Prognostic Criteria of Severe Protein Malnutrition

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THROUGH ignorance and poverty many African mothers feed their infants and older children on diets consisting almost entirely of maize. Consequently clinical evidence of protein malnutrition (kwashiorkor, sindrome policarencial infantil, distrofia da farinacei) is common in this group of the population. Advanced cases are characterized by nutritional edema and acute nutritional dermatosis, and these patients usually die within days or weeks if left untreated.

Depending on the selection of cases and the methods of treatment the death rate in protein malnutrition ranges from less than 10 per cent in some centers to over 50 per cent in others.[1,2] At Baragwanath Hospital, the mortality in advanced protein malnutrition was 40 per cent when treatment consisted almost entirely in the administration of skimmed milk.[3] It dropped to 20 per cent when intravenous electrolyte therapy was added for the patients showing clinical evidence of dehydration.

During the past three years the mortality in protein malnutrition at this hospital has remained unchanged at 20 per cent. This study was undertaken in an attempt to determine the clinical signs which distinguish the patients who die of the disease from those who survive on our present treatment. An ability to identify such "bad risk" patients on admission to the hospital might enable us to make further progress in the treatment of this very common condition.

MATERIAL AND METHODS

The investigation was based on clinical and certain biochemical data obtained from 100 children admitted to this hospital with the diagnosis of severe protein malnutrition during the winter of 1957. All children showed evidence of nutritional edema and/or acute nutritional dermatosis. The latter was encountered in the various stages of development described by Trowell *et al.*,[4] ranging from the earliest erythematous blotching of the skin which fades on pressure to exfoliating black "enamel paint" plaques with oozing raw surfaces. Patients who did not show evidence of either edema or acute dermatosis were excluded from this series. Fatalities occurring during the first 24 hours after admission to hospital were included, as were all those children suffering from associated debilitating illnesses. The birth date was known in all except three patients.

The clinical and biochemical data in this paper are those found on admission to the hospital unless the contrary is specifically stated. The clinical state of hydration of the patients was judged by the elasticity of a fold of skin raised over the anterior chest wall or the upper abdomen (at other sites edema may interfere with the test). Impaired elasticity, however slight, was interpreted as clinical evidence of dehydration, except in patients with extreme wasting, where looseness of the skin from loss of subcutaneous fat rendered the test valueless.

The body weight and height of the patients were compared with American averages,[5] because reliable data for African children were not available.

Serum sodium and potassium concentrations were measured by flame photometry on venous blood which was withdrawn from the internal jugular vein before the patients had received any intravenous therapy. Blood sugar levels were determined by the "true sugar" colorimetric method.[6] Rectal swabs were taken

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from all patients and were plated on SS agar and desoxycholate citrate agar. The chests were x-rayed, except in a few patients who died shortly after admission to the hospital.

All children were treated with an acidified milk formula containing 3 per cent protein, 4.5 per cent lactose, and 1.3 per cent fat. Milk feeds totaled 150 to 200 ml per kg of body weight per day. Each child was given 50 mg of ascorbic acid per day, but no other vitamin supplements.

Intravenous fluid therapy was used only for dehydrated patients. It was guided, wherever possible, by serum sodium and potassium values. When this information was not available, patients were given our standard electrolyte solution which contains 38 meq/l of sodium, 27 meq/l of potassium, and 65 meq/l of chloride in 5 per cent of invert sugar. During the first 24 hours of intravenous therapy, the patients usually received 200–220 ml per kg of body weight of this solution. In children with acidotic respiration, this was preceded by an intravenous infusion of 0.166 N molar sodium lactate in quantities of 60 ml per kg of body weight. Milk feeds were usually started within 12 hours of commencement of intravenous therapy. During the first 24 hours, feeds amounted to 60–90 ml per kg of body weight. On subsequent days the feeds were increased to about 200 ml per kg of body weight per day, while the volume of the intravenous fluids was correspondingly reduced. No patient in this series received intravenous plasma or blood.

CLINICAL AND BIOCHEMICAL FINDINGS

There were 20 deaths in this series, of which 7 occurred within the first 24 hours of admission to hospital. Clinical and biochemical data of the fatal cases compare with those of the survivors as follows:

Age

Figure 1 shows that the age distribution of the fatal cases did not differ significantly from that of the survivors. Therefore, the patients' age gave no indication of the prognosis.

Growth and Development

Retarded growth was observed in nearly all cases (Fig. 1), the height of the patients being from 2 to 4 inches below the American average; but the degree of retardation was similar in fatal cases and survivors and could not, therefore, be considered to be of prognostic significance.

Figure 1 shows that the body weight of all the patients was below average, despite the fact that 89 of them were edematous. In 15 (75 per cent) of the fatal cases, the weight was

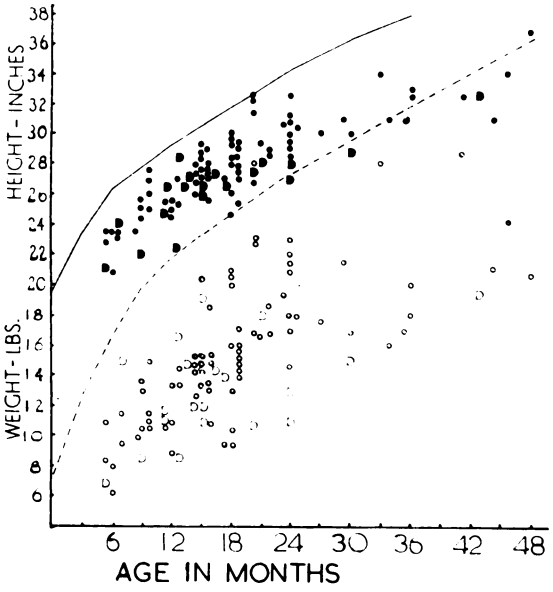

Fig. 1. Height (black dots) and weight (white dots) of patients in relation to age. Fatalities are represented by semicircles. The unbroken line represents the average height of American children, and the broken line the average weight. Five patients, older than 4 years, are not shown.

50 per cent or more below average, whereas this degree of wasting was found in only 24 (30 per cent) of the nonfatal cases. It would appear, therefore, that the prognosis of protein malnutrition is unfavorable if the condition is associated with marked loss of body weight.

Dermatosis

An acute nutritional dermatosis, with or without exfoliation, was a bad prognostic omen. It was encountered in 15 (75 per cent) of the fatal cases but in only 38 (48 per cent) of children who recovered. A dermatosis of the chronic type, consisting of "burnished," "crackled,"

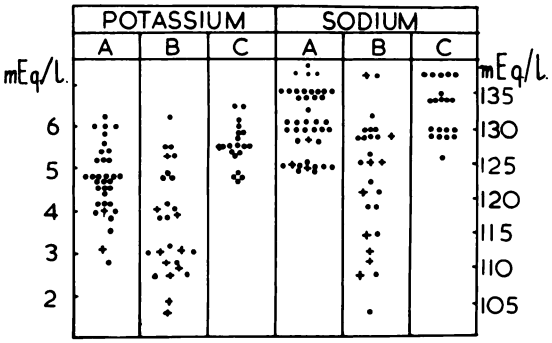

Fig. 2. Serum potassium and sodium values in 3 groups of children: *A*, patients without evidence of dehydration; *B*, patients with clinical evidence of dehydration; *C*, normal controls. Fatalities are represented by crosses.

TABLE I

Incidence of Dehydration and Nutritional Edema in 100 Malnourished African Children

Condition of patient	No. edematous	No. nonedematous	Total no. patients
Clinically dehydrated	25 (8)[a]	10 (5)	35 (13)
Not dehydrated	57 (5)	1 (0)	58 (5)
State of hydration uncertain	7 (2)	—	7 (2)
TOTAL	89 (15)	11 (5)	100 (20)

[a] Numbers in parentheses are fatal cases.

"mosaic," and "sooty" skin areas,[4] was present in 3 (15 per cent) of the fatal cases and in 30 (38 per cent) of the survivors, and therefore its presence did not influence the prognosis adversely. Two (10 per cent) of the fatal cases and 12 (15 per cent) of the surviving cases showed no evidence of a dermatosis.

Edema, Clinical Dehydration, and Abnormal Electrolyte Levels

The influence of nutritional edema and clinical dehydration on the mortality is shown in Table I. Of 57 children who were edematous, but showed no evidence of dehydration, only 5 (8.8 per cent) died. Edema was associated with dehydration in 25 patients, and 8 (32 per cent) of these died.

In 7 patients, of whom 2 died, extreme wasting and loss of subcutaneous fat made it impossible to assess the clinical state of hydration by skin elasticity. Among the remaining 93 children, there were 35 with varying degrees of dehydration, and 13 (37 per cent) of these died. In 58 patients, clinical dehydration could not be detected, and of these only 5 (9 per cent) died.

Low serum sodium and potassium levels were common in dehydrated patients (Fig. 2) and were associated with a high mortality, despite intravenous replacement therapy.

Liver Enlargement

An enlargement of the liver to $1^1/_2$ inches (2 fingerbreadths) or more below the costal margin in the right midclavicular line was more common in children who succumbed to the disease: it was found in 9 (45 per cent) of the fatal cases and in only 11 (14 per cent) of the survivors. Postmortem examinations were carried out on only 2 of these cases, and both had grossly fatty livers which resembled putty in color and consistency.

Hypothermia

A body temperature below 95°F was a grave prognostic sign. Two patients arrived at the hospital with temperatures of 87°F and 87.7°F, respectively, and both died within a few hours. Three others developed hypothermia in the hospital. Of these, 2 died and 1 recovered after the temperature had fallen to 88.8°F. Serum potassium levels were investigated in only 3 of the hypothermic children and were found to be 3.2, 2.9, and 2.6 meq/l, respectively.

Clouding of Consciousness

Occasionally death was preceded by drowsiness or sudden stupor. In one such case in this series, the blood sugar level was 13 mg/100 ml shortly before death, and in another fatal case a level of 44 mg/100 ml was obtained.

Infection

The death rate was not influenced by the presence of certain infections. *Shigella* organisms were isolated from 10 children, with only one death, and *Salmonella* organisms were found in 5 children, all of whom survived. Active pulmonary tuberculosis was encountered in 10 children. One of these, a child with severe tuberculous bronchopneumonia, died

within a few hours of arrival at the hospital. The remaining 9 patients survived.

DISCUSSION

This survey has shown that, with the therapy in current use at this hospital, the prognosis in protein malnutrition is grave in the presence of one or more of the following signs: severe wasting, acute dermatosis, dehydration and low sodium and potassium levels, marked enlargement of the liver, and hypothermia. Drowsiness and stupor may indicate hypoglycemic attacks which are commonly fatal.

No prognostic significance could be attached to age, retardation of growth, chronic dermatosis, and associated shigellosis, salmonellosis, or pulmonary tuberculosis.

The "atrophic" type of malnutrition was stated by Altmann[7] to have a serious prognosis, and this was confirmed in the present investigation. Starvation is known to be fatal in many adults when 50 per cent of the initial body weight has been lost, and the greatest weight loss recorded in a mammal was in a dog which had lost 65 per cent of its initial body weight at death.[8]

An acute nutritional dermatosis is always an indication of an advanced degree of protein malnutrition.[4] In this part of Africa such skin lesions are found exclusively in patients who have been consuming a faulty diet containing mainly maize, the local staple food. We have of late treated these patients with plasma infusions, and the results appear to be favorable. The acute dermatosis is not seen in children who develop protein malnutrition while subsisting on a diet of wheat products or oatmeal. In the absence of a nutritional dermatosis the prognosis is better, a fact observed previously by Altmann.[7]

Despite the fact that the water content of the skin of malnourished dehydrated patients is higher than that of normal controls,[9] it is useful to retain the concept of "dehydration" in clinical practice. In this series, evidence of clinical dehydration was commonly associated with marked lowering of the serum electrolyte levels. Furthermore, the mortality of the dehydrated children was nearly 40 per cent, and thus 4 times higher than the death rate of well-nourished dehydrated children at this hospital. It has been stated that the unsatisfactory response of malnourished dehydrated children to intravenous fluid therapy is due to renal dysfunction.[10]

Hypothermia revealed itself as a highly fatal complication of protein malnutrition. It is not caused by climatic conditions. It is often a manifestation of severe hypopotassemia, which causes muscular atony or paralysis, resulting in impaired production of body heat.

Marked enlargement of the liver was much more common in fatal cases, an observation already made by Altmann.[7] Parasitic infestations, which could cause such enlargement, are extremely rare in this part of Africa. At autopsy the enlarged liver is usually found to be the seat of extensive fatty changes. Unexpected death, preceded by a brief period of stupor, is particularly common in this type of patient. In one case included in this series, and in a number of others,[11] we have been able to prove that this mode of death, with which other workers are well acquainted,[4a] is due to severe hypoglycemia.

SUMMARY

Observations on 100 children with manifestations of severe protein malnutrition show that a fatal outcome is more likely in the presence of one or more of the following factors: (1) advanced emaciation, in this instance a body weight 50 per cent or more below average; (2) acute nutritional dermatosis; (3) clinically detectable dehydration, which in the patients in this series was often associated with markedly lowered serum sodium and potassium levels; (4) marked enlargement of the liver; and (5) hypothermia.

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