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PRINCIPLES OF TREATMENT AND PREVENTION OF SEVERE PROTEIN MALNUTRITION IN CHILDREN (KWASHIORKOR)*

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It is now generally recognized that kwashiorkor is the result of a severe deficiency of dietary protein at an age when the essential amino acids are required in relatively large quantities for growth. In most children developing kwashiorkor the protein intake is deficient, not only in quantity, but also in quality. Thus, the diets that are responsible for the syndrome usually contain protein that, due to its low biological value, is poorly utilized.

If protein deficiency occurs in children who are receiving an adequate or even excessive quantity of calories, as has been reported in Jamaica,[1] the resulting clinical picture is that of classic kwashiorkor. This form is characterized by edema, lesions of the skin, hair changes, apathy, anorexia, enlarged fatty liver, and low serum protein. These children also have abundant subcutaneous fat and recover rapidly with a high protein diet; when they loose their edema there is no wasting evident.

In the majority of the regions of the world in which kwashiorkor is found, however, children after weaning receive diets that are deficient not only in protein but also in calories. The clinical picture differs from that of classic kwashiorkor in that the children often show a considerable degree of tissue wasting, and the response to treatment is much slower. They are characterized by a reduction in statural growth and in weight, marked diminution or even absence of subcutaneous fat, and a much greater degree of muscular wasting; the liver, although it shows fatty change, is usually not increased in size. Since these children have a marasmic appearance when their edema is lost, this form of malnutrition is spoken of as marasmic kwashiorkor.

The diets of children developing kwashiorkor are not only low in protein, but are also deficient in other essential nutrients, particularly in the marasmic form of the disease. For this reason and also because their absorption is reduced,[2, 3] a deficiency of fat-soluble vitamins is a particularly common accompaniment of kwashiorkor.[4] Signs suggestive of B-complex vitamin and iron deficiencies are also frequently found associated.[5-7] Due largely to

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variations in the customary diet, the relative importance of these various vitamin and mineral deficiencies that complicate the clinical appearance vary greatly.

Our concept of the various types of kwashiorkor and their relationship to marasmus is presented graphically (FIGURE 1). This chart shows a continuous range of types between marasmus, which is due basically to a severe lack of food, but with a normal protein-to-calorie ratio, and kwashiorkor, which is basically produced by a deficiency of protein combined with almost any other

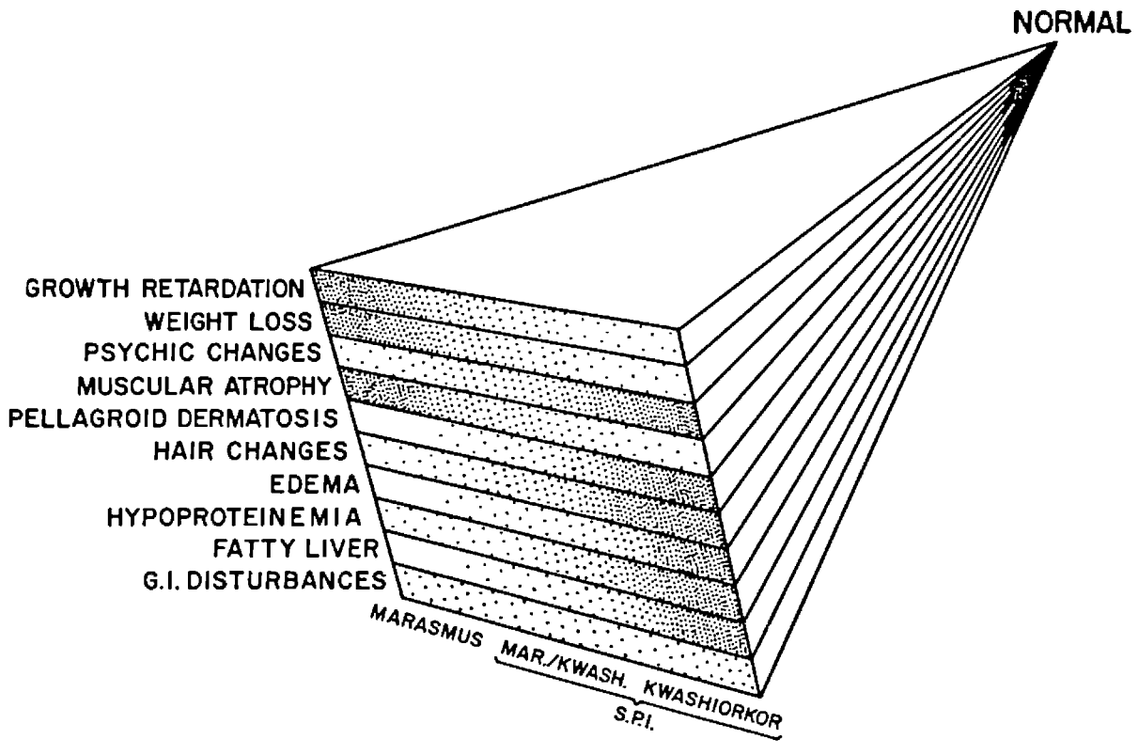

FIGURE 1. Schematic representation of the interrelation of kwashiorkor and marasmus. At the left of the pyramid base the intensity of the stippling suggests the frequency with which the signs and symptoms listed appear in marasmus. At the right the occurrence of the same signs and symptoms in "classic" kwashiorkor are portrayed. In between are all combinations between these two extremes. The term *síndrome pluricarencial de la infancia* (S.P.I.) is used in Latin America to cover both "classic" and marasmic kwashiorkor; the great majority of the cases are of the latter type. The severity of the signs and symptoms is indicated by the distance from the apex. Reproduced by permission of the Institute of Nutrition of Central America and Panama (INCAP), Guatemala City, Guatemala, C. A.

degree of caloric intake. The body of the pyramid indicates the degree of severity, which is also a continuous transition from the well-nourished child (represented by the apex) to the most severe form of any of the types of malnutrition mentioned. In the intermediate part of the pyramid are represented the cases of prekwashiorkor and the other mild forms of protein deficiency which occur in a high percentage of children in underdeveloped areas. The closer to the apex of this pyramid, the less pronounced become the signs and symptoms and the narrower becomes the degree of differentiation between the various types.

This diagram is not merely theoretical, since the cases encountered under field conditions show every conceivable variation in signs and symptoms as represented in the diagram. It should be emphasized, however, that when

the extreme of partial or complete starvation is reached (marasmus), the signs of specific protein deficiency are no more manifest than are those of other specific nutrients, all of which are, of course, grossly deficient.

Although many cases gradually develop kwashiorkor due to the inadequacy of the diet alone, in most cases other factors operate as contributory or precipitating causes.[8] These help to determine the relatively small number of children who will develop the clinical syndrome in a population in which the majority are fed on inadequate diets. Among these factors, acute and chronic infections are important. In Central America, at least, the most common of the infections that serve to precipitate kwashiorkor is diarrhea of infectious origin. Other infections that are likely to act similarly are malaria and the contagious diseases of childhood. Socioeconomic factors such as the death of a parent, abandonment, or loss of work by the head of the family are also frequently involved.

We have recently observed a child who developed diarrhea while on repeated metabolic balance trials with milk feeding. With moderate diarrhea of short duration, this child showed a markedly reduced absorption of nitrogen and a negative balance.[8] Diarrhea not only limits the absorption of nitrogen, but also considerably increases its excretion, so that the net retention drops. The situation is made even worse by the common and unfortunate practice of withdrawing solid food from the child who develops diarrhea and substituting starch gruels. Educational efforts should be aimed, not only at the correction of diets given to children with diarrhea, but also at avoiding the dangerous practice of using laxatives or purgatives in the treatment.

Principles of Dietary Treatment

There is no doubt that the administration of a diet rich in proteins of high nutritive value is an effective treatment of kwashiorkor.[9-12] The majority of authors recommend the use of either half-skim or skim milk, particularly because of the proportionately high content of protein of such food. Some consider also that the lower fat content, as compared with that of whole milk, is beneficial because the capacity of the sick child to digest fat is seriously impaired. However, Gómez obtained equally satisfactory results using whole milk,[13] and Dean has recently recommended the addition of 30 to 50 gm. of fat to diets for the treatment of kwashiorkor.[14] The conclusion that a normal amount of fat in the diet is not harmful is strongly supported by the work of Holt in children with diarrhea from other causes.[15] Although both our own studies[16] and those of Gómez[17] demonstrate that fat is poorly absorbed during the first few days of treatment, the amount absorbed is proportional to the quantity of fat ingested, and the child soon recovers most of his ability to use dietary fat.

The profound anorexia that is characteristic of children with kwashiorkor and the reduced activity of the digestive enzymes[18-20] make it necessary to begin treatment with relatively small amounts of protein, generally in the range of 2 gm./kg. The prompt recovery of enzyme activity[20] and returning appetite make it possible to increase this rapidly to values in the range of

5 gm./kg. at the end of the first week or during the second. This intake can later be increased still further in order to correct the protein depletion as rapidly as possible. Nitrogen balance studies indicate clearly that, within a broad range, nitrogen retention in kwashiorkor does increase with a rising intake, although the percentage of nitrogen retained out of the total absorbed will drop, of course, as the protein intake increases[21, 22] or as nitrogen stores are gradually repleted.[16]

It is very important that the caloric intake be sufficiently high to avoid the use of protein by the body to supply energy and, as mentioned previously, this is the rationale behind the use of added fat in therapeutic diets.[14] There have been reports of the poor tolerance of sugars, especially sucrose and lactose[23, 24] and, for this reason, the use of bananas as a calorie source has been suggested. There is no objection to the use of bananas, since they are well tolerated and are an excellent calorie source. The reports of intolerance to sugars are based, however, only on clinical observations and need further study. As soon as appetite and tolerance permit, the child should be given fruit juices, green and yellow vegetables, meat, eggs, and other foods necessary to give the balanced diet required for complete recovery.

Vitamin and Mineral Supplements

With an initial diet of milk alone, there occurs a prompt recovery from all of the signs and symptoms of kwashiorkor, including those that might be attributed to a lack of vitamins of the B complex. It is not only unnecessary to use therapeutic vitamin preparations; the use of such preparations may actually be harmful. In the experience of Magalhaes Carvalho,[25] for example, the administration of high doses of vitamin B complex increases the mortality from kwashiorkor, a phenomenon that Frontali[26] explains as due to the greater demand for labile methyl groups for the transformation of nicotinic acid into trigonellin. The greater deficiency of methyl groups may in turn aggravate the liver damage.

There is no demonstrated benefit from the use of either folic acid or vitamin B_{12}, since the anemia, although frequently macrocytic, responds satisfactorily to milk alone, unless there exists a marked iron deficiency.[3] Despite the fact that the serum levels of vitamin C tend to be low, at least in Central American cases,[27] the deficiency does not reach the point where obvious clinical signs are observed, and it is a simple matter to add fruit juice and other natural ascorbic acid sources to the diet.

We do consider justifiable, however, the addition of moderate doses of vitamin A from the beginning of treatment, especially when half-skim or skim milk is used. Partially defatted milk does not correct the deficiency of vitamin A, which has been amply confirmed by studies of the vitamin A content of blood serum and liver tissue,[3] and which may even be so severe as to cause ocular lesions.

The majority of children show only a mild anemia, which is usually normocytic or slightly macrocytic in character. Even in uncomplicated cases, however, there is a tendency for the serum iron values to be low and for micro-

cytosis to develop with dietary treatment unless supplementary iron is given. Accordingly, the relatively early addition of iron to help fill depleted iron stores is recommended.

Other Therapeutic Procedures

(1) *Blood transfusions.* In general, blood transfusions have no advantages over proper diet therapy alone. Although blood transfusions for the treatment of kwashiorkor were introduced many years ago[28] and are still used and recommended today,[29] our own experience demonstrates that they are rarely necessary. It is still desirable to employ them, however, in the occasional very severe case where the child is in imminent danger of death due to collapse and shock and in cases with very severe anemia.

(2) *Plasma and protein hydrolyzates.* The parenteral administration of plasma or proprietary protein hydrolyzates, which has often been recommended to combat the hypoproteinemia of kwashiorkor, does not appear to be justified. There is abundant evidence from the protein balance studies of Gómez[22] and Holemans and Lambrechts,[21] as well as from our own unpublished work, that protein given orally is sufficiently absorbed and well retained even at the beginning of treatment.

(3) *Antibiotics and chemotherapy.* In general, we favor the routine use of an antibiotic such as penicillin during the first 8 to 10 days of hospitalization, since secondary infections are very frequent. Bronchopneumonia is particularly common and may be asymptomatic and therefore not recognized clinically. This complication is found at autopsy to be a frequent cause of death during the early days of hospitalization.[30, 31] When a secondary infection can be definitely diagnosed, it is important that the treatment be initiated promptly to avoid the stress which may interfere with or even prevent recovery. Similarly, malaria and amebiasis should be treated as soon as diagnosed.

Intestinal parasitism due to helminths ordinarily should not be treated until recovery is well advanced. The child with the kwashiorkor syndrome is not well able to tolerate the type of treatment required for parasite eradication, and the presence of intestinal helminths does not appear to interfere significantly with recovery.

(4) *Electrolyte solutions.* Either in the immediate history of the child or during the first few days of hospitalization, diarrhea is an almost constant feature of the syndrome, and vomiting is frequent. Dehydration, therefore, is often severe, even in the presence of edema. This accentuates electrolyte imbalance. Potassium deficiency is likely to be particularly severe, since it is aggravated by both the diarrhea and vomiting as well as by the protein deficiency.[32-34]

Failure to correct electrolyte disturbances is now believed to be the most frequent cause of death during the first 48 to 72 hours of hospitalization,[31] and their correction should be one of the first therapeutic measures taken. In cases that are only moderately severe, the oral administration of appropriate electrolyte solutions gives good results, but in severe cases it is necessary to resort to parenteral administration. The problem of electrolyte therapy

has received particular attention in the work of Gómez *et al.*[32] and is discussed in more detail by Gómez elsewhere in this monograph.[35]

(5) *Enzymes and lipotropic substances.* While it is true that there is a marked deficiency in the action of duodenal enzymes at the time of admission, they recover very rapidly with the initiation of dietary treatment, as shown by Véghelyi[20] and confirmed by our own observations on the prompt return of the child's ability to absorb both the nitrogen and fat in either milk or vegetable mixtures. The use of special enzyme preparations appears, therefore, to be unnecessary.

The same can be said for the various preparations with lipotropic activity that have been used because of the frequency and severity of fatty infiltration of the liver;[36, 37] this disorder is promptly and completely corrected by the feeding of protein of high biological value.

Response to Amino Acid Mixtures

It would be helpful to know whether kwashiorkor is produced primarily by an over-all deficiency of protein or whether it is associated with imbalances in individual amino acids such as occur when the small amount of protein that the child receives is derived largely from a single food of vegetable origin (as is the case of Central American children developing kwashiorkor on a predominantly corn diet). The fact that occasional cases are encountered in which the child has received its protein from mother's milk, although in grossly inadequate quantities, suggests that it is not amino acid imbalance per se.

An important contribution made by the South African group[38, 39] has shown that a clear-cut improvement of all of the major signs of kwashiorkor can be brought about by vitamin-free casein or a mixture of synthetic amino acids. The improvement occurs not only in the anorexia, apathy, cutaneous lesions, and edema, but also in serum protein, and results in what they designate as a satisfactory "initiation of cure."

Our own experience with amino acid mixtures* is limited to a single individual to whom a mixture of 18 synthetic amino acids similar to that used by Hansen *et al.*[39] was given for a period of 18 days. This treatment resulted in the "initiation of cure" as defined by these workers, that is, the edema and skin lesions began to disappear relatively soon and serum protein increased. The child remained apathetic and anorexic, however, and there was not the same degree of recovery in serum amylase, and in the pseudocholinesterase previously observed in cases treated with either milk[12] or a vegetable protein mixture.[40] As will be seen in TABLE 1, there was a decrease in the serum levels of all of the vitamins except vitamin A, which apparently was mobilized from tissue stores.

It does not invalidate the concept that kwashiorkor is due to protein deficiency to emphasize that no experimental treatment that fails to provide the necessary vitamins can be expected to be successful for more than a relatively

* This work is being carried out in collaboration with Eugene E. Howe, from the Merck Sharp & Dohme Research Laboratories, Philadelphia, Pa., who prepared the amino acid mixture.

short initial period. All that we know of nutrition in general, and of vitamin metabolism in particular, indicates that under these circumstances vitamin deficiencies, if not limiting initially, will become so later as a result of inadequate intake, especially when body stores are depleted as in the case of kwashiorkor. For this reason, the objection that the results obtained with synthetic amino acid mixtures are limited only to an "initiation of cure" is meaningless.

The results show that protein administration must be the central point of any rational therapy even though appropriate amounts of all other nutrients should obviously be given for best therapeutic results. They also lend added emphasis to the administration of vitamins in "physiological" rather than so-called "therapeutic" doses. As these studies are continued, more information of fundamental value in guiding therapy will undoubtedly be obtained.

TABLE 1

BLOOD CONSTITUENTS AT ADMISSION WITH KWASHIORKOR AND FOLLOWING 18 DAYS TREATMENT WITH SYNTHETIC AMINO ACIDS (14-MONTH-OLD BOY)

Per 100 ml.*	On admission	After amino acid therapy	Per 100 ml.*	On admission	After amino acid therapy
Total protein (gm.)	4.12	5.73	Vitamin A (μg.)	6.4	21.0
B_1 in RBC (μg.)	8.8	4.8	Carotene (μg.)	1.0	3.0
Free B_2 (μg.)	0.0	0.0	Vitamin E (mg.)	0.04	0.02
Total B_2 (μg.)	1.61	1.25	Cholinesterase (U)†	0.21	0.46
B_2 in RBC (μg.)	24.6	17.2	Amylase (U)‡	6	0
Ascorbic acid (mg.)	0.22	0.10	Alk. phosphatase (mM/1/hr.)	5.85	3.70

* All determinations in serum except red-blood cell, thiamine, and riboflavin.
† Actually "pseudocholinesterase" measured in Michel units.
‡ Smith Roe units.

Dietary Measures for the Prevention of Kwashiorkor

(1) *Use of cow's milk.* There is no doubt that the consumption of adequate quantities of cow's milk following weaning will prevent kwashiorkor. Unfortunately, there are a number of factors that limit the consumption of cow's milk in areas where the kwashiorkor syndrome occurs. These factors are, principally, the inadequate production and high cost of milk. The insufficient production of milk is often due to poor animal management, nutritional deficiencies in the rations, poor control of ectoparasites and endoparasites, and inadequate facilities for the conservation and distribution of feedstuffs and of milk. In many regions these factors can be corrected and milk production greatly increased, but only through major long-term national efforts and considerable expense. In other regions the agricultural limitations may be such that the production of sufficient milk cannot be anticipated. Furthermore, under the circumstances of most underdeveloped areas, the permanent large-scale importation of milk is likely to be economically impracticable and undesirable.

The high cost of milk prevents its sufficient use by low-income families in

areas where kwashiorkor is endemic. The problem of safe handling, including storage and distribution in both the dairy and the home is another major obstruction to the use of fresh fluid milk. The use of powdered milk has a number of practical advantages, and efforts that have been made to set up milk-drying plants in underdeveloped areas, wherever justified by potential milk production, are to be commended.

It must also be recognized that in many regions there are cultural objections to the use of animal milk.[41] Often such milk is unfamiliar to the people. This difficulty is more easily overcome than an acquired fear of milk, a phenomenon based on unfavorable experience with contaminated, adulterated, and poorly preserved milk that has been responsible for producing diarrhea. All of these considerations suggest that, especially in the near future, complete reliance cannot be placed on milk as a practical means of preventing kwashiorkor in most regions of the world in which it is a serious problem, despite the fact that, from a nutritional point of view, milk is ideal.

(2) *Use of animal protein.* The extensive use of such other sources of animal protein as meat and eggs also involves the serious problems of insufficient production, high cost, and prejudice against their use for feeding small children. It has been suggested that fish, especially in the form of industrial preparations of fish flour or similar products, can be of great value in infant feeding. While such products can undoubtedly contribute to the solution of the problem in a number of areas, not all countries have sufficient fish to make industrial development practicable. Fish flours would also encounter the same resistance observed to the introduction of any new food, especially one that is radically different from that commonly consumed in the region.

(3) *Use of plant protein.* In view of the difficulty of solving the problem of protein malnutrition by the increased production and use of animal products alone, the consideration of plant sources of protein becomes imperative. The excellent monograph by Dean on *Plant Proteins in Child Feeding*[42] has stimulated active work on the problem in a number of regions, and recently the specialized agencies of the United Nations concerned with nutrition, WHO, FAO, and UNICEF,* have cooperated in promoting these developments.

The major difficulty in the use of vegetable proteins is the relatively poor biological value of proteins from single plant sources. There are also the potential problems of an excess of crude fiber, low digestibility, and the presence of toxic or interfering substances. There is the further possibility that processing can introduce toxicity or lower nutritive value. There are times when processing will be beneficial, particularly in making certain of the essential amino acids more available, but the conditions must be controlled.

Despite all of these problems, an increased use of local proteins of vegetable origin appears to be the most promising means of preventing protein malnutrition in many areas of the world, at least under the conditions that now prevail. Information as to the amino acid content and digestibility of vegetable protein sources, although very incomplete, is still sufficient to enable suitable

* World Health Organization, Food and Agriculture Organization, and the United Nations International Children's Emergency Fund.

combinations to be planned for chemical and microbiological analysis and for animal trials of their biological value. More precise information about amino acid requirements would help, however, in combining vegetable proteins to give mixtures whose net protein value is relatively good. Such vegetable protein combinations have the advantage not only of being relatively cheap, but also of fitting the habitual diet patterns of young children in the majority of regions in which kwashiorkor is a problem.

It would be desirable to devise a product that could be prepared in the home from local raw materials. This is scarcely practicable, since special knowledge and skill are required to combine vegetable proteins in the right proportions, and since many of the cheapest and best protein sources cannot be used directly for food without special processing. We believe, therefore, that vegetable protein mixtures designed for the prevention of kwashiorkor must be manufactured from low-cost ingredients within the agricultural resources of each region.

In planning vegetable protein mixtures, it is necessary to take into consideration the following 8 factors: (1) the amino acid content of the individual ingredients and the final product, (2) the possible presence of toxic or interfering factors, (3) the need for obtaining exact specifications for each of the components, (4) the necessity of avoiding processes that damage the quality of the protein, (5) the desirability of using products of local origin, (6) the fact that the final product must be inexpensive and easily preserved, (7) the requirement that it may be easily prepared in the home as an infant food by mothers of low-income families, and (8) the demand that it must not run counter to existing dietary habits and prejudices.

Even after all of these requisites seem to be met, the product should not be recommended for commercial production and mass consumption until the 4 following biological trials have been carried out: (1) the testing of the product for toxicity in at least 2 species of animals, (2) the demonstration of the biological value of its protein by animal growth studies, (3) the testing of its acceptability and effectiveness in children under careful observation, and (4) field trials completed in selected communities or small population groups.

Although the primary objective is to provide a supplementary source of protein of good quality, it is desirable that a vegetable protein mixture contain, also, adequate quantities of the vitamins and minerals that are likely to be lacking in the usual diet. INCAP has attempted to follow these principles and procedures in developing vegetable mixtures for the prevention of protein malnutrition in infants and young children in Central America. The work has resulted in a mixture that soon will be ready for field trials. It contains:

Components	Percentage
Dried corn *masa*	50
Sesame meal	35
Cottonseed press cake	9
Torula yeast	3
Kikuyu leaf meal	3

The specifications for each of these ingredients have been recently published.[40] *Masa* is the dough prepared from lime-treated corn that is usually made into flat cakes and cooked to make tortillas. It is the basic food of the rural and poor urban populations of Mexico and Central America and is dried and powdered to form one half of the mixture. The sesame and cottonseed press cake, which may both be produced locally in considerable quantities and at low cost as a by-product of oil extraction, are rich in protein of relatively good quality, and their amino acids help to complement those of corn.

Fresh young kikuyu grass is dried to produce a meal that provides the major

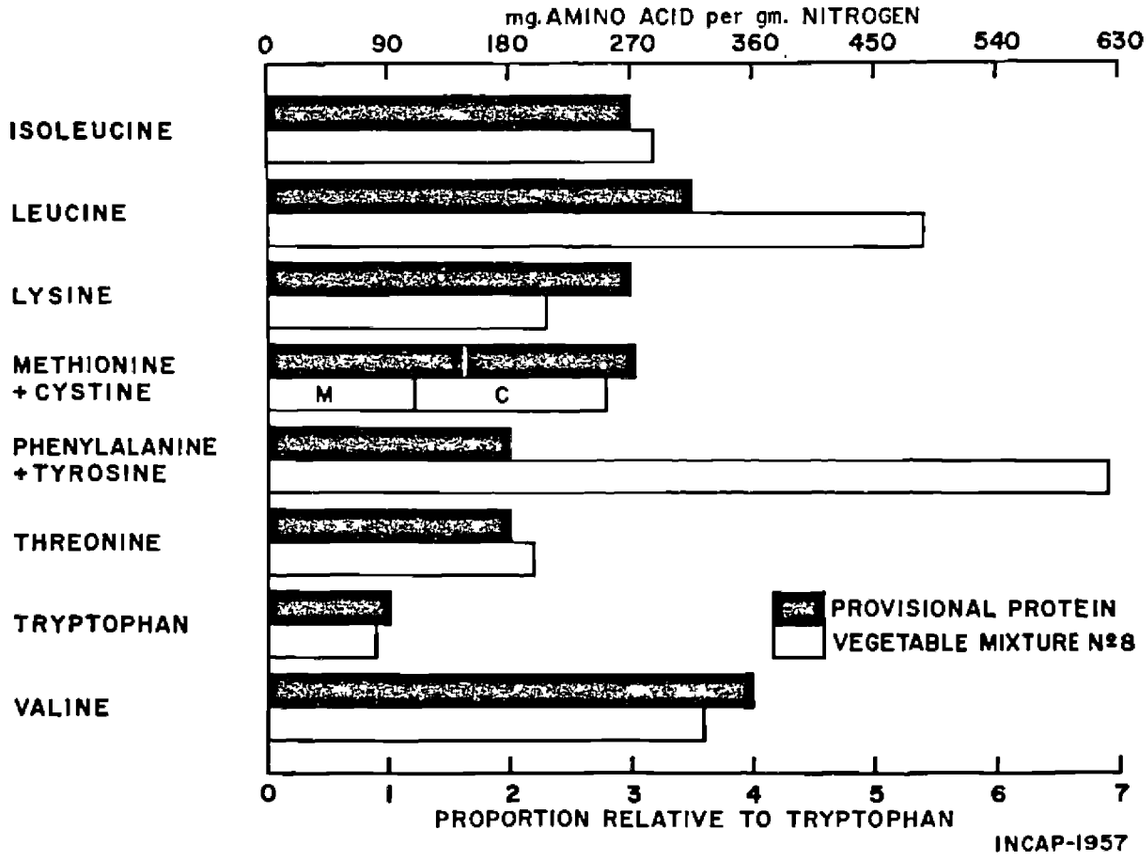

FIGURE 2. Amino acid pattern of provisional protein and INCAP Vegetable Mixture No. 8. Reproduced by permission of the Institute of Nutrition of Central America and Panama (INCAP), Guatemala City, Guatemala, C. A.

source of vitamin A activity in the mixture. It is important that this or a similar dehydrated leaf meal be added to provide provitamin A, since vitamin A deficiency is a serious problem in Central America, particularly in the preschool child. The torula yeast furnishes an inexpensive natural source of additional niacin, riboflavin, and thiamine.

The degree to which the amino acid pattern of the mixture corresponds to that of the reference protein proposed by the FAO Committee on Protein Requirements[43] is shown in FIGURE 2. It will be seen that the mixture contains adequate quantities of most of the essential amino acids per gram of nitrogen. Small deficiencies by calculation of tryptophan, methionine, lysine, and valine are present. The magnitude of these deficiencies will vary somewhat with the particular corn used.[44, 45] The satisfactory degree to which the mixture would supply the estimated requirements for major vitamins and

minerals,[46] if it were fed as the principal food and sole source of protein, is shown in TABLE 2. The mixture does not supply vitamin C since, in the countries of Central America, this vitamin is abundant in fruits and fruit juices that are available and can be given easily to the young child.

The mixture has thus far been fed to children only in the form of an *atole*, a purée, or a dessert. The *atole* is prepared by cooking the mixture in a double boiler with enough water to make a thin gruel and is flavored with sugar. The purée is prepared in the same way, except that less water is added, and salt and oleomargarine are used for flavoring. The dessert is essentially the purée flavored with sugar and vanilla and served cold. It is obvious that the mixture may be prepared and served in many other ways, and a precooked form is envisaged.

Tests in animals have shown that this mixture is of good protein quality for rats, and for baby chicks when the added requirement for lysine is met.[40] To date, 11 children have received this mixture. Among these is 1 who was fed

TABLE 2
AMOUNTS OF MAJOR NUTRIENTS SUPPLIED BY INCAP VEGETABLE MIXTURE NO. 8 COMPARED WITH ESTIMATED REQUIREMENTS*

	Calories	Protein, gm.	Vitamin A, mg.	Thiamine, mg.	Riboflavin, mg.	Niacin, mg.	Iron, mg.	Calcium, gm.
Recommended*	1140	40†	1.20	0.6	1.0	5.7	7	1.0
150 gm. Veg. Mix. No. 8	750	38	1.17‡	2.1	0.9	12.6	60	1.3

* INCAP's recommendations for children 1 to 3 years old.[46]
† This figure is now believed to be more than double the amount required when the protein is of high biological value.[43]
‡ Vitamin A activity calculated from carotene content.

the mixture for a period of 100 days as the sole source of protein and 4 others who have received it from the time of their admission with moderate-to-severe kwashiorkor. The results have been uniformly good, and no complications have been encountered. Furthermore, the intake and output of nitrogen was measured in 5 children receiving their dietary protein entirely from the vegetable mixture for 5 days. The results were then compared with similar periods immediately before or after in which the child received the same amount of protein from milk. The average absorption of the milk protein was 81 per cent, and that of the vegetable protein, 73 per cent. The average retention of the total nitrogen fed was 17 per cent in each case, a clear indication that the child was utilizing the protein of the vegetable mixture as effectively as that of milk.

Amino Acid Supplementation

Now that the industrial production of certain of the essential amino acids at low cost is practicable, the possibility of improving the utilization of vegetable proteins by their supplementation with synthetic amino acids has been discussed.[47, 48] In theory such a measure could be of great value, both for

the prevention of kwashiorkor and for the improvement of diets that are protein deficient because of the poor quality of their protein. In most underdeveloped areas in which protein deficiency is a problem, the amount of protein consumed by school children and adults would be satisfactory if only its biological value were higher. In some populations of the Guatemalan highlands the diet contains as much as 75 gm. of protein primarily from corn and still is deficient in tryptophan and methionine; there is also a marked imbalance among the essential amino acids. Thus, amino acid supplementation, if proved safe and effective, should be considered seriously.

Unfortunately, there is not yet sufficient knowledge, either of the availability of amino acids in most vegetable foods or of the optimum proportions for human nutrition, to be sure of the right amounts to add. The work of Elvehjem[49] has clearly shown that small excesses of the essential amino acids have a harmful rather than beneficial effect on protein utilization, and we have recently found that a small excess of methionine added to lime-treated corn consumed as tortillas decreases rather than increases nitrogen retention.[40] It is obvious that much more study is required before amino acid supplementation can be recommended as a practical preventive measure.

Nutrition Education for Prevention

Although economic factors and the unavailability of protein-rich foods are the basic reasons for the occurrence of kwashiorkor, ignorance and food prejudices also play an important role. For this reason nutrition education constitutes a vital part of any program for its prevention.

Central American parents are slow to give supplementary foods to children during lactation, and breast milk may be the only food received by the child until it is weaned. Prolonged lactation is, of course, very advantageous under the conditions prevailing in most regions where kwashiorkor is common, but supplementary food must be given well before the end of the first year. The fear of supplementary foods appears to be based largely on the frequency with which they are associated with diarrhea in young children; such diarrhea is always attributed to the food itself and not to poor hygiene.

At the time of weaning, these prejudices persist or are even accentuated; instead of giving the weaned infant special foods, a selection is made among those received by the rest of the family, which tends to eliminate foods richest in protein. For example, black beans, which are customarily consumed by the adults and which are a relatively good source of protein, are not given to the young child, but he receives instead some of the water in which the beans have been cooked. Even when meat is available to the family, it is not considered a suitable food for the young child, who is given instead only the broth.

An even worse situation occurs when the food intake of the child is drastically reduced because of diarrhea. In this event, solid foods and milk, if the child is receiving any, are withdrawn, and thin cereal gruels (*atoles*) or preparations of starch are given instead. In some of the countries the use of barley or rice or sugar water is customary, and a severe nutritional deficiency rapidly develops. These poor feeding practices for children with diarrhea are found not only at all social and economic levels, but are even encouraged by some

physicians. A purgative is commonly given to children with diarrhea on the mistaken theory that it will help get rid of the worms that are believed to be responsible. All of these factors can be combated by nutrition education.

An excellent example of this has been the success of the instructions given to the mothers who come to take their children home after hospital treatment for kwashiorkor. The majority of these children remain in good nutritional condition, as noted on subsequent follow-up visits, even though there have been no obvious changes in the socioeconomic conditions of the family.

Environmental Sanitation for Disease Control

Infectious episodes are frequent precursors of the development of kwashiorkor and have been identified as precipitating or contributing causes. In this connection, special mention should again be made of infectious diarrhea, both because of its primary effect on nitrogen absorption and retention and because of the errors that are made in its treatment. Recent INCAP studies carried out in 2 towns in the Guatemalan highlands showed that an average of 5.5 per cent of children under 5 years of age have clinical diarrhea at any given time. Since the incidence of *Shigella* in these populations varies from 1.5 to 15.5 per cent,[8] it is probable that shigellosis is responsible for a significant proportion of these cases. Amebiasis, malaria, measles, whooping cough, and various other communicable diseases have a similar effect.

It is clear, therefore, that efforts directed toward improving environmental sanitation and controlling communicable diseases should considerably reduce the number of children developing kwashiorkor, even though they will not eliminate the chronic malnutrition present in most of the children in rural and poor urban groups in the so-called underdeveloped areas.

Summary

Severe protein malnutrition occurs in any combination of protein and calorie deficiency, ranging from the adequate caloric intake of classic kwashiorkor to the severe deprivation of both protein and calories that results in marasmus. Furthermore, under actual field conditions, protein malnutrition occurs combined with the deficiency of various other nutrients. Rational dietary treatment must take these variables into consideration, together with the biochemical and pathological alterations that occur in a child with kwashiorkor. Early correction of the electrolyte imbalance accentuated by diarrhea is imperative, but the generally satisfactory nature of the response to dietary therapy alone makes unnecessary the resort to blood or plasma transfusions, intravenous or oral protein hydrolyzates, enzyme preparations, and the therapeutic use of vitamins. On the other hand, the frequency of infection and the lowered resistance of the child make desirable the almost routine use of antibiotics. Intestinal parasites, although frequently present, should not be treated until after the child has recovered.

While the use of milk continues to be an ideal basis for therapy and prevention, properly constituted vegetable protein mixtures are almost equally effective for treatment and are the most promising means of prevention for many

areas of the world. Much more work is required to determine the possible value and practicability of the amino acid supplementation of vegetable foods in areas in which animal protein is in short supply.

Since diarrheal disease is widely prevalent in areas in which kwashiorkor is endemic and contributes to the development of severe protein malnutrition, improved environmental sanitation should reduce the number of cases of kwashiorkor. A major factor in the effective prevention of kwashiorkor will always be nutrition education directed toward improved feeding practices for the weaned infant and the young child.

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