of blood volume and frequent heart failure. The increased dermal salt and water losses during the nutritional recovery syndrome are added as the stigmas of the edematous state fade. These factors justify the development of specific recommendations concerning nutrient requirements for the rehabilitation of the child with PCM.

Hansen and Jenkinson[29] studied electrolyte balance in children on protein-free diets for the first two to six days following admission. The continuing losses of these children are virtually identical to those of our subjects in the A period. The continuing losses in period A can be viewed as the minimal requirement necessary to prevent negative balance during periods of reduced oral intake or intravenous therapy.

**Therapeutic diet.** At the most practical level, the implications of these requirements can be related to the common practice of using whole cow's milk for nutritional rehabilitation.[1] In order to receive 100 cal. per kilogram per day,* milk intake must reach 150 ml. per kilogram per day, which also provides an intake of protein of 5.4 Gm. per kilogram per day. These data (Fig. 4) allow us to predict that this level of nitrogen intake would require a urine volume averaging 140 ml. per kilogram per day, which leaves little water for the insensible requirement of 65 ml. per kilogram per day or fecal requirement of an additional 12 ml. per kilogram per

*This figure is chosen for the purpose of discussion. In practice, much higher caloric intakes are commonly administered.[17,18]

day. This level of K intake, 5.4 mEq. per kilogram per day, falls short of the continuing loss during the A and T periods (Table II) and does not satisfy the deficit requirement at admission. The sodium intake of 3.3 mEq. per kilogram per day is not high enough to induce Na retention and make heart failure likely.

Human milk or one of the commercial substitutes, if offered at the same caloric intake, would provide about 2 Gm. of protein per kilogram per day. This intake would provide inadequate protein to exceed the continuing loss of 2.6 Gm. per kilogram per day of protein. The continuing water losses would be exceeded by 30 ml. per kilogram per day, a figure within the range of requirements in Table VI. The K requirement would be three times that provided in such a formula, and the level of sodium intake would be analogous to that in the study by McCance and co-investigators.[8] On a low sodium formula, the renal K losses could be increased to five times that contained in human milk.

The ideal diet should offer at least 3.5 Gm. of protein per 150 ml. and 100 calories, a K content not less than 8 mEq., and a Na content not more than 4 mEq. per kilogram of body weight per day. A liter would provide 23 Gm. of protein, 660 calories, at least 58 mEq. of K, and less than 30 mEq. of Na. This requirement could simply be achieved by a dilution of two parts of whole cow's milk with one part of a 15 per cent dextrimaltose solution containing 1.5 per cent KCl or 110 mEq. of K per liter. Sodium intake on such a diet would be 2.2 mEq. per kilogram per day, a value at the lower limit of the range given in Table VI. The remainder of the specifications would have been met by such a dilution of whole cow's milk. An additional advantage would be a reduced lactose load.[32]

If the child with PCM is committed to the catabolic state because of vomiting or other clinical conditions which prevent adequate oral or nasogastric feeding, the observations made in the A period of our study and made by Hansen and Jenkinson[29] on a protein-free diet can provide the basis for the estimation of temporary maintenace water and electrolyte requirements. In order to compensate for average continuing losses, an oral or intravenous solution of 55 mEq. of K and 25 mEq. of Na can be infused with 5 per cent dextrose at 120 ml. per kilogram per day. The presence of antecedent deficits greater than those of our study patients or continuing excessive loss through diarrhea and vomiting will require modifications of this electrolyte formula. These variations are reflected in the range of requirements indicated in Table VI. This solution contains a large quantity of potassium and should not be administered to the anuric child; neither should it be administered more rapidly than 5 ml. per kilogram per hour. By monitoring serum K concentrations hyperkalemia can be prevented.

Several groups[17, 33, 34] have practiced a gradual induction of nutritional rehabilitation with a delay of up to two weeks before a full therapeutic diet is offered. In the present investigations, the protocol called for a delayed institution of the therapeutic diet. The results have been better (mortality rate less than 5 per cent) with this diet than in a sister hospital where whole cow's milk diet was administered to patients with similar cases of PCM from the day of admission. This experience leads us to reinforce the recommendation that the full therapeutic diet be achieved only after several stepwise increments during the first week of hospitalization. As an example, on the first two days of hospitalization, the child with PCM should receive 100 ml. per kilogram per day of oral maintenance fluid and 50 ml. per kilogram per day of the modified milk. On the third and fourth day, 50 ml. per kilogram per day of the oral maintenance fluid and 100 ml. per kilogram per day of the modified milk can be given. On the fifth day, the modified milk can be increased to 125 ml. per kilogram per day with 25 ml. per kilogram per day of the electrolyte solution. Only on the sixth and seventh days does the child receive all of his fluid from the therapeutic diet. Significant gastrointestinal disturbances are an indication for a slower rate of increase in diet.

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