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Protein-Calorie Malnutrition in Children

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In the less developed countries of the world, infant mortality is two to four times higher than in those which are technically highly developed. The discrepancy in mortality of children 1 to 4 years of age, however, is tenfold greater, from twenty to forty or more times higher in the less developed countries. The principal factor underlying this higher mortality in preschool children, particularly in the second year of life, is the nutritional inadequacy of the supplements to breast milk and of the diet provided in the months immediately after weaning (1).

Nearly all children among the lower socioeconomic groups of less developed countries are breast-fed, and develop fairly normally in the first months of life Neonatal mortality is high, however, because of unskilled attendance at childbirth and unsanitary conditions. There is also a very high mortality among those few infants who are not breast-fed. For the majority of young children in these countries it is only in the second half of the first year that the quantity of breast milk becomes increasingly inadequate as a protein source; unfortunately, it is frequently supplemented only by watery cereal gruels and infusions which fail to supply needed protein. Depending upon the culture and circumstances, weaning may occur at this time, or be postponed until late in the second year of life

Regardless of when weaning finally occurs, the substitute for breast milk is very often the same diluted low protein, high carbohydrate preparation. Even where animal milk is available and an accepted infant food, its cost is likely to prevent its use in adequate quantities. In these circumstances growth and development are likely to become slowed and resistance to infection decreased. Depending upon the time of weaning this begins in the first or second years of life and continues for several years.

Eventually, the child is able to demand solid food for himself, prejudices against allowing him to share the family diet are

outgrown and his protein requirement per unit of body weight decreases. It is only then that normal growth, development, and resistance to infection are again encountered. In the meantime, marked irreversible retardation in growth and development has occurred and many children have died. Recent studies have suggested that the developmental retardation may be psychomotor as well as physical (2, 3).

Types of Protein-Calorie Malnutrition

If, as sometimes happens, carbohydrate is forced upon the child in amounts adequate to meet his Calorie requirements, with very little protein supplied by the diet, the clinical signs and symptoms of protein deficiency will develop with very little loss of subcutaneous fat or growth retardation. The child may actually be fat and blubbery at the time when he develops edema, skin and hair changes, apathy, anorexia, and other characteristics of severe protein deficiency or kwashiorkor. This is the so-called sugar-baby type of kwashiorkor (4).

On the other hand, the child may experience months or years of grossly inadequate diets, fail to grow and develop and lose both adipose tissue and lean body mass, until an abrupt decrease in the proportion of protein to Calories results in the signs of kwashiorkor being superimposed. It is most common for kwashiorkor to be superimposed on some degree of prolonged partial starvation and this combination is commonly referred to as marasmic kwashiorkor. It also often happens that the child is given a diet after weaning so grossly inadequate that the consequences are slow starvation and the development of nutritional marasmus. For reasons which will be mentioned later, the child with marasmus suffers profound loss of all adipose tissue and much of his muscle mass without developing the signs and symptoms of protein malnutrition *per se*.

The Institute of Nutrition of Central America and Panama (INCAP) has attempted to classify cases of protein-Calorie malnutrition according to the way in which kwashiorkor and marasmus are combined in a given child (5). Figure 1 illustrates the way in which a young child losing weight for age due to an inadequate diet may progress from N, the normal state, to M, a state of marasmus. If the diet is calorically adequate but grossly deficient in protein, the child fails to gain in weight for age, and develops kwashiorkor along the line N–K before the deficit has become marked. The dotted line "a" indicates that with successful therapy such a child, upon regaining normal weight for height, would not make up all of the weight lost for his age.

The clinical histories suggested by lines "b", "c" and "d" are more common among preschool children in areas where kwashiorkor is common. The child illustrated by dotted line "b", after a quantitatively inadequate diet for some months, has entered a period when protein was even more inadequate relative to Calories, perhaps due to the discontinuance of a relatively small amount of breast milk. Then, just as his status was beginning to improve a little, something additional happened to worsen his protein intake relative to caloric need, perhaps an episode of diarrhea or severe upper respiratory infection.

In the case of the child illustrated by the dotted line "c," the development of measles after many months of a quantitatively inadequate diet could well account for the abrupt subsequent development of kwashiorkor. The child portrayed by the dotted line "d" was obviously already severely marasmatic at the time when something caused his status to deteriorate in the direction of kwashiorkor. A very common cause of this type of line would be an episode of diarrhea in a severely undernourished child followed by partial recovery, recurrence of diarrhea and finally death with the signs and symptoms of kwashiorkor.

It is obvious that during recovery combinations of factors could cause the child's weight for age to follow any of these types of clinical course. Figure 2 is an attempt to classify the clinical states associated with the preceding combinations of Calorie and protein deficiency. For practical public health purposes, Dr. Frederico Gómez of Mexico has proposed the classification of malnourished preschool children on the basis of the degree of retardation in weight for age (6). Children with a deficit of more than 40 percent of normal weight for age during the first 3–4 years of life can be assumed, for public health purposes, to have severe malnutrition, and to require medical attention, usually hospitalization for their rehabilitation. Similarly, children with

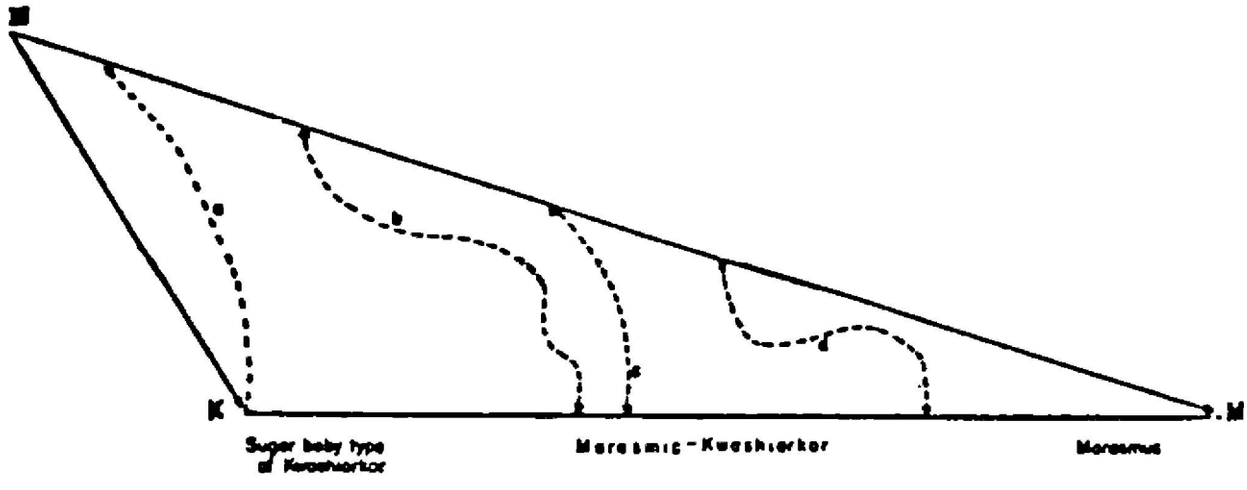

FIGURE 1.—Development of different types of protein malnutrition in children.

a deficit between 25 and 40 percent of normal weight for age will usually recover without hospitalization, providing they receive supplementary food and the mother is willing and able to follow instructions regarding their treatment. If edema is present, however, regardless of the degree of weight loss, the child must be considered to have kwashiorkor and should receive hospital treatment.

In the case of children with a weight deficit between 10 and 25 percent, and without edema, nutrition education of the mother will usually suffice to prevent further deterioration of the child's condition. If supplementary food is available for distribution to the less severely malnourished children, this group should receive it also. It is apparent from the diagram that pre-kwashiorkor and kwashiorkor may be superimposed on any degree of retardation in weight for age, that is, on any degree of chronic caloric deficiency.

The emphasis placed on infection in the preceding discussion is fully justified by clinical and field observations. Because of the unsanitary environment and greatly increased susceptibility to infection, young children in less developed areas have a high incidence of diarrhea, often three or four episodes per year (7). Respiratory infections are also more frequent and severe. These infections and the common contagious diseases of childhood precipitate kwashiorkor in malnourished children by decreasing appetite, causing a reduction in the protein content of the diet given by the parents or even the physician and increasing the metabolic loss of nitrogen. Giving strong purgatives to children with diarrhea further worsens their nutritional status.

Of the common contagious exanthemas measles is most often associated with the subsequent development of kwashiorkor (8, 9). Diarrhea occurs as a symptom in most cases of measles in malnourished children. Measles also results in the almost complete

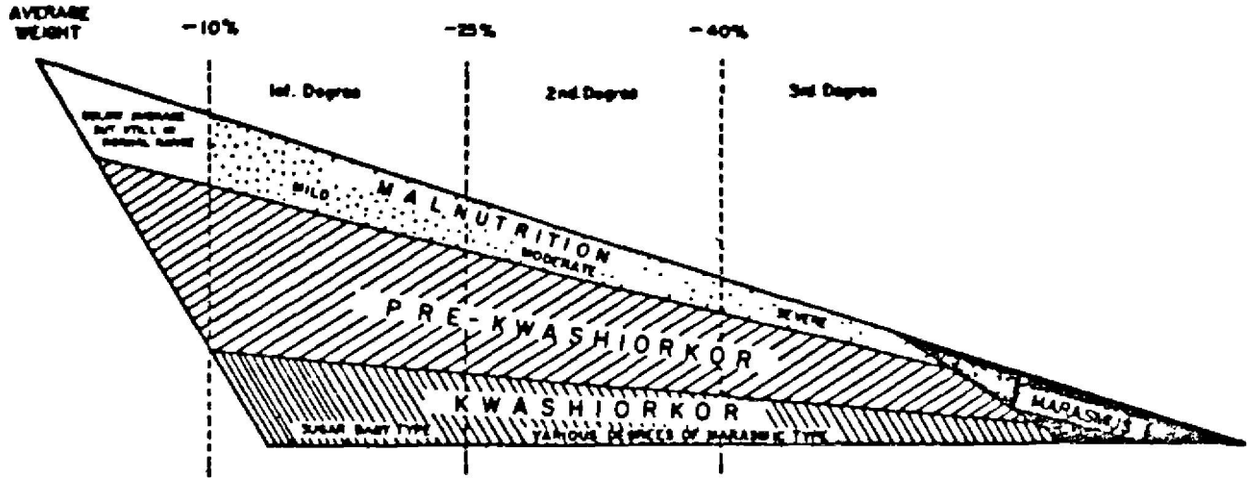

FIGURE 2.—Classification of different types of protein malnutrition in children.

withdrawal of solid food as well as a greatly increased excretion of nitrogen in the urine. There is widespread evidence that the majority of cases of kwashiorkor are precipitated by an infectious episode in a child whose diet, although grossly deficient, would not in itself have led to the clinical signs of protein deficiency (10).

Occasionally, some other cause of stress may be the precipitating factor. Dean has emphasized the frequency with which the abrupt physical separation of the child from its mother which occurs in Uganda acts in a closely similar way to infection in precipitating kwashiorkor (11).

Marasmus and kwashiorkor should be thought of as two independent clinical processes, epidemiologically related and frequently occurring together in the same child. Anything which will decrease the proportion of useful protein to Calories in the diet below a certain critical level will result in the appearance of the clinical signs of kwashiorkor, superimposed on whatever degree of Calorie malnutrition may be present. It is obvious that infectious disease will bring about just such an abrupt change through both its effect on food intake and on nitrogen loss.

The biochemical explanation advanced for the failure of starving children and adults to develop the signs of clinical protein deficiency is that they are using the amino acids from their muscles as a source of glucose produced by gluconeogenesis in the liver and for the synthesis of essential proteins. It is known that starvation as well as such causes of stress as trauma, infection, fear and anxiety stimulate the hypothalamus and through it ACTH secretion by the anterior pituitary (12). This in turn increases the output of 17-hydroxyglucocorticoid hormone by the adrenal cortex. This hormone causes the skeletal muscles to give up amino acids and stimulates amino acid uptake and use by the liver (13). In these circumstances, such fat stores as may be available, along with glucose, are used by the muscles as an energy source. A possible hypothesis is that if the stimulus to this mechanism is the need for glucose, it will be inhibited by a high carbohydrate-low protein diet, with the secondary effect that essential amino acids will not be made available from the muscles for protein synthesis.

Characteristics of Kwashiorkor

The characteristics of kwashiorkor have been extensively reviewed (5, 10, 14, 15). The salient features are as follows:

Clinical

The most constant feature is the appearance of edema, which may be mild and limited to the extremities, or of any degree of

severity up to generalized anasarca. Anorexia is so characteristic that some children must be tube-fed in order to initiate therapy successfully. Apathy is generally profound and the child, when aroused, is likely to be irritable. Diarrhea is almost always present to some degree.

The hair shows three types of alterations: in color, texture and implantation. It becomes dry, thin and brittle, with a tendency for curly hair to straighten. Dark hair becomes much lighter in color and may acquire a reddish tinge. The more severe the deficiency the lighter the color of the hair. When a child with mild protein deficiency develops kwashiorkor, and is then given a high protein therapeutic diet, bands may be seen in the hair reflecting this history. The name "flag sign" has been given to this phenomenon, first described by Dr. Peña Chavarria of Costa Rica (16) and illustrated in Figure 3. It is also usually possible to pull out clumps of hair easily and painlessly.

Skin lesions may be minimal or quite severe. The dermatosis of kwashiorkor is characterized by hyperkeratosis and hyperpigmentation with areas of desquamation and actual excoriation. It resembles closely the skin lesions of pellagra, but is not confined to areas exposed to the sunlight.

Hematology

The characteristic anemia of kwashiorkor appears to be a mild and normocytic, normochromic one. Associated with a hypoplastic bone marrow, however, the microcytic hypochromic anemia characteristic of iron deficiency may be superimposed, especially where hookworm infection is also present. A superimposed megaloblastic anemia associated with deficiency of one or more B-complex vitamins seems also to be equally common. A superimposed anemia presumably associated with vitamin E deficiency has also been described (17). Not surprisingly, the anemia found in kwashiorkor is of mixed origin.

Biochemistry

A low serum total protein concentration due to a decreased serum albumin is the most universally recognized biochemical change. There is also a tendency for the beta-globulin fraction to be decreased, and a relative rise in the alpha-2 globulin has been reported. Total alpha-amino nitrogen in plasma reflects a general lowering of most amino acids, particularly tryptophan, cystine, valine, tyrosine and methionine (18, 19). The rate of albumin synthesis is decreased and antibody formation inhibited (20, 21, 22). All the various lipid fractions which have been determined, including neutral fats, fatty acids, phospholipids and cholesterol, have been found to be low in the blood of children with kwashiorkor, but

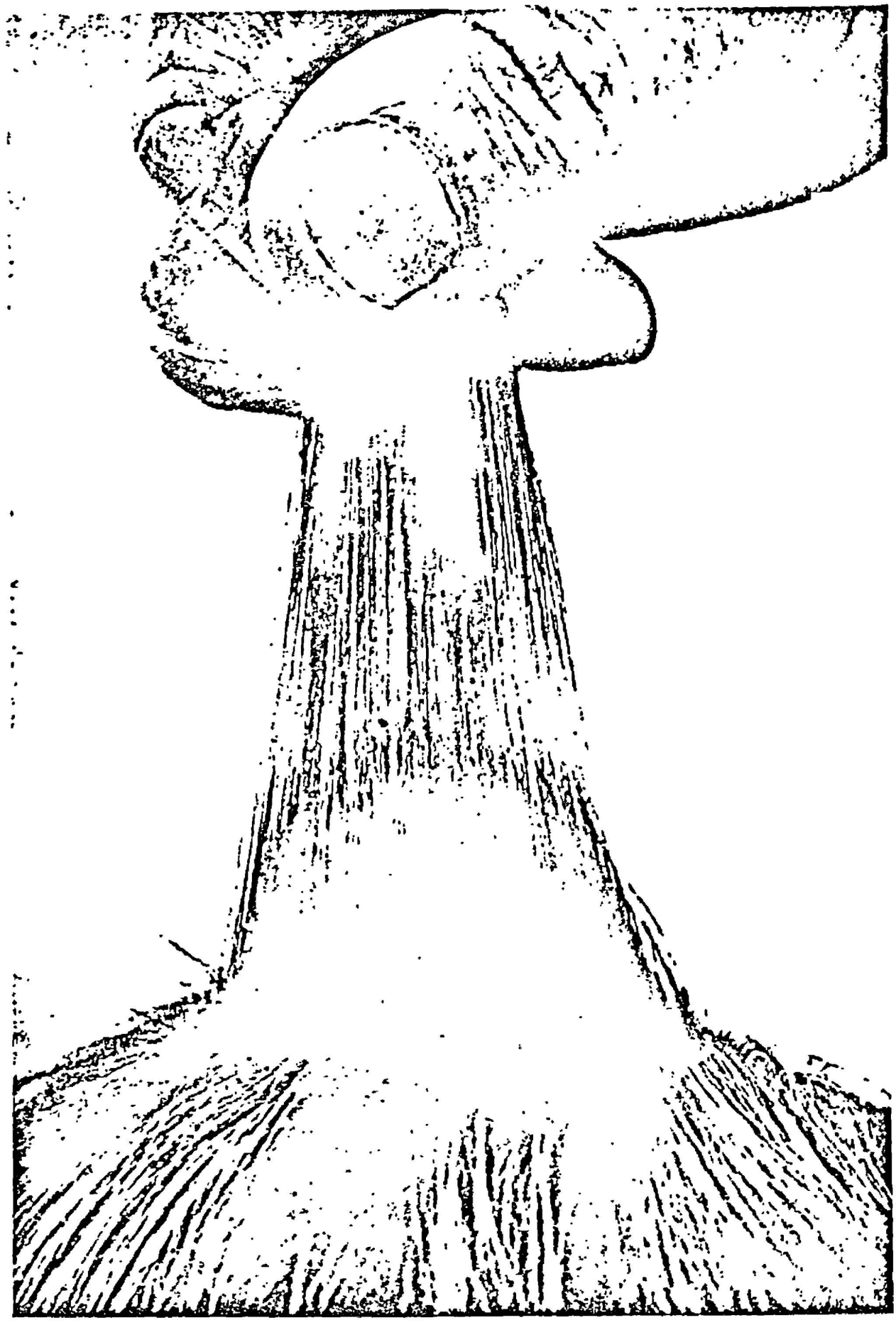

FIGURE 3.—"Flag sign," showing previous episode of protein malnutrition.

rise rapidly with treatment. The same is true for the fat-soluble vitamins A and E. There is evidence that vitamin A transport is impaired by the lack of carrier lipoprotein. Perhaps related to this, vitamin A intestinal absorption tests give a flat curve on admis-

sion, which is corrected by 3 to 5 days of protein therapy (23, 24). Glucose levels tend to be relatively low.

Major diagnostic features of kwashiorkor and indicators of recovery are the reduced levels of enzyme activity in blood plasma (18). Amylase, pseudocholinesterase, alkaline phosphatase, and carbonic anhydrase have been studied the most. There is also a decrease in the xanthine oxidase, cholinesterase, and D-amino acid oxidase activity in the liver. Most other liver enzymes are not affected, although alkaline phosphatase activity is generally increased.

A major biochemical characteristic of kwashiorkor is potassium depletion. Other electrolyte changes are secondary consequences of diarrhea. Magnesium deficiency has been stated to be responsible for some cases of tetany in kwashiorkor (25). Low plasma iron and copper levels are attributed primarily to a reduction in plasma protein (26).

Physiology

The heart is relatively small and increases rapidly in size with dietary treatment (27). Low electrocardiographic voltage and minor alterations in rhythm and the T-wave have been reported (28). Despite large amounts of fat in the liver, liver function appears to be essentially normal.

Altered gastrointestinal function is indicated by the increased volume of feces and poor absorption of fat and fat-soluble vitamins. A reduction in renal plasma flow has also been reported, associated with dehydration and diminished blood volume. Clearance of inulin and endogenous creatinine indicate a lowered glomerular filtration rate.

Particularly significant is the finding of Castellanos and Arroyave (29) of low 17-hydroxy- and 17-ketosteroid excretion in the urine, indicating a decrease in glucocorticoid activity. Since they find normal excretion of 17-hydroxysteroids in the urine of children with marasmus, these findings are compatible with the differences in plasma glucocorticoid levels in kwashiorkor and marasmus postulated above.

Diminished electroencephalographic voltage and excessively slow rhythmic activity have been reported to disappear as recovery progresses. Responses to standard psychomotor tests are greatly impaired.

Pathology

In kwashiorkor, the liver and the pancreas are the most seriously and constantly affected organs (30, 31). Small fat droplets generally appear first in the periportal area of the liver lobule and spread progressively toward the central vein. Eventually

large fat globules appear that displace the nuclei and other cell structures of almost every cell in the liver. There is an increase in the prominence of reticulin fibers, but no true cirrhosis.

In the pancreas there is a shrinkage of the acinar cells, a loss of zymogen granules, and atrophy of the basal pro-enzyme plate. Fibrosis may occur but is not a constant finding. The islet cells are not affected. Consistent anatomical lesions of the pituitary, adrenal, and kidney are not seen.

As is suggested by the clinical lesions, the skin shows atrophy of the epidermis with varying degrees of hyperkeratosis and parakeratosis. Skin appendages are markedly atrophic. The striated muscle shows signs of atrophy, presumably reflecting previous marasmus.

Treatment

Because of the diarrhea which is frequently associated with kwashiorkor and the potassium loss characteristic of severe protein deficiency, rehydration and restoration of electrolyte balance may be the first consideration in the treatment of acute kwashiorkor. The basic treatment of kwashiorkor, however, is dietary (32). Initiation of cure depends almost entirely on supplying orally a relatively high protein and Calorie intake, but other deficiencies will soon become limiting if the diet is not balanced with regard to essential nutrients.

By the second day of therapy, the child should be receiving at least 2 gm of protein of good biologic value per kilogram of body weight per day, and soon thereafter 3 to 5 gm cow's milk—fresh, canned, or reconstituted from dry powder—is usually the most convenient source of protein, but vegetable mixtures combined to provide a reasonably good concentration and quality of protein are also effective.

Because infection is so commonly present as a serious and even fatal complication, even without febrile response and other pathognomonic signs, penicillin or other antibiotics should probably be given routinely from the time the child with kwashiorkor is first seen. The diet based on milk or vegetable mixture should be progressively supplemented with other foods, so that by the second or third week of treatment the child is receiving a complete and varied diet, including eggs, meat, cereals, vegetables, and fruit. Caloric intake should be high enough to insure good protein utilization. While this varies with the age of the child, an intake of at least 150 Calories per kilogram of body weight is generally desirable. Because of the rapid regeneration of hemoglobin, care must be taken to include an adequate amount of dietary or supplementary iron.

The two measures most important in reducing the time necessary for recovery are insuring that the child actually consumes the quantities of protein recommended, and minimizing cross-infections acquired in the hospital. The former requires closer nursing attention than is common in the hospitals where kwashiorkor is likely to be treated. The latter requires a maximum of physical separation of patients rather than the overcrowding so characteristic of hospitals likely to have a burden of kwashiorkor cases. The child with marasmus also needs attention to complicating infections, but, most importantly, must receive a high protein and Calorie intake for many months.

Concluding Remarks

I have outlined the various forms of protein-Calorie malnutrition as they are commonly seen in technically underdeveloped countries throughout the world. There will, of course, be many local variations due to differences in the age and nature of weaning and to the simultaneous presence of other deficiencies. For example, both kwashiorkor and marasmus may have superimposed upon them the xerophthalmia and keratomalacia characteristic of vitamin A deficiency. The way in which either iron deficiency or nutritional megaloblastic anemia may be superimposed on the mild anemia of protein deficiency has already been mentioned.

The basic principles elaborated are believed to apply to all countries in which these conditions occur. Kwashiorkor and marasmus are common in most of the countries of the Far East but do not seem to be quite as serious public health problems as in most of Latin America, Africa, the Middle East, and India.

Ignorance, poverty, and lack of availability of suitable food are all factors; their relative importance varies with the circumstances of each population. It is hoped that this conference will provide first-hand information on kwashiorkor and marasmus, as they now occur in the countries of the Far East.

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