30 June 1961, Volume 133, Number 3470 SCIENCE

CURRENT PROBLEMS IN RESEARCH

Protein Malnutrition in Young Children

Malnutrition is still a major factor in the high morbidity and mortality in underdeveloped areas.

Nevin S. Scrimshaw and Moisés Béhar

It is disconcerting to discover that even today in many parts of the world half of the children born in low-income groups die before they are five years of age and that a significant proportion of these deaths are attributable directly or indirectly to malnutrition. It is now evident that most deaths from protein malnutrition occur after weaning, and that the mortality of children from one to four years old in a country is the best index of the seriousness of protein malnutrition (*1*). For example, the mortality of children one to four years of age in the United States and in most countries of Western Europe is now around 1 per 1000, while in most technically underdeveloped countries the proportion varies from 10 to 45 per 1000.

Careful investigation was made of a series of individual deaths of children in four rural Guatemalan towns in which the mortality of the 1- to 4-year age group was 50.3 per 1000. It was found that nearly two-fifths died from the deficiency disease kwashiorkor, and that the remaining deaths were nearly equally attributable to infectious diarrhea and to systemic infections very few of which would have been fatal if the children had been well nourished (*2*).

The widespread occurrence of kwashiorkor is shown in Fig. 1, but its seriousness is better indicated by the data in Table 1, which shows the mortality of children from one to four years of age in representative countries where kwashiorkor is rare or unknown as contrasted with deaths occurring in countries where kwashiorkor is common.

Another form of severe malnutrition in children, which is often fatal, is marasmus. This disease develops when the child is deprived not only of adequate protein but also of calories and other nutrients. For both physiological and cultural reasons, marasmus is more common in children below one year of age, while kwashiorkor is more prevalent in children during the second and third years.

Research on the problem of protein malnutrition in children is now being actively carried on throughout the world, and this article attempts to define the present status of our knowledge in a still dynamic and rapidly progressing field (*3*).

Clinical Characteristics

Protein deficiency in growing children cannot be described as a single clinical syndrome because it is usually associated with some degree of calorie inadequacy. The relative magnitude of this deficiency and of deficiencies of other nutrients determines the resulting clinical picture (*4*). The clinical spectrum of severe protein deficiency ranges from deficiency accompanied by an adequate or even excessive caloric intake to that accompanied by a lack of calories so great that this lack becomes the limiting factor and few signs and symptoms of protein deficiency are apparent. The principal reason why investigators cannot fully agree on the line of demarcation between kwashiorkor and marasmus is the difficulty of establishing limits within this continuous spectrum, which is illustrated diagrammatically in Fig. 2. Cases combining characteristics of both are frequently identified as "marasmic kwashiorkor" (*5*).

The clinical picture depends greatly on the relative degree or intensity of protein and calorie deficiencies. If consideration is limited to the advanced states of each, the main clinical signs and symptoms of the kwashiorkor type are pitting edema (which is a *sine qua non* of the diagnosis), a variable degree of dermatosis characterized by hyperkeratosis, hyperpigmentation, and desquamation, which are illustrated in Fig. 3.

The hair shows three types of alteration: its implantation is affected, so that it falls out spontaneously or can be painlessly removed with little effort. It becomes dry, thin, and brittle, and curly hair tends to straighten. The color is also usually altered. When periods of malnutrition alternate with periods of relatively adequate dietary intake, depigmented bands appear in the hair. The name "flag sign" has been applied to this phenomenon, which is illustrated in Fig. 4. Changes paralleling those in the hair may also be observed in the nails.

Psychic changes always occur to some extent, with a mixture of apathy and irritability prevailing. Anorexia and diarrhea are also very common. Even when clinical diarrhea is not present, the stool volume is greater than in normal children, a finding characteristic of malabsorption syndrome. Muscular hypotonicity is also frequently observed.

Dr. Scrimshaw is the director of the Institute of Nutrition of Central America and Panama (INCAP), Guatemala. Dr. Béhar is assistant director.

Fig. 1. Geographical distribution of kwashiorkor.

In marasmus the predominant signs are retardation in growth and development, as evidenced by height and weight and bone maturation; extreme muscular wasting; and a virtual lack of subcutaneous fat. It should be noted, however, that even in children at the kwashiorkor extreme of the spectrum, such as those described in Jamaica as "sugar babies" (*5*), there is some growth retardation and muscular wasting. The contrasting appearance of children with kwashiorkor and marasmus is shown in Figs. 5 and 6.

Signs and symptoms attributable to specific vitamin or mineral deficiencies are commonly observed both in children with kwashiorkor and in those with marasmus. Examples are eye changes characteristic of vitamin A deficiency and lesions of the conjunctiva and oral mucosa associated with riboflavin deficiency. The frequency of such symptoms varies greatly from one region to another. They appear to be superimposed on the basic manifestations of protein and calorie deficiency and are not, therefore, considered to be characteristics of these syndromes.

Hematology. Some degree of anemia is always found in kwashiorkor, although it is usually mild, unless another major cause of anemia is also present. All the major types of anemia may occur in children with kwashiorkor (*6*). The type depends primarily on whether a deficiency of iron, vitamin B_{12} or folic acid or an infection is superimposed on the protein deficiency. The exact role of protein deficiency per se in the production of some types of anemia is still not known.

Other alterations in the blood include a tendency to leucopenia or diminished leucocytic response to infections, as well as some inconstant alterations in the coagulation system (*7*).

Biochemistry and Physiology

Protein. Low total serum protein is a diagnostic characteristic of kwashiorkor. It is due almost entirely to a low level of albumin and is sometimes partially obscured by a relatively high level of gamma globulin resulting from a concurrent infectious process. There is a tendency for the beta-globulin fraction to be both relatively and absolutely decreased; a relative increase in the alpha-2 globulin has also been found (*8*). Studies with I^{127}-labeled albumin indicate that the lowering of this fraction is due to a decrease in rate of synthesis and not to abnormal catabolism (*9*).

Total α-amino nitrogen in plasma is abnormally low because most amino acids are present in decreased amount. The greatest reductions are found in tryptophan, cystine, valine, tyrosine, and methionine. Low levels of urea in both blood and urine indicate decreased protein metabolism. There is also evidence that the synthesis of antibodies is inhibited in kwashiorkor (*10*).

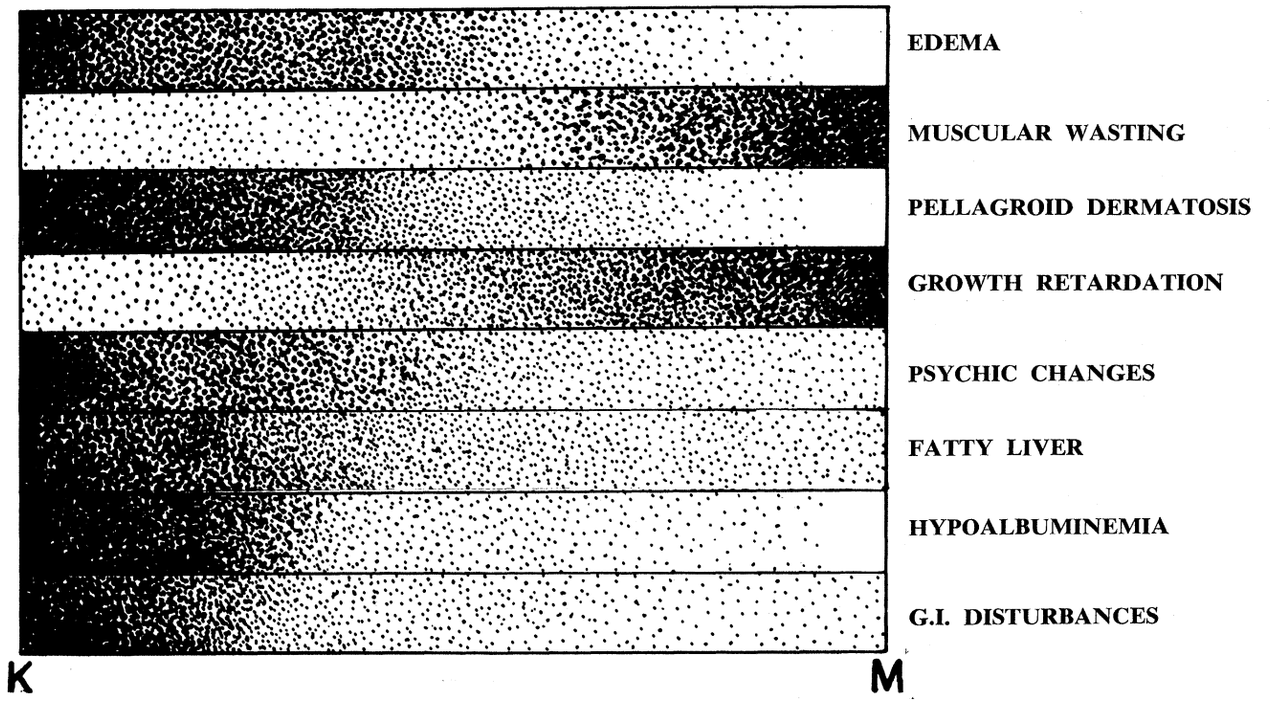


Fig. 2. Schematic representation of the interrelationship of kwashiorkor (*K*) and marasmus (*M*).

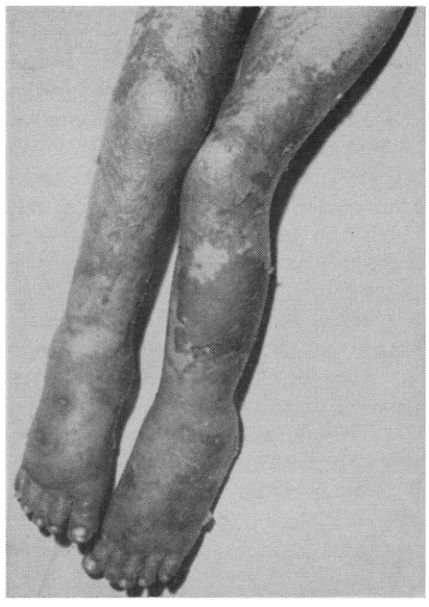


Fig. 3. Edema and skin lesions in a child with kwashiorkor.

In acute cases of kwashiorkor, the level of blood creatinine tends to be relatively high, presumably because of reduction in urinary excretion, which is even too low to be accounted for by the decrease in muscle mass.

A very marked increase in the proportion of urinary nitrogen excreted as purine derivatives has been taken as evidence of cellular breakdown in kwashiorkor (*11*). Other abnormal substances in the urine, which indicate impairment of important metabolic pathways, are β-aminoisobutyric acid and ethanolamine (*12*).

The only tissue proteins measured have been those of liver and muscle. It appears that, although the liver protein in kwashiorkor is greatly diluted by fat, it is not decreased in absolute amount in relation to body size. However, a lowered ratio of nitrogen to deoxyribonucleic acid has been reported (*13*), suggesting a true loss of protoplasmic nitrogen. In any case, the level of nitrogen in the liver of children with kwashiorkor is markedly decreased over that for normal children of the same age. There is also a marked loss of muscle nitrogen in kwashiorkor, the degree depending largely upon the degree of preexisting marasmus.

Lipids. All the various lipid fractions which have been determined in blood of children with kwashiorkor, including neutral fat, fatty acids, phospholipids, and cholesterol, have been found to be low, and levels of these substances rise rapidly in the course of treatment. An increase in fat content of the liver, found by gross and microscopic examination, is another diagnostic criterion. In true marasmus, on the other hand, the amount of liver fat is decreased.

Carbohydrate. Blood glucose levels are generally low. Although glucose tolerance is sometimes reduced, so that the diabetic type of glucose tolerance curve is observed, this is not a constant feature of the disease (*14*).

Enzymes. The protein deficiency of kwashiorkor is severe enough to cause profound alterations in the activities of many enzymes (*15*). In marasmus, enzyme activity is apparently not affected.

In the acute stage of kwashiorkor, lipase, trypsin, and amylase activities in the duodenal secretion are lowered almost to zero, and marked reductions in serum pseudocholinesterase, amylase, carbonic anhydrase, and alkaline phosphatase are recognized characteristics of the syndrome. The activity of these enzymes returns rapidly to normal with the administration of an adequate diet. Alkaline phosphatase levels, however, show a slight further drop before rising with therapy.

The activity of a number of enzymes has also been measured in fresh liver tissue obtained by needle biopsy from children with kwashiorkor (*16*). The outstanding finding is a decrease in xanthine oxidase activity per unit of protein, although cholinesterase and D-amino acid oxidase activity are also definitely lowered. In one case, in which death occurred soon after hospitalization, diphosphopyridine nucleotide cytochrome *c* reductase activity was also decreased. In the remaining cases, the activity of this enzyme and of glycolic acid oxidase, both riboflavin-dependent, was not affected, nor were the pyridine nucleotide-dependent enzymes lactic dehydrogenase and malic dehydrogenase or the pyridoxine-dependent transaminase. Alkaline phosphatase activity in the liver is generally increased. These findings suggest that, although the activity of many key enzymes is maintained even in the presence of extreme protein deficiency, some are sufficiently affected to initiate the train of events culminating in death.

Electrolytes and other minerals. Potassium depletion is a major biochemical characteristic of kwashiorkor and is a direct consequence of the protein deficiency (*17*). Other electrolyte changes are secondary consequences of diarrhea (a symptom almost always present in kwashiorkor) or vomiting, which may also accompany the deficiency. Interpretation and correction of electrolyte changes in kwashiorkor is complicated by the abnormal distribution of water and the severe degree of potassium depletion.

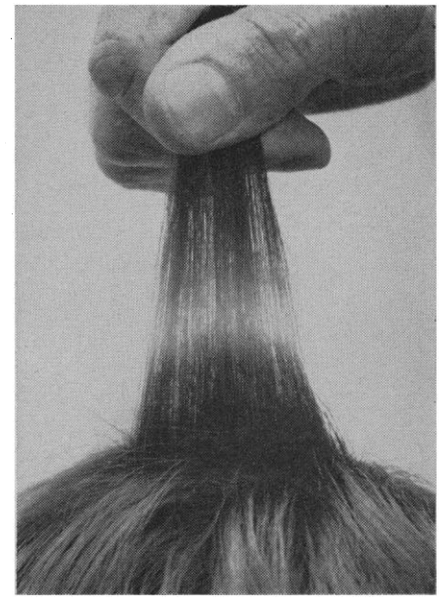
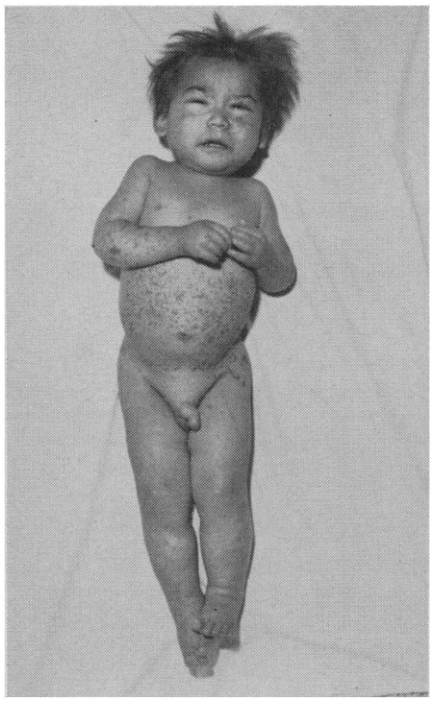


Fig. 4. "Flag sign" in the hair of a child recovering from kwashiorkor. The band of depigmentation corresponds to the period of acute deficiency.

There is no evidence of an initially altered calcium-phosphorus ratio in kwashiorkor, nor is there a significant degree of bone hypocalcification. When insufficient calcium is included in the therapeutic diet, tetany due to hypocalcemia may occur during recovery. Magnesium deficiency has recently been reported in kwashiorkor and may also be responsible for some cases of tetany (*18*). It has been postulated that the reduction in intracellular ions may lead to a breakdown of cellular metabolism by interfering with vital enzymatic activities (*19*).

Table 1. Specific mortality rates, per 1000 population, of children 1 to 4 years of age in selected countries (1955–56) (*39*).

Countries where kwashiorkor is rare or unknown	Mortality rate	Countries where kwashiorkor is common	Mortality rate
Argentina	3.8	Colombia	20.3
Australia	1.3	Ecuador	28.8
Belgium	1.6	Egypt	60.7
Canada	1.5	El Salvador	22.7
France	1.6	Guatemala	42.7
Japan	3.8	Guinea	55.4
Netherlands	1.2	Mexico	24.0
Sweden	1.0	Thailand	14.5
United States	1.1	Venezuela	12.5



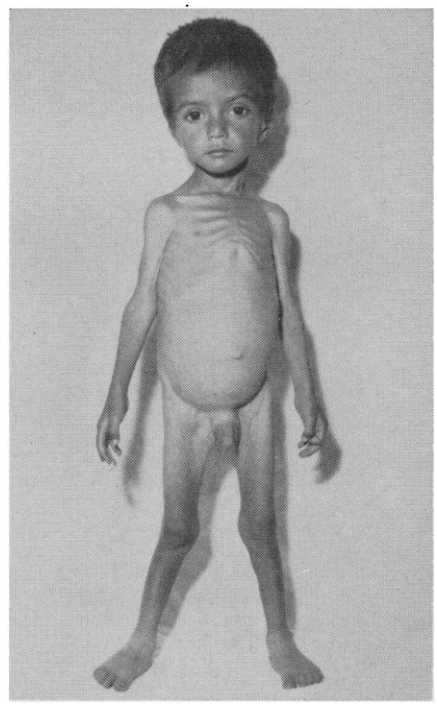


Fig. 5 (left). Child 1 year and 11 months old with kwashiorkor, as observed in Central America. Note the edema, the psychic changes, the changes in skin and hair. Fig. 6 (right). Child 4 years and 5 months old with typical marasmus, showing marked muscular wasting and lack of subcutaneous fat.

Levels of iron and copper are extremely low in the plasma of children with kwashiorkor. The explanation appears to lie in a reduction in transport protein—a hypothesis substantiated in the case of iron by the finding of a low iron-binding capacity (*20*). The iron content of the liver may be increased or decreased, according to the previous dietary history of the child.

Fat-soluble vitamins. Levels of vitamin A and carotene in the serum of children with kwashiorkor are extremely low. It was assumed that this was due to low intake of vitamin A, until recent studies demonstrated that children with acute kwashiorkor upon admission to the hospital did not have an increase in serum vitamin A after a 75-milligram oral dose of vitamin A palmitate. After three to five days of intensive protein therapy, however, a similar dose gave the same sharp increase in serum vitamin A that is found in normal children (*21*). It was also found that, in most cases, serum vitamin A levels rose with protein therapy, even when the diet contained no carotene or vitamin A. Analysis of liver biopsy material demonstrated that this phenomenon occurred whenever there were adequate stores of vitamin A in the liver, and that in those few cases where there was gross depletion of vitamin A in the liver, administration of protein alone produced no serum response (*22*). From this and similar studies, it appears probable that the transport of vitamin A and possibly of vitamin E, which also occurs in abnormally low amounts in blood plasma of children with kwashiorkor, is inadequate because of the lack of a protein carrier.

No vitamin D deficiency has been observed. Little is known about vitamin K levels in kwashiorkor, except that in the majority of cases prothrombin time is not seriously affected.

Water-soluble vitamins. Blood levels of thiamine and riboflavin are within normal limits in children with kwashiorkor. Even though the pigmented skin lesions superficially resemble those of pellagra, there is no evidence of niacin involvement. The urinary excretion of N-methylnicotinamide, in cases in Central America at least, is within normal limits. Levels of serum ascorbic acid are relatively low but are not in the range commonly associated with clinical deficiency (*8*). No significant alterations of levels of vitamin B_{12} in the blood have been found (*23*).

Endocrine function. Children with kwashiorkor have a low urinary excretion of 17-ketosteroids and 17-hydroxysteroids. The latter finding, together with near-normal eosinophil counts, suggests that there is a marked decrease in glucocorticoid activity. In marasmus, on the other hand, the excretion of 17-hydroxysteroids in the urine is normal or high, and eosinophil counts are greatly reduced, suggesting hyperactivity of the adrenal cortex. Further evidence has been obtained from experiments carried out in animals fed diets simulating those of children developing either kwashiorkor or marasmus (*24*).

Cardiovascular function. In the marasmic type of kwashiorkor seen in Central America, a relatively small heart, which rapidly increases in size with treatment, is found upon radiological examination (*25*). Electrocardiographic findings have been reported to show principally low voltage and minor abnormalities, including alterations in the T wave and changes in rhythm (*26*).

Gastrointestinal function. To judge by the volume of feces excreted by children with kwashiorkor, these children suffer from a malabsorption syndrome which is not completely corrected even after some weeks of treatment. Good digestion and absorption of proteins still take place during the acute state, but fat is poorly handled at first. Although fat absorption improves very rapidly as the child recovers, some degree of steatorrhea persists even into late recovery (*27*).

Hepatic function. Despite the marked histological alterations in the liver, the common tests for liver function have been found to give results within normal limits, with the possible exception of Bromsulphalein retention, which is frequently high (*28*).

Renal function. A reduction in renal plasma flow has been reported; this is found particularly when there is dehydration and therefore appears to be related to the diminished volume of circulation. The glomerular filtration rate, as indicated by clearance of inulin and endogenous creatinine, is also reduced (*29*). Although there is some evidence of reduced antidiuretic activity, the mechanism of water retention in kwashiorkor is not yet clear and may be primarily a physiological response of the kidney to the electrolyte and water disturbances.

Neurological function. Electroencephalographic studies have shown diminished voltage and excessively slow rhythmic activity. Some authors have

also reported abnormal focal activity and other alterations (*30*). These abnormalties tend to disappear as recovery progresses.

Gesell tests, or similar procedures for evaluating psychic development, when carried out after a few days of treatment, show marked retardation. It has been reported that when the child has recovered, he reaches normal levels for his age (*31*). Others have reported, however, that the child is still mentally retarded after complete clinical recovery (*32*). The duration of illness and opportunities for learning must be taken into consideration in the interpretation of these data.

Pathology

In kwashiorkor, the liver and the pancreas are the most seriously and constantly affected organs (*8*). The most evident alteration in the liver is a diffused fatty change which starts at the center of the lobule and eventually affects nearly all of the parenchymal cells, as illustrated in Fig. 7. As a result, the sinusoids are generally collapsed. Small acute inflammatory foci may also be present. Although an increase in the reticular fibers is common, we do not believe that true fibrosis has been demonstrated in uncomplicated cases of kwashiorkor.

Atrophic changes in the exocrine pancreas include shrinkage of the acinar cells, reduction in the number of enzyme granules, and a loss of the basal proenzyme plate. In a few severe cases there is a definite increase in fibrotic tissue. The salivary and intestinal glands are similarly affected. The intestinal wall is sometimes so atrophic as to be nearly transparent.

No significant cellular changes in the pituitary have been observed. The thyroid gland contains follicles which are smaller than normal and have cuboidal epithelium. The testes and ovaries show only minimal signs of maturation as compared to those of normal children of the same age. The adrenals tend to be small in size and weight. Histopathologically, two different and opposite patterns are observed in the cortex, one compatible with hypofunction and the other with hyperfunction of these glands.

The skin shows atrophy of the epidermis with a varying degree of hyperkeratosis and parakeratosis. The skin appendages are also atrophic.

The striated muscle shows atrophy, with a varying degree of loss of striation. Usually no anatomical lesions are found in the kidney except, in some cases, a fatty degeneration of the tubules. When there is severe hypokalemia, a typical vacuolar degeneration occurs.

Epidemiology

The major factors involved in the etiology of protein malnutrition are summarized graphically in Fig. 8. They are diverse in nature and include agricultural, economic, cultural, and medical causes.

Food production is, of course, fundamental. In the underdeveloped areas of the world where protein malnutrition is prevalent, production of protein-rich foods, and particularly those of animal origin, is nearly always insufficient to meet the nutritional needs of the population. The per capita availability of these foods in different areas of the world, listed in Table 2, indicates that low-production areas correspond very closely to areas where kwashiorkor is common.

This low production is mainly the result of failure to employ modern techniques of agriculture and animal husbandry. The productive capacity is further reduced by debilitating infectious and nutritional diseases.

The per capita availability of foods does not in itself give an accurate idea of their distribution among the different socioeconomic groups. In addition, the lack of facilities for transportation and preservation often results in a decrease in the availability of animal foods in some areas and among some population groups within a country.

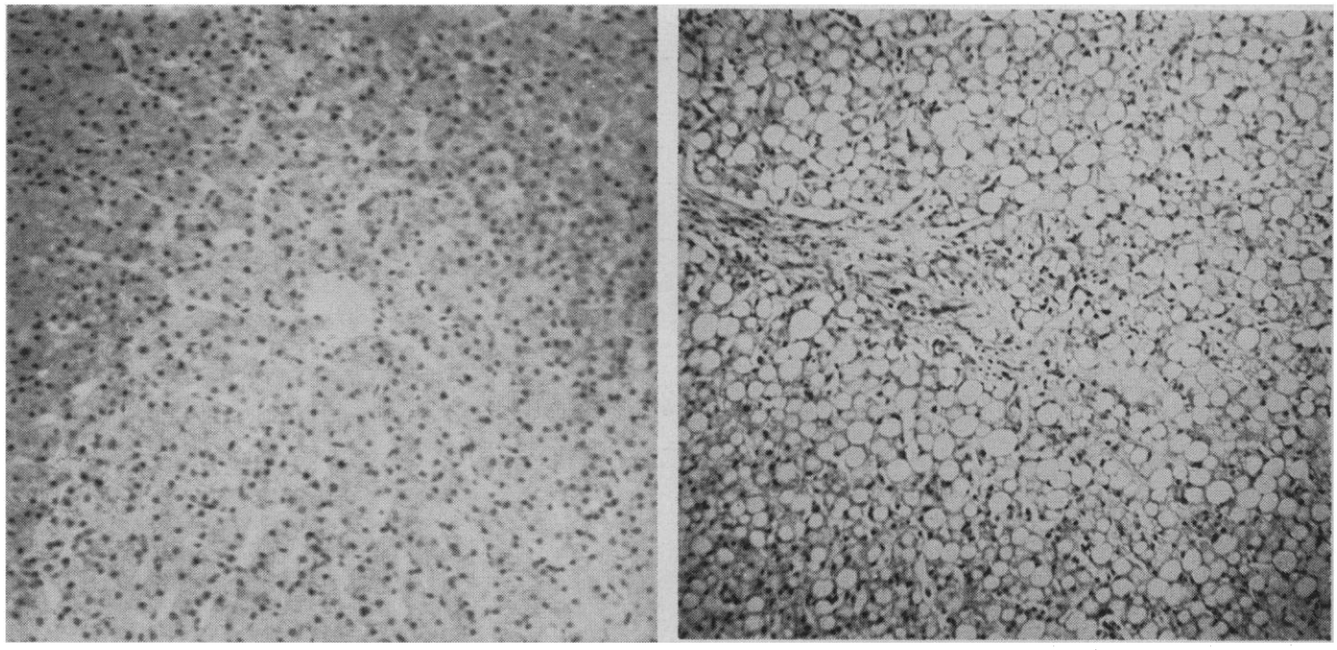


Fig. 7. Normal liver (left) and liver of a child with kwashiorkor (right), in which fat fills each hepatic cell, giving the liver a honeycomb appearance (hematoxylin and eosin stain; × 100).

Table 2. Per capita availability of foods, in grams per day (*40*).

	Countries included (*N*)	Milk	Animal protein	Total protein
Regions where kwashiorkor is unknown or rare				
North America	2	722	64	94
Oceania	2	642	66	98
Western Europe	15	573	43	85
Regions where kwashiorkor is common				
Latin America	7	222	22	62
Near East	3	93	20	84
Africa	5	93	19	65
Far East	6	30	12	51

The availability of food to the family, furthermore, does not accurately indicate its consumption by the individual members. Particularly in populations which do not have enough protein-rich food, small children suffer most from an inequitable distribution within the family. There are many reasons for this, but most of them are due to the mother's ignorance of the nutritional needs of small children and the ways of satisfying them, and from unfortunate cultural beliefs and taboos.

In the areas where protein deficiency is prevalent, most infants are breast-fed for a relatively long time, but without proper supplementation. For several years after weaning, children receive a diet which is often much poorer in proteins than that of any other member of the family. When these children become ill, the protein of their diet is likely to be reduced still more.

A further reduction in diet is often made by the child himself, by failure to eat all the foods actually offered him, because of anorexia, which is presumably the consequence of an infectious process or of the poor diet itself. Anorexia may also develop for psychological reasons when the child receives less attention from the mother than he is accustomed to after the birth of a younger sibling.

The amount of protein absorbed by the child is decreased by heavy intestinal parasitic infections, severe diarrheas, the physical state of the food, the quality of the protein, and the presence of interfering substances. His nitrogen retention is also diminished by such factors as catabolic losses due to infectious processes, the biological value of the protein, and use of protein to meet caloric needs. The amount of nitrogen finally retained by the child determines his nutritional status with respect to protein.

In the classical epidemiological terms of agent, environmental factors, and host factors in the etiology of disease, the agent of kwashiorkor is generally considered to be a deficiency in protein or, more specifically, in the amounts and proportions of the essential amino acids. Of equal importance, however, in determining whether or not the disease appears with a given diet are the environmental factors (such as those determining the availability of protein-rich foods), the stress of infections, and sociocultural factors. Host factors include the decrease in protein requirement per unit of body weight with increasing age of the child and genetic variations in protein needs. Ordinarily, a child develops kwashiorkor only when several of these factors are interacting.

Our concept of the interrelationship between the development of kwashiorkor and marasmus is given schematically in Fig. 9. A normal child, indicated by the apex *N* of the triangle, when starved, would rapidly lose weight and pass through various degrees of malnutrition along the line *N–M*, to end in marasmus, designated as *M*. A child deprived of protein but given an abundance of calories would lose some weight in relation to age by not growing, but would move rapidly toward kwashiorkor along the line *N–K*.

Only in exceptional circumstances, however, would a child move smoothly along one of these two lines. Usually there is a long preliminary period of weight loss during which the child moves parallel to the line *N–M* until stress factors and dietary changes move him rapidly toward the base line *K–M*, which represents the continuous spectrum between marasmus and kwashior-

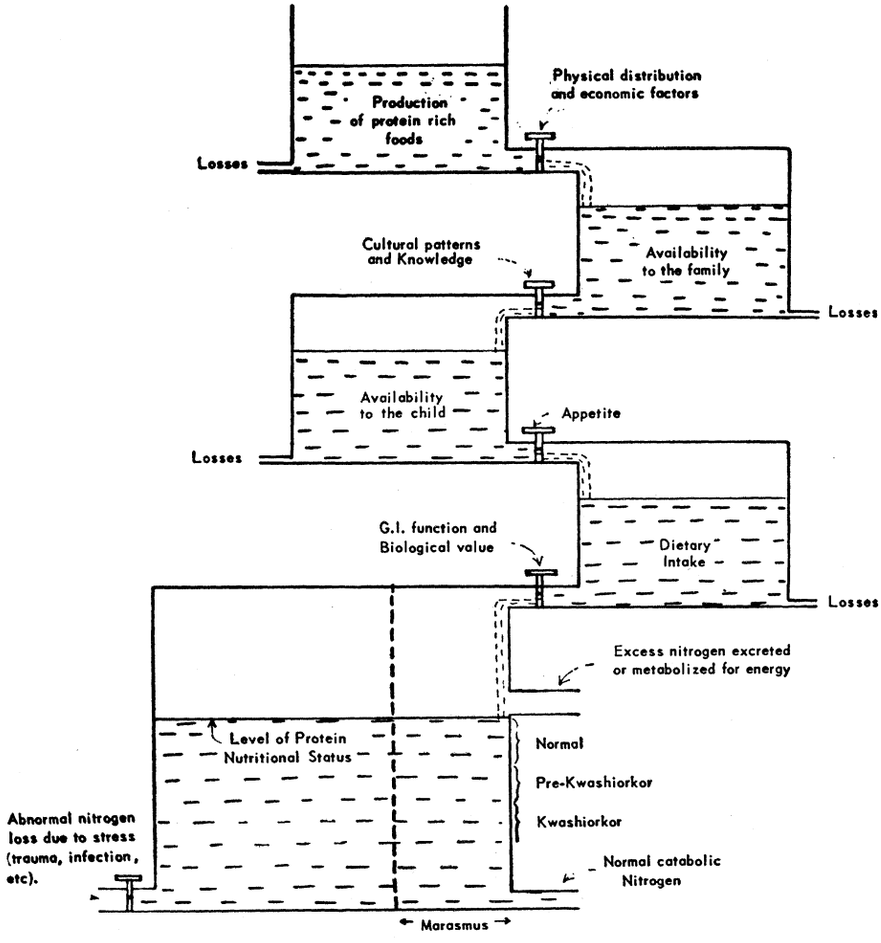


Fig. 8. Schematic representation of factors determining protein nutritional status.

kor illustrated in Fig. 8. Such a course is suggested by line *c* in Fig. 9.

Another common course, illustrated by line *b*, is that in which a child loses weight because of insufficient food and passes through an episode which moves him away from line *N–M* toward line *K–M*. He may then move again toward *M* in an intermediate zone parallel to line *N–M*, until a new episode results, this time, in moving him all the way to line *K–M*, with the resulting clinical appearance of marasmic kwashiorkor. Line *d* indicates that, as a child approaches marasmus, it is possible for him to move into the zone of kwashiorkor under stress, then move back toward the *N–M* line and display clinical symptoms of marasmus before an adverse change results in the superimposition of kwashiorkor.

All these lines could be taken equally well to represent the possible course of recovery, if they are followed in the reverse direction. Line *a* indicates that in the "sugar baby" type of kwashiorkor, the child, after recovery from the acute episode, is still somewhat below normal weight for his age.

On this basis, Fig. 10 indicates that it is possible to identify the clinical syndrome which the child presents at any point within this triangle. It can be seen that classification of malnutrition on a basis of percentage below standard weight—a system developed by some authors (*33*)—is useful under this scheme only in the limited area parallel to line *N–M*. The term *pre-kwashiorkor* is used to define those children who already have a few mild signs and symtoms of kwashiorkor and who should be considered on their way to developing the full-blown syndrome.

Treatment

The basic treatment of kwashiorkor is dietary. The child should be given a diet providing 3 to 5 grams of proteins of good biological value per kilogram of body weight per day. Cow's milk in any form is a convenient and effective source of protein. However, good results can be obtained with adequate combinations of proteins of vegetable origin (*34*) and even with mixtures of amino acids (*35*). Other foods should be progressively added so that by the second or third week of treatment the child is receiving a complete and varied diet, including fruits, vegetables, eggs, meat, and cereals, as well as milk.

Caloric intake should be high enough to insure good protein utilization. After the first few days of adaptation to the diet, an intake of about 150 calories

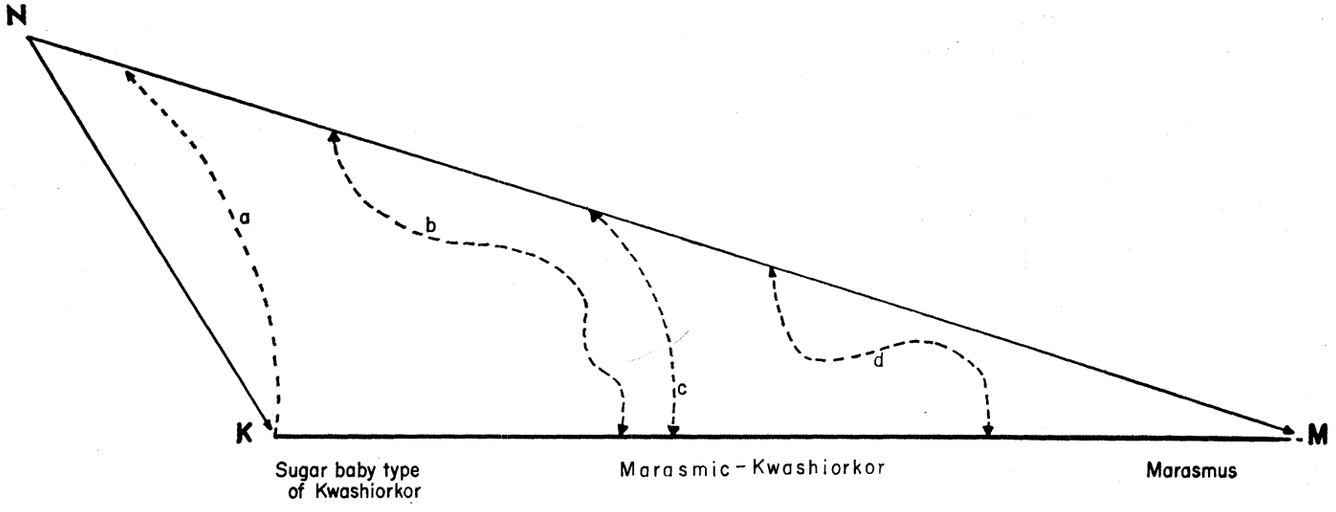


Fig. 9. Schematic representation of the development of the different types of protein malnutrition in children.

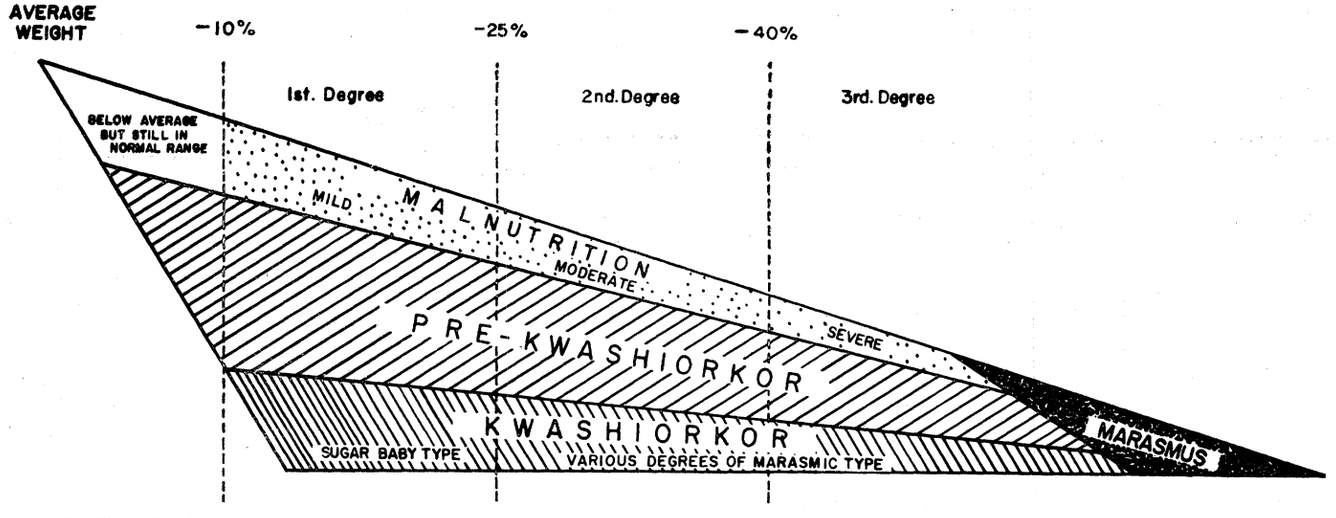


Fig. 10. Classification of the different types of protein malnutrition in children, based on the concept represented in Fig. 9. The classification developed by Gómez *et al. (33)* is shown by the dashed lines.

per kilogram of body weight, together with adequate protein, gives good results in most patients with kwashiorkor. In cases of marasmus or in very marasmatic cases of kwashiorkor, a higher intake of calories may be necessary after the initial phase of recovery.

It has been repeatedly demonstrated that, with good dietary treatment, there is no need for additional vitamins or minerals in most cases. Only when clinical or biochemical evidence of a severe deficiency of a specific nutrient is observed is it desirable to administer a vitamin or other specific nutrient. Children with megaloblastic or iron-deficiency anemias or ocular signs of vitamin A deficiency are among those requiring specific treatment.

Immediately after admission to the hospital and before initiation of the dietary treatment, measures should be taken to correct electrolyte imbalance in these children, particularly if clinical dehydration is present. Particular attention should be given to correcting potassium deficiency.

An antibiotic or a sulfonamide, or both, should also be given during the first few days of hospitalization, even if the child does not give evidence of infection. Severe infections, particularly bronchopneumonia, may develop with few clinical manifestations and be responsible for unexpected deaths during the first few days after admission. Obviously, if infection is found at any stage it should be treated promptly and effectively, since it interferes with adequate recovery.

It has also been found that good nursing and general care in the hospital, including adequate control of intake, isolation from infectious cases, cleanliness, frequent changes in position during the period of apathy, and affectionate attention at all times, are extremely important for good recovery.

Prevention and Unsolved Problems

Preventive measures should include prompt and adequate attention to individual cases of malnutrition, with special emphasis on the education of the parents; supplementary feeding programs for vulnerable groups, not only as a source of additional food but also as a means of education; and long-term projects to maintain a stabilized situation.

The first step in the long-term prevention of protein malnutrition in a country should be to increase, by all practical means, the availability of protein of good quality, particularly for the feeding of young children. Traditionally, providing foods of high protein quality has required an increase in the production of milk, cheese, meat, eggs, and fish. In most underdeveloped areas the means of increasing production of these foods are readily at hand but the cost is too high.

It now appears more practical to extend the usefulness of a given quantity of milk by adding it to vegetable mixtures (*36*), or to develop low-cost all-vegetable mixtures, such as Incaparina (*34, 37*), which have a protein content similar to that of milk and other products of animal origin. Also, advances in food technology have largely overcome the processing difficulties encountered in the past in making fish flour, meat meals, and soya preparations.

In areas where kwashiorkor occurs, mothers need to be taught to use locally available sources of protein, whether milk and dairy products, fish or fish flour, vegetable mixture, soya products or other legumes. It is also important that mothers learn to continue giving these protein sources to the child during episodes of illness. It may be necessary to combat erroneous beliefs which actually proscribe these foods for young children. Of major importance, also, is the processing and storage of foods so as to preserve or enhance their nutritive value.

Even when good food is consumed, several preventable conditions may interfere with its utilization. Heavy infestations of ascaris and other intestinal parasites, as well as frequent diarrhea of infectious origin, require specific therapy, and improved environmental sanitation is necessary to prevent their occurrence. Improved sanitation thus becomes a major factor in the prevention of kwashiorkor, along with immunization against smallpox, diphtheria, whooping cough, and tetanus, and (hopefully) also against measles. Prompt and effective therapy for acute infections, both intestinal and systemic, will, of course, help to limit their adverse effects on nutritional status.

Need for low-cost protein-rich foods: The prevention of kwashiorkor requires the further development of foods which furnish protein of good quality at low cost, and which can be produced in technically underdeveloped areas. Powdered skim milk is a partial solution for some regions, and fish flours and soya products may also be useful. It is evident, however, that the oilseeds are the most promising low-cost sources of protein for many areas.

The work of the Institute of Nutrition of Central America and Panama has shown that both cottonseed and sesame flours, if properly processed, can be combined with cereal grains in low-cost, palatable mixtures which have a protein content and quality comparable to that of foods of animal origin. The product, Incaparina, contains corn, sorghum, cottonseed flour, and *Torula* yeast and is already produced commercially in several Latin-American countries. Similar mixtures could be developed with local resources in countries where protein-containing foods of animal origin are in short supply or are too costly for low-income groups, and where neither cottonseed flour nor soya are available as cheap sources of vegetable protein.

Susceptibility of malnourished children to infection: While it is well established that children suffering from protein malnutrition are more susceptible to infection than normal children, little is known of the mechanisms involved. Antibody synthesis is impaired in protein-depleted animals and, apparently, also in protein-depleted man, but this is not the sole mechanism of resistance to infection and may not even be the most important one. Adverse effects of protein malnutrition on tissue integrity, leucocyte activity, and production of nonspecific protective substances have been proposed as possible mechanisms, but their relative importance is not known.

Mechanisms involved in the development of kwashiorkor: The sudden development of kwashiorkor in children with underlying malnutrition is usually associated with the stress of infection. While it is known that infections decrease nitrogen retention by increasing urinary nitrogen excretion, the critical point at which the changes of kwashiorkor set in is a matter of great uncertainty. Much more information is needed concerning the mechanism of this change and concerning the frequent development of kwashiorkor in children with the marasmic type of malnutrition. Until we acquire an understanding of the combination of circumstances responsible for the sudden development of kwashiorkor in one child and not in another under apparently similar conditions of dietary deficiency and other

stress, we will be handicapped in our efforts at diagnosis and prevention.

Regional variations: Although the basic characteristics of the kwashiorkor syndrome have been fairly well agreed upon, there remain baffling differences in the signs associated with the disease in different areas. While some of these differences may be due to genetic differences in skin pigmentation and in texture and color of hair, others seem more likely to be the result of variations in deficiencies of specific amino acids or of concomitant deficiencies of other nutrients. Elucidation of these differences should yield valuable information about the relationship of specific nutrients to those clinical signs which are inconstant accompaniments of the syndrome and about the interrelationships between a deficiency of protein and a deficiency of other nutrients. Particularly intriguing is the concept that kwashiorkor-producing diets differ in deficiencies of specific amino acids and that these differences account for some of the regional variations in clinical signs, even though a deficiency of any essential amino acid may produce the interference with protein anabolism which results in kwashiorkor.

Adverse Consequences and Sequelae

Thus far, attempts to demonstrate permanent sequelae from protein malnutrition alone have failed. There have been no sufficiently prolonged follow-up studies in which permanent sequelae have been sought. The effect of protein malnutrition in a child on the development of degenerative disease in an adult will, of course, be exceedingly difficult to determine. The recent demonstration of impaired intellectual capacity in malnourished children (*38*) is of tremendous importance and needs further investigation.

References and Notes

1. J. M. Bengoa, D. B. Jeliffe, C. Pérez, *Am. J. Clin. Nutrition* **7**, 714 (1959).
2. M. Béhar, W. Ascoli, N. S. Scrimshaw, *Bull. World Health Organization* **19**, 1093 (1958).
3. We are greatly indebted to Dr. Dorothy Wilson, chief, Kwashiorkor Project, Division of Clinical Investigation, Institute of Nutrition of Central America and Panama (INCAP), for assisting in the preparation of this article. This is INCAP publication No. I-204.
4. H. C. Trowell, J. N. P. Davies, R. F. A. Dean, *Kwashiorkor* (Arnold, London, 1954); M. Béhar, F. Viteri, R. Bressani, G. Arroyave, R. L. Squibb, N. S. Scrimshaw, *Ann. N.Y. Acad. Sci.* **69**, 954 (1957–5[illegible] D. B. Jelliffe, *J. Pediat.* **54**, 227 (1959).
5. D. B. Jelliffe, G. Bras, K. L. Stuart, *West Indian Med. J.* **3**, 43 (1954).
6. G. Mehta and C. Gopalan, *Indian J. Med. Research* **44**, 727 (1956); F. Walt, *J. Trop. Pediat.* **5**, 3 (1959 L. G. Macdougall, *Trans. Roy. Soc. Trop. Med. Hyg.* **54**, 37 (1960).
7. C. Merskey and J. D. L. Hansen, *Brit. J. Hematol.* **3**, 39 (1957).
8. M. Béhar, G. Arroyave, C. Tejada, F. Viteri, N. S. Scrimshaw, *Rev. col. méd. Guatemala* **7**, 221 (1956).
9. D. Gittlin, J. Cravioto, S. Frenk, E. L. Montaño, R. Ramos-Galván, F. Gómez, C. A. Janeway, *J. Clin. Invest.* **37**, 682 (1958).
10. J. Olarte, J. Cravioto, B. Campos, *Bol. méd. hosp. infantil (Mex.)* **13**, 467 (1956).
11. R. G. Whitehead and C. E. Matthew, *E. African Med. J.* **37**, 384 (1960).
12. J. C. Edozien, E. J. Phillips, W. R. F. Collins, *Lancet* **1**, 615 (1960).
13. J. C. Waterlow and T. Weisz, *J. Clin. Invest.* **35**, 346 (1956).
14. D. Slone, L. S. Taitz, G. S. Gilchrist, *Brit. Med. J.* **1**, 32 (1961).
15. J. C. Waterlow, *Federation Proc.* **18**, 1143 (1959).
16. H. B. Burch, G. Arroyave, R. Schwartz, A. M. Padilla, M. Béhar, F. Viteri, N. S. Scrimshaw, *J. Clin. Invest.* **36**, 1579 (1957).
17. J. D. L. Hansen and V. Jenkinson, *S. African J. Lab. and Clin. Med.* **2**, 206 (1956).
18. R. D. Montgomery, *Lancet* **2**, 74 (1960).
19. J. Metcoff, S. Frenk, I. Antonowicz, G. Gordillo, E. López, *Pediatrics* **26**, 960 (1960).
20. M. E. Lahey, M. Béhar, F. Viteri, N. S. Scrimshaw, *ibid.* **22**, 72 (1958); J. C. Edozien and I. O. K. Udeozo, *J. Trop. Pediat.* **6**, 60 (1960).
21. G. Arroyave, F. Viteri, M. Béhar, N. S. Scrimshaw, *Am. J. Clin. Nutrition* **7**, 185 (1959).
22. G. Arroyave, D. Wilson, J. Méndez, M. Béhar, N. S. Scrimshaw, *ibid.* **9**, 180 (1961).
23. L. G. Macdougall and G. I. M. Ross, *J. Pediat.* **57**, 589 (1960).
24. H. Castellanos and G. Arroyave, *Am. J. Clin. Nutrition* **9**, 186 (1961).
25. N. S. Scrimshaw, M. Béhar, G. Arroyave, C. Tejada, F. Viteri, *J. Am. Med. Assoc.* **164**, 555 (1957).
26. C. Schyns and E. DeMaeyer, *Acta cardiol.* **12**, 413 (1957).
27. G. Mehta, P. S. Venkatachalam, C. Gopalan, *Indian J. Med. Research* **44**, 231 (1956).
28. A. A. Kinnear and P. J. Pretorius, *Brit. Med. J.* **1**, 1528 (1956).
29. G. Gordillo, R. A. Soto, J. Metcoff, E. López, L. García Antillón, *Pediatrics* **20**, 303 (1957).
30. G. K. Nelson and R. F. A. Dean, *Bull. World Health Organization* **21**, 779 (1959).
31. M. Geber and R. F. A. Dean, *Courrier* **6**, 3 (1956).
32. B. Robles, R. Ramos-Galván, J. Cravioto, *Bol. méd. hosp. infantil (Mex.)* **16**, 317 (1959).
33. F. Gómez, R. Ramos-Galván, S. Frenk, J. Cravioto, R. Chávez, J. Vázquez, *J. Trop. Pediat.* **2**, 77 (1956).
34. N. S. Scrimshaw, M. Béhar, D. Wilson, F. Viteri, G. Arroyave, R. Bressani, *Am. J. Clin. Nutrition* **9**, 196 (1961).
35. J. D. L. Hansen, E. E. Howe, J. F. Brock, *Lancet* **2**, 911 (1956).
36. R. F. A. Dean, *E. African Med. J.* **37**, 378 (1960).
37. Incaparina, as its name indicates, is a product developed by INCAP.
38. R. Ramos-Galván, J. L. Pérez Navarrete, J. Cravioto Muñoz, *Bol. méd. hosp. infantil (Mex.)* **17**, 455 (1960).
39. Data taken from "Summary of Four-Year Reports on Health Conditions in the Americas," *Pan American Sanitary Bureau Regional Office of the World Health Organization, Scientific Publication No. 40* (Washington, D.C., 1958); *Demographic Year Book 1957* (United Nations, New York, 1957); *Enquête demographique 1954–1955* (Haut Commissariat de la République Française).
40. Data taken from *The State of Food and Agriculture 1960* (Food and Agriculture Organization of the United Nations, Rome, 1960).

Why Did Daedalus Leave?

Underdeveloped countries are aiding the developed by exporting one of their most precious commodities: talent.

Stevan Dedijer

The study of the social behavior of scientists is one of the least developed branches of one of the youngest of the social sciences: the sociology of science. Even the belles-lettres, as C. P. Snow recently pointed out, have practically ignored scientists. The rare and tenuous tracks back through time, marking an awareness of this type of human behavior, stop in Greek mythology. In the legend about Daedalus (*1*), the first mortal inventor in their mythology, the Greeks described the behavior of a man passionately devoted to what today would be called the solution of problems in applied research and completely free of any social and ethical norms.

Daedalus starts his career with murder: he kills from professional jealousy his colleague Talos and flees to the court of king Minos of Crete. There, by appropriate inventions, Daedalus solves a series of problems of questionable moral and political worth: he constructs a machine enabling Minos' wife to copulate with a bull, he devises the labyrinth so that Minos can hide the shameful monster born as the result of the previous invention, and finally he invents a device for

The author is at present at the Universitetets Institut for Teoretisk Fysik, Copenhagen, Denmark.