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WORLD REVIEW *of* NUTRITION *and* DIETETICS

Treatment and Prevention of Kwashiorkor

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PITMAN MEDICAL PUBLISHING CO. LTD.

4

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Contents

I. INTRODUCTION

Knowledge of the biochemical, physiological and pathological characteristics of kwashiorkor has grown rapidly since the appearance of the monograph on *Kwashiorkor in Africa* by Brock and Autret (1952), and has been summarized in a number of recent reviews (Trowell, Davies and Dean, 1954; Brock, 1954; Scrimshaw *et al.*, 1956; Béhar *et al.*, 1956). Intensive study of the syndrome in many different parts of the world has resulted in a clarification of the features of kwashiorkor common to all regions in which it occurs as well as the identification of those associated signs and symptoms which are the result of local conditions. This has been facilitated by the interchange of ideas at several international conferences and by the exchange of visits among workers from different countries. There has also grown up a common body of successful experience in the treatment of kwashiorkor and a genuinely international approach to the problems of its prevention. These developments have been stimulated and assisted to a precedent-setting degree, by two of the specialized agencies of the United Nations, the World Health Organization (W.H.O.) and the Food and Agricultural Organization (F.A.O.), and both U.N.I.C.E.F. and U.N.E.S.C.O. are now co-operating in this effort.

The specific purpose of this review is to describe present knowledge and concepts of the treatment and prevention of kwashiorkor derived from world-wide investigations and experience. For a systematic coverage of the clinical, biochemical and pathological characteristics of the syndrome the reader is referred to the reviews listed; reference to these aspects of kwashiorkor is made only as they relate to or serve to guide therapy or prevention.

The authors have attempted not only to include controversial points and divergent opinions but also to evaluate them in the light of the latest knowledge available and the consensus of experienced workers. In so active a field of research this desirable but difficult procedure will inevitably lead to some errors of both omission and commission. It is hoped, nevertheless, that this type of summary, at a time when international interest in the problem has been so greatly aroused, will contribute to the widespread efforts being made to reduce morbidity and mortality from kwashiorkor by disseminating knowledge of effective treatment and by instituting practical measures for prevention.

II. CONCEPT OF KWASHIORKOR AS A DISEASE ENTITY

Kwashiorkor is recognized as a disease syndrome arising as result of severe deficiency of dietary protein relative to caloric intake and characterized typically by retardation of growth and development, oedema, apathy, anorexia, alterations in the colour and texture of the hair, lesions of the skin, and diarrhoea. It occurs most commonly in young children because at this period of life protein requirements are relatively high and diets are most likely to be deficient in protein. It is frequently accompanied by deficiencies in other nutriments which differ somewhat from one region to another and complicate the clinical picture. Not only do the associated deficiencies of vitamins and minerals vary but also the relative adequacy of the caloric intake. When protein deficiency occurs in a child whose caloric intake is adequate, the result is the classical type of kwashiorkor in which tissue-wasting is not a conspicuous feature. With excessive caloric intakes, subcutaneous fat may be increased and the child develop the so-called "sugar-baby" type of kwashiorkor (Fig. 14.1) described in Jamaica (Jelliffe, Bras and Stuart, 1954). As kwashiorkor occurs throughout Latin America, most of Africa, India, and the Middle and Far East it is combined with a deficiency of calories sufficient to cause pronounced wasting and presents a continuous clinical spectrum merging with marasmus (Fig. 4.2). These intermediate clinical forms, representing combinations of marasmus and classical kwashiorkor, could more properly be designated as marasmic kwashiorkor, but since they are the prevalent form of the disease, this is not customary. Because it is the common type, instructions for the therapy of "kwashiorkor" are generally given with the marasmic case in mind. Fig. 4.3 shows the underlying wasting evident in a child with marasmic kwashiorkor once the oedema is lost. These concepts must be kept in mind since severe caloric deficiency complicates both treatment and prevention.

Regardless of the degree of associated caloric deficiency, the fundamental aetiological factor in the development of kwashiorkor is a marked deficiency in the amino acids necessary for protein metabolism. This may come about because dietary protein is inadequate in quantity or quality, but more frequently it is deficient in both total amount and biological value. Any factor decreasing either nitrogen absorption or nitrogen retention will contribute to the development of protein deficiency and may precipitate kwashiorkor in cases of border-line protein intakes. The high frequency with which diarrhoea of infectious origin and other infectious diseases decrease nitrogen retention prior to the appearance of kwashiorkor will be discussed in detail in the section on prevention. It has not been possible to isolate the effects of single amino acids from those of the essential amino acids as a group. Since, unlike the vitamins, a deficiency of one essential amino acid blocks the utilization of the others, it is almost impossible to design suitable experiments on this point without jeopardizing the child.

While some of the associated nutrient deficiencies depend on inadequacies in the local diets, which are not necessarily constant from region to region, others, like the deficiency of the fat-soluble factors, vitamin A and E, appear to depend upon interference with intestinal absorption (Trowell, Moore and Sharman, 1954; Arroyave *et al.*, 1959). Some deficiencies, such as those of iron and ascorbic acid, may not be apparent at the time of the acute episode but develop rapidly if the therapeutic diet does not supply these factors in adequate amounts.

III. PRINCIPLES OF TREATMENT

A. Dietary Measures

1. Meeting Protein Needs

(a) *The Amount of Protein*

All investigators are in agreement that large amounts of protein of high biological value are of primary importance in therapy, but the actual amounts administered vary widely. Carvalho (1947) reports satisfactory results with 3 to 4 g of milk protein per kg body weight per day, and DeMaeyer (1954) recommends 4·5 g per kg per day. Some investigators, however, on the basis of balance studies which indicate a direct relationship between the absorption and retention of nitrogen and the quantity of protein ingested, advocate much higher protein dosages. While Dean (1953) has used as much as 15 to 20 g per kg per day, he admits that no further beneficial effect is obtained from such high protein intakes, and recommends the use of 8 to 10 g per kg per day, which is approximately the same dosage as is used by workers in India (Gopalan and Ramalingaswami, 1955).

When the child consumes the food readily and milk is the major protein source, we generally employ intakes varying between 5 and 7 g per kg per day. Such levels are not usually attained, however, until the second week of treatment. Owing to the profound anorexia, intolerance to food, and the danger of abnormal distention of the stomach and intestine, it is necessary to initiate treatment at much lower levels of intake, particularly in severe cases. During the first 24 hours, 1 to 2 g per kg can generally be administered and this amount increased from 2 to 5 g per kg during the second to fourth day of treatment. It should also be clear that if intakes as high as 5 to 7 g of protein per kg are employed, these will gradually drop as the child gains in weight and as nitrogen stores are filled. Furthermore, the successful treatment of kwashiorkor with mixtures of vegetable origin, even though the intake conveniently attainable does not exceed 3 to 5 g of protein per kg because the bulk of food which the child can consume is limited, indicates that higher protein intakes are not necessary for complete and satisfactory recovery.

Recommendations regarding protein intakes which are based on weight have the limitation that cases of kwashiorkor vary from normal or even excessive weight for age to extreme underweight. In the marasmic case, calculation of protein intake on a weight basis according to the estimated requirements of a child of this weight may result in an absurdly small total protein intake while calculation on the basis of chronological age as given in most tables of requirements (British Medical Association, 1950; Canadian Council on Nutrition, 1950; National Research Council, 1953; Institute of Nutrition of Central America and Panama, 1953) results in an impossibly high one. The present recommendations for the 3 to 7 g per kg in the treatment of kwashiorkor attempt to take these factors into consideration and leave considerable room for judgement as to whether the lower or higher intakes within this range are most appropriate in a specific case. If the total protein intake based initially on 5 to 7 g of protein per kg is kept constant, the increasing weight of the recovering child results in a gradual reduction of the protein intake per kg to the 3 to 5 g per kg range and eventually less. This is frequently the natural course of events since the child's willingness to eat and capacity to utilize large quantities of food decreases gradually as consolidation of cure approaches completion.

(b) *Proteins of Animal Origin*

Milk has been generally recommended as the most convenient source of protein for the treatment of kwashiorkor. Skimmed milk has been widely used because it has proportionally more protein and less fat than whole milk, and is recommended by many authors (Brock and Autret, 1952; DeMaeyer, 1954; Dean, 1953; Trowell, 1954; Raoult, 1954; Silva, 1954) as the most effective and practical way of administer-

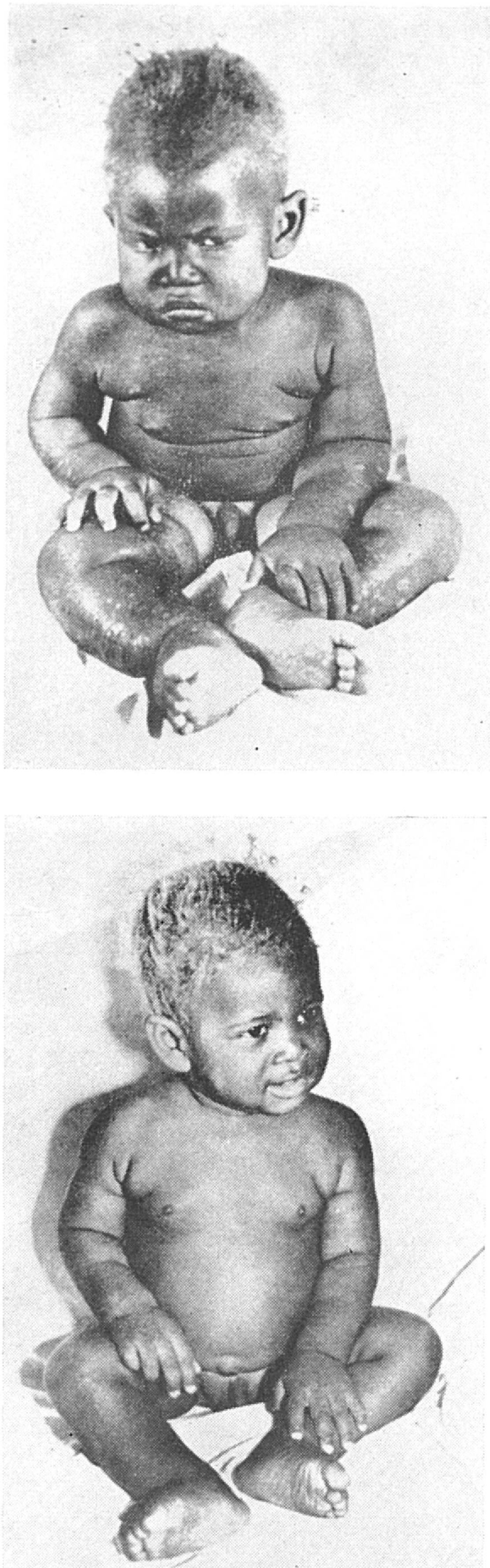


Fig. 4.1. Thirteen-month-old Boy With "Classical" Kwashiorkor (Sugar-baby), on Admission (Above) and 6 Weeks after Treatment (Below)

Notice the abundance of subcutaneous fat and the swiftness of recovery.

(*Composite photograph from Plates X and XI of the article "Kwashiorkor and Marasmus in Jamaican Infants" by Jelliffe, D. B., Bras, G. and Stuart, K. L., in the "West Indian Medical Journal,"* **3**, 43, 1954. *Use of this illustration was kindly authorized by Dr. Jelliffe.*)

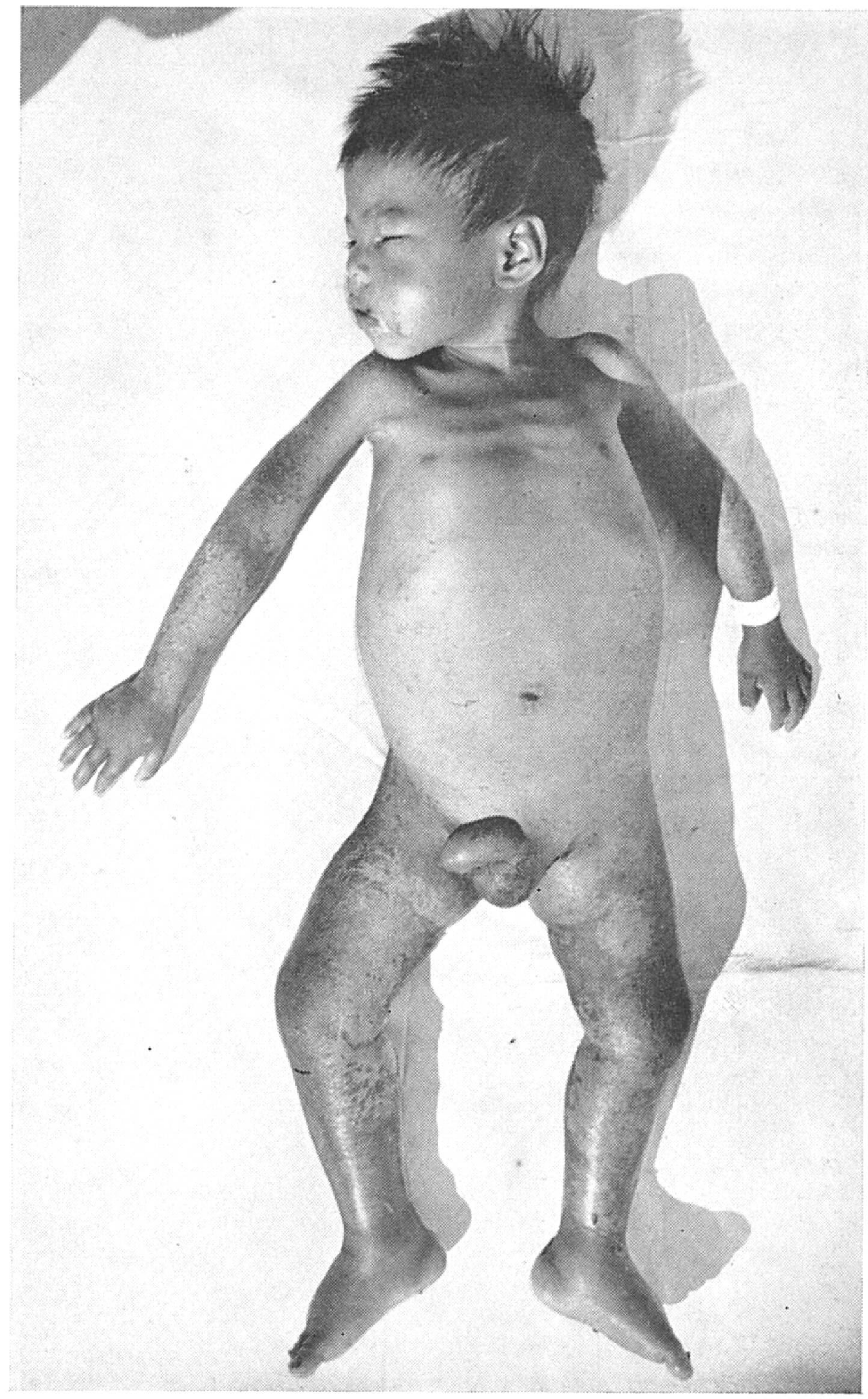


Fig. 4.2. Boy, 3 Years 9 Months of Age, with Marasmic Kwashiorkor as Usually Observed in Central America

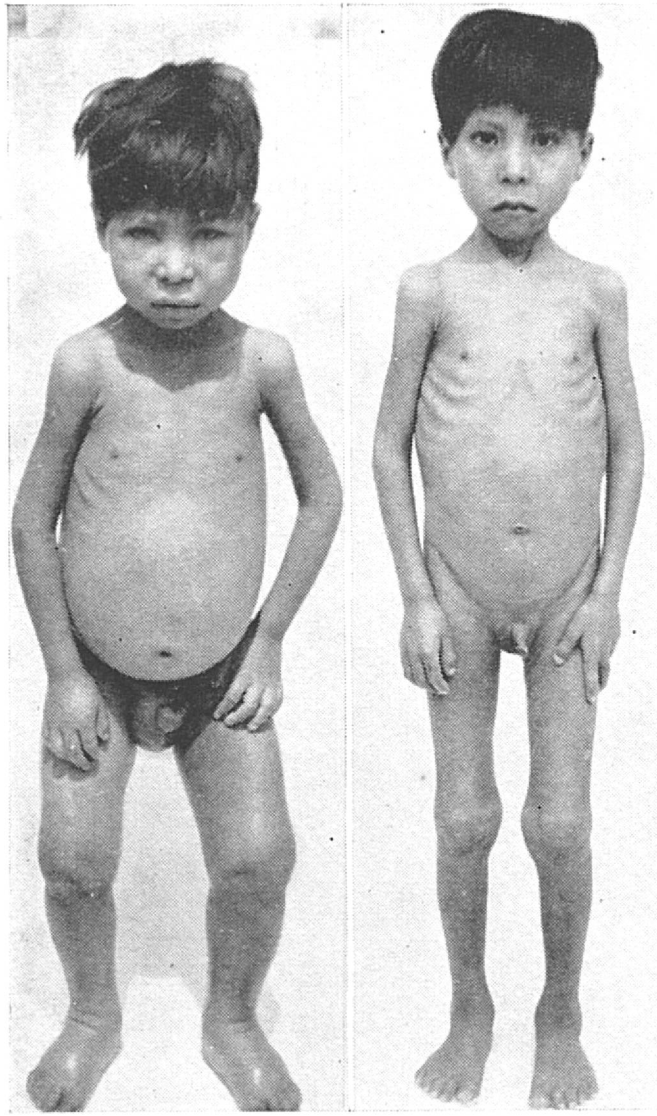
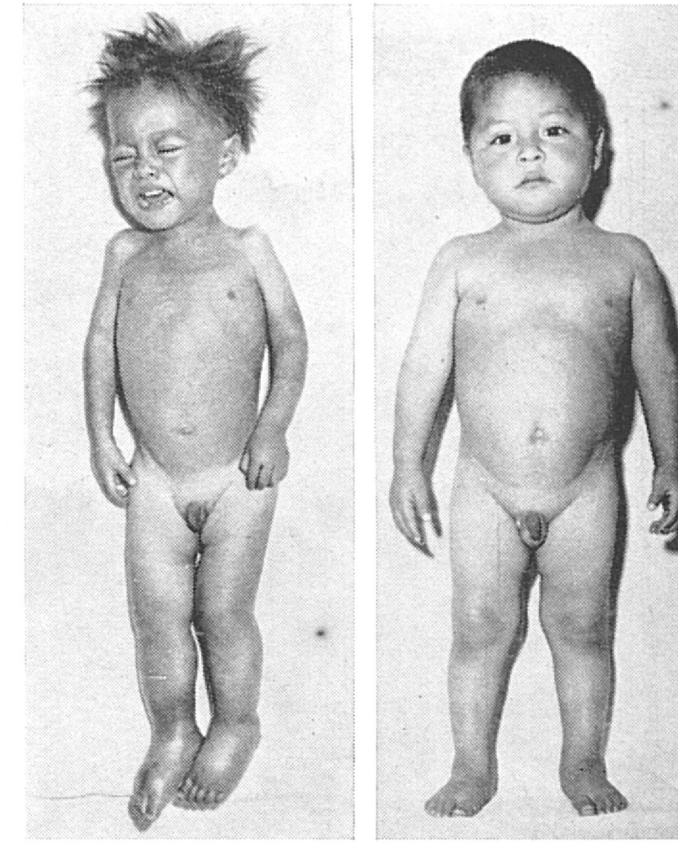


Fig. 4.3. Boy, 8 Years 11 Months of Age, with Marasmic Kwashiorkor, on Admission (Left) and 10 Days after Treatment (Right)

Notice how the loss of oedema makes more apparent the underlying wasting.

Fig. 4.4. Boy, 2 Years 8 Months of Age, with Kwashiorkor, on Admission (Left) and 19 Weeks after Treatment (Right) with INCAP Vegetable Mixture 8 as the Only Source of Protein



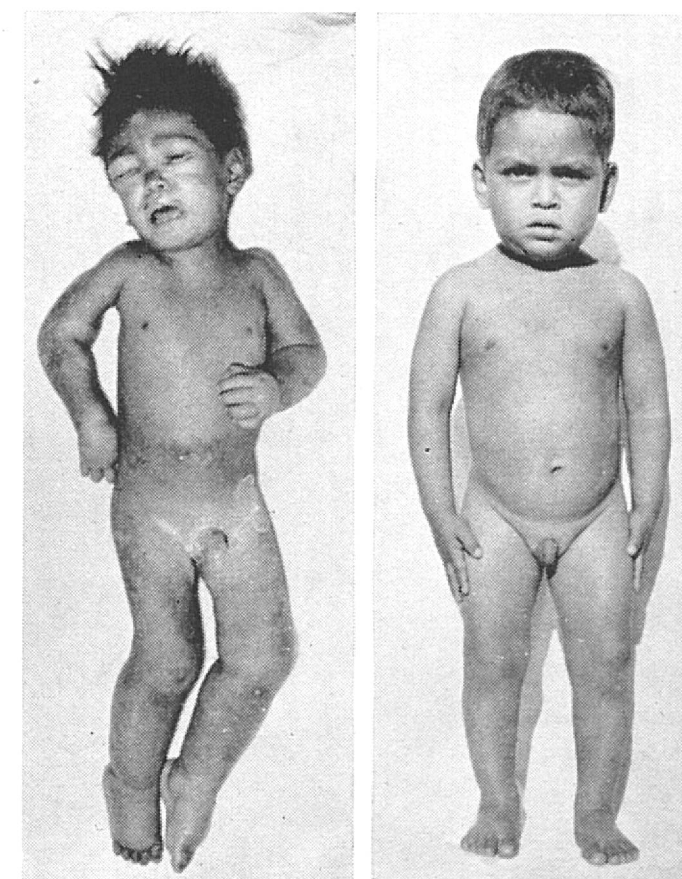


Fig. 4.5. Boy, 2 Years 8 Months of Age, with Kwashiorkor, on Admission (Left) and 15 Weeks after Dietary Treatment (Right) Initiated with Milk

ing the proteins needed in the therapy of kwashiorkor; half-skimmed milk, however, has given equally good results (Béhar, Viteri and Scrimshaw, 1957; Béhar *et al.*, 1958). Some workers (Achar and Benjamin, 1951; Gerbasi, 1956) prefer an acidified half-skimmed milk in the initial stages of the treatment, believing it to be more easily digestible in the presence of the gastric hypochlorhydria and initial enzyme deficiencies of kwashiorkor (Véghelyi, 1948; Gómez *et al.*, 1954*a*; Badr-El-Din and Aboul Wafa, 1957). Whole milk has also been used successfully from the beginning of treatment (Gómez *et al.*, 1958), although there are some reports of intolerance to it (DeMaeyer, 1954; Dean, 1953; Trowell, 1954). Both Dean (1953) and DeMaeyer (1954) have recommended the addition of calcium caseinate (Casilan, Casec) to milk to augment the protein content even more and state that this addition has also proved beneficial for the diarrhoea almost always present in these children at the time of hospitalization.

It is universally recognized, therefore, that milk proteins constitute an excellent treatment of kwashiorkor. The form in which they are administered is not important as long as the anorexia and inability to tolerate large quantities of food which are common in the acutely ill child are considered. Good results can be achieved with any of the recommended milks through the use of proper dilutions and dosages. We have achieved equally good results using either skimmed milk, half-skimmed milk or acidified half-skimmed milk. Similarly, Brock *et al.* (1955) have not found any difference in effectiveness between skimmed milk and casein. The possible influence of the quality and quantity of the fat and carbohydrate components of milk will be considered later.

The view that milk owes its initial therapeutic efficacy entirely to its protein content is strongly supported by the success of Brock *et al.* (1955) and Hansen, Howe and Brock (1956) in initiating cure of kwashiorkor with vitamin-free casein or even with suitable mixtures of synthetic amino acids. They are able to bring about disappearance or marked improvement of all the clinical characteristics of kwashiorkor with these preparations, although, as they point out, the other essential nutrients are soon needed for continued recovery.

Other proteins of animal origin (meat, eggs, etc.) have not been used in the initial stages of the treatment of kwashiorkor, mainly because of the inherent difficulties in the administration of these products to the anorexic child. It is recommended, nevertheless, that they be added as soon as convenient after the initial anorexia has disappeared. We have usually found it possible to introduce them not later than the end of the second or during the third week of hospitalization even in severe cases.

(c) *Proteins of Vegetable Origin*

Proteins of vegetable origin have been employed in the treatment of kwashiorkor in some areas, not in the expectation of obtaining better results than with milk, whose value and convenience are undisputed, but in an effort to assay their biological value as alternative protein sources for prevention. Suitable vegetable protein sources are required since milk supplies are often inadequate in the underdeveloped areas of the world in which protein malnutrition is prevalent, particularly for the vulnerable socio-economic groups in which kwashiorkor occurs.

Gómez *et al.* (1952) compared the progress of malnourished children treated with either a soya preparation or cow's milk, and were unable to detect any differences in recovery by the clinical and biochemical criteria employed except for a slower rise in total serum protein; the final serum protein levels in the two groups were identical. Dean (1953) reported satisfactory results in the treatment of kwashiorkor with a soya preparation, although both the disappearance of the oedema and the rise of serum albumin occurred at a somewhat slower rate than in similar cases treated with skimmed milk. The more extensive trials of the treatment of kwashiorkor with proteins of vegetable origin carried out in India (Venkatachalam *et al.*, 1956) and Central America (Scrimshaw *et al.*, 1957*a*) have evaluated vegetable protein sources for both treatment and prevention. In India, 59 children were treated with a diet based on Bengal gram as the only source of protein; another group of 19 similar children received their proteins from Bengal gram and rice. Forty-nine additional children receiving a skimmed-milk diet of equal protein content served as controls. The results of the treatment with proteins of vegetable origin were considered satisfactory although the disappearance of oedema and the rise of serum albumin again were slower than with milk; this was particularly true for the Bengal gram–rice diet. Although these findings suggest that the amino acid balance was not optimal in the vegetable protein diets employed, the skin lesions and the fatty infiltration of the liver disappeared as rapidly as with milk and no differences were observed in the rates of haemoglobin regeneration.

In Central America we have worked with two formulae based on plant products which are or can be made locally available. INCAP Vegetable Mixture 8 contains 50 per cent dried corn masa, 35 per cent sesame meal, 9 per cent cottonseed press-cake, 3 per cent torula yeast and 3 per cent kikuyu-leaf meal (Scrimshaw *et al.*, 1957*b*). This preparation has been given to children with moderate to severe kwashiorkor and has resulted in uniformly good recoveries without complications (Fig. 4.4). INCAP Vegetable Mixture 9 contains 28 per cent corn masa, 28 per cent sorghum masa, 38 per cent cottonseed press-cake, 3 per cent torula yeast and 3 per cent kikuyu-leaf meal and is more economical to produce in Central America in the present circumstances. Preliminary indications are that this formula also gives excellent results.

The development of vegetable mixtures will be discussed in more detail under prevention since this is the primary purpose for which they have been developed. Although the foregoing results leave no doubt that, if necessary, proteins of vegetable origin can be successfully employed in the treatment of kwashiorkor, the vegetable protein sources for this purpose must be carefully chosen, and skilfully combined. Their amino acid patterns must complement one another to correct the unbalanced pattern of amino acids characteristic to a greater or lesser degree of all vegetable proteins from a single food source.

2. Caloric Intake

The caloric intake is of secondary importance in the initial stages of treatment, although the diet should contain sufficient calories to ensure good protein utilization. It is extremely difficult, however, to begin treatment with a diet supplying the desired caloric content, owing to the anorexia and food intolerance of the child with acute kwashiorkor. Accordingly, we may give as few as 30 to 50 cal per kg during the first day and raise this level gradually to 100 cal per kg by the fifth or sixth day of therapy. Although this caloric intake seems low for severely malnourished children, it will ensure sufficient nitrogen retention to initiate recovery. This finding agrees with observations of Gómez *et al.* (1957*a*) which seem to indicate that with severe protein depletion nitrogen retention is still possible even in the presence of a low caloric intake when sufficient protein is given.

As soon as possible after anorexia has disappeared, and the digestive enzymatic activity has been restored, most authors recommend that the caloric intake should be increased gradually to about 150 cal per kg. This can be reached toward the end of the first week or during the second week of treatment (DeMaeyer, 1954; Dean, 1953). An increase in calorie intake is necessary for good weight gain and satisfactory recovery after the loss of oedemas and during that part of recovery which Brock calls the "consolidation of cure" (Brock *et al.*, 1955). This is the variable period after disappearance of the acute signs and symptoms during which the child is gaining weight and gradually becoming ready for discharge from the hospital. A high caloric intake is particularly important when the child is suffering from the marasmic type of kwashiorkor, and is very much under-weight after the loss of oedema.

Gómez *et al.* (1958) have given as many as 200 to 250 cal per kg to children recovering from marasmic kwashiorkor. It is probable, however, that diets with such a high caloric content, of predominantly carbohydrate origin, are largely responsible for the "nutritional recovery syndrome" described by these authors. The symptoms, which include enlargement of the liver, ascites, increased superficial circulation over the abdomen and hypertrichosis, have not been reported with comparable frequency or severity by other workers, although we have occasionally noted these symptoms in milder form in children of the marasmic type recovering on very ample diets. This syndrome would appear comparable to that observed with the rapid refeeding of persons in prison and concentration camps following World War II, and it should be regarded, tentatively at least, as an indication that the upper limits of refeeding are being exceeded.

3. Sources of Carbohydrate

Some authors have suggested that the child with kwashiorkor has a decreased tolerance for certain sugars, especially lactose and sucrose (DeMaeyer, 1954; Dean, 1953; Trowell, 1954; Dean, 1956). Dean (1953, 1956) and DeMaeyer (1954), for example, believe that the high lactose content of skimmed milk may aggravate the tendency to diarrhoea, and recommend the use of bananas and rice as carbohydrate sources in the initial phase of treatment. Nevertheless, most workers consider milk with added sucrose entirely satisfactory, and in using acidified half-skimmed milk we have not encountered any difficulties. Acidified milk does contain less lactose than non-acidified milk since part of the sugar is transformed into lactic acid, but there is no evidence that this particular change is of significance. In common with other investigators, we find bananas to be well tolerated even as part of the initial treatment and use them regularly as a carbohydrate supplement.

The vegetable mixtures developed as protein sources contain carbohydrate in a very satisfactory form for the treatment of kwashiorkor. The tendency for diarrhoea to disappear more quickly with the use of these vegetable mixtures than with milk has been repeatedly noted (Venkatachalam *et al.*, 1956; Gopalan, 1956), and, as Dean (1953) has suggested, may be due to the differences in carbohydrate content of the two types of dietary regimens.

4. Amount and Type of Fat

The proper amount and kind of fat to be included in diets for the treatment of kwashiorkor, especially during the early stages of recovery is still a matter of controversy. There is little doubt that the ability to absorb fat and fat-soluble factors is initially impaired, but this seems to be recovered very rapidly when adequate protein is supplied. The evidence for this comes directly from studies of fat (Holemans and Lambrechts, 1955; Gómez *et al.*, 1956) and of vitamin A absorption (Arroyave *et al.*, 1959), and indirectly from measurements of the lipase activity in the duodenum (Véghelyi, 1948). Recovery of ability to absorb oral vitamin A occurs in 3 to 5 days with optimum dietary treatment (Arroyave *et al.*, 1959), and intestinal enzyme activity is restored within 3 days (Véghelyi, 1948).

Certainly, early in treatment fat absorption becomes proportional to fat intake (Holemans and Lambrechts, 1955; Gómez *et al.*, 1956; Robinson *et al.*, 1957). Furthermore, as Holt (1956) has strongly emphasized, the presence of excessive fat in diarrhoeal stools in the initial stages of treatment is not a contra-indication to the incorporation of fat in the diet. While adding fat to the diet may increase faecal fat in this circumstance, it also increases fat absorption so that useful additional calories are provided which spare protein and facilitate recovery.

For these reasons we cannot accept the point of view that children with kwashiorkor cannot tolerate fat of any kind (Trowell, 1954) nor that milk fat should not be given (Dean, 1953). We are impressed, however, with the success of Dean and Skinner (1957) in feeding 30 to 50 g of vegetable fat from soya or cottonseed. They report that this quantity is well tolerated and aids greatly in maintaining adequate caloric intake. The INCAP Vegetable Mixture 8, which has proved to be well tolerated even in severe cases of kwashiorkor, contains 35 per cent of sesame oil meal with a fat content of 33 per cent and thus supplies about 20 g of fat from this source as fed to a 10 kg child by the end of the fifth day of treatment.

Fat is not only a valuable source of calories, but also provides essential fatty acids which may be of benefit to the child, particularly since the characteristic diets leading to the development of kwashiorkor are often almost wholly devoid of fat. In general it does not seem justifiable to restrict fat intake with the possible exception of the first two or three days of treatment.

While we prefer to begin treatment with only the fat supplied by half-skimmed milk, whole milk is substituted by the end of the first week and additional fat of vegetable origin added to the diet so that 15 to 20 per cent of the total calories in the therapeutic diet are supplied by fat.

5. Vitamin Requirements

The associated vitamin deficiencies in kwashiorkor vary in nature and severity from one region to another, depending upon the diets which the children receive prior to developing the disease. Vitamin A and some of the B-complex vitamins are particularly likely to be deficient, because the diets in underdeveloped areas in general frequently result in these deficiencies. In Central America, lip and tongue changes suggestive of riboflavin deficiency are frequent in the general lower-income groups (Pérez, Arce Paiz and Maza, 1955). Studies carried out at INCAP on pre-school children have also revealed the serum levels (Carrascosa, 1956) and urinary excretion of this vitamin to be reduced (Arroyave, Sandstead and Schumacher, 1958).

The fact that vitamin A deficiency is observed even in regions where the dietary intake of this nutrient is not excessively low has led Trowell, Moore and Sharman (1954) to suggest that the deficiency of vitamin A is due largely to the poor fat absorption. When both low intakes and poor absorption occur, avitaminosis A may be of such magnitude as to produce severe ocular lesions (Oomen, 1954), such as Bitot's spots and keratomalacia. In Central America, eye lesions are frequent but usually not severe. They include dryness of the cornea and thickening of the conjunctiva. Serum levels of vitamin A and carotene, however, are nearly always very low (Scrimshaw *et al.*, 1956; Béhar *et al.*, 1956; Scrimshaw *et al.*, 1955).

Ascorbic acid deficiency in kwashiorkor has been reported only occasionally since most underdeveloped areas have abundant natural sources of this vitamin. In Central America we have encountered no clinical evidence of ascorbic acid deficiency; serum levels of this vitamin are relatively high in most individuals. Although we frequently find low serum levels of this vitamin in kwashiorkor, they are not at the zero or near-zero limits associated with clinical scurvy.

Because signs suggestive of vitamin deficiency and skin lesions of a pellagroid type are almost universally present, it is not surprising that many early investigators tried the administration of therapeutic doses of vitamins in the treatment of kwashiorkor. Experience has demonstrated, however, that this is not only unnecessary but may prove detrimental. Carvalho (1947) reports greater mortality in a group of children who were given B complex than in another group treated identically but without B complex supplement and attributes the higher mortality to a greater fatty infiltration of the liver. Furthermore, Brock *et al.* (1955) have demonstrated that "initiation of cure", that is, the initial recovery which includes loss of oedema and apathy, frank improvement of skin lesions, recovery of appetite, etc., which usually occur before the twenty-first day of treatment, is achieved with vitamin-free casein and even with a mixture of synthetic amino acids.

While some authors (DeMaeyer, 1954; Gerbasi, 1956) routinely administer an oral preparation supplying physiological amounts of the common vitamins, this is not necessary for good recovery if attention is given to supplying all of the essential nutrients in a balanced diet. Trowell (1954), Altmann (1948) and

Gómez *et al.* (1954*b*) report good recoveries without the use of any vitamin products. We do not use them at all when employing vegetable mixtures which are balanced to contain sufficient vitamin A activity and B-complex vitamins. When ocular lesions are present, however, and we are using half-skimmed milk, which fails to supply sufficient vitamin A, we give 3,000 to 5,000 I.U. of vitamin A orally but only until adequate natural sources of this vitamin can be introduced into the diet.

There is no evidence that a deficiency of vitamin B_{12} plays a role in kwashiorkor. Even though the anaemia of kwashiorkor is frequently macrocytic in type (Scrimshaw *et al.*, 1956; Adams, 1954; Mehta and Gopalan, 1956) the bone marrow, in Central America at least, is not megaloblastic. Furthermore, not only does this anaemia respond well to the administration of skimmed milk but the serum vitamin B_{12} values are within normal limits.[1] Since megaloblastic anaemias have been reported in kwashiorkor (Adams, 1954; Mehta and Gopalan, 1956), it is possible that in these cases vitamin B_{12} deficiency is superimposed on the primary protein deficiency of kwashiorkor as may occur with other vitamins of the B complex. Dean (1953) has recommended massive doses of vitamin B_{12} when weight gain appeared stationary during the consolidation of cure. Other authors have found no response to the administration of this vitamin (Trowell, 1954; Silva, 1954). We have been unable to confirm the claim of benefit from vitamin B_{12} administration and have markedly reduced the frequency and duration of stationary periods in weight gain during recovery by taking precautions to reduce the spread of intercurrent infections, particularly that of diarrhoea of infectious origin.

6. Mineral Needs

The characteristic anaemia of kwashiorkor is normocytic or macrocytic in type and generally mild unless complicating factors are present. In regions where chronic malaria or hook-worm occurs in young children, severe microcytic, hypochromic anaemia may be present initially and require specific iron therapy as part of the initial treatment. Even when the anaemia is not of the iron-deficiency type, it must be recognized that the stores of body iron are limited. With a therapeutic diet based on milk, there is a rapid haematopoiesis, without an iron intake adequate to meet the increased iron requirements. The child may then develop a microcytosis and a decreased mean corpuscular haemoglobin concentration, despite a continuing rise in the red blood-cell count. In these circumstances iron has become a limiting factor and the administration of supplementary iron will evoke a second reticulocyte response and the gradual return of the mean corpuscular volume to normal.

Accordingly, we consider it desirable to begin the administration of an iron preparation during the second or third week of treatment, and have obtained good results with the oral administration of 300 to 600 mg of ferrous sulphate per day in single or divided doses. As other investigators have also reported (De Maeyer, 1954), such a preparation can be safely administered at this stage of recovery without intolerance.

7. Other Dietary Supplements

In view of the fatty infiltration of the liver, some early reports recommended the use of lipotropic agents (Meneghello, 1949). However, Carvalho (1947) does not find products such as choline chloride or desiccated pancreas to be useful, and most investigators now believe that the fatty infiltration of the liver in kwashiorkor is not related to a deficiency of lipotropic factors. Particularly since this infiltration recedes quickly and completely upon administering proteins of a high biological value, the use of lipotropic preparations does not appear justifiable.

8. Summary of the INCAP Dietary Regimen

Although a variety of protein and caloric sources can be successfully employed, we find it most convenient to begin the treatment of severe kwashiorkor cases with acidified half-skimmed milk diluted to half strength with water to which 5 per cent sugar has been added. Because of anorexia, this is administered in doses of 120 cc every 2 hours (eight times a day), or if not well tolerated or accepted in this amount, in smaller doses of 60 cc every hour (17 times a day). These quantities supply from 1 to 2 g of protein and from 30 to 60 cal per kg during the first 24 hours. It may be given by gastric tube if necessary in extreme anorexia. If it is well tolerated the concentration is increased to three-quarters strength during the second 24 hours and to full strength by the third or fourth day. The amount of formula given is increased as rapidly as accepted to 180 cc every 3 hours (six times daily) and then to 240 cc at the same intervals (five times daily), so that the child receives approximately 5 g of protein and 100 cal per kg by the fourth to sixth day of hospitalization. We begin to give the child bananas as soon as he will accept solid food, usually on the second or third day after admission.

During the second week of therapy the child is gradually changed to whole non-acidified milk and the amount is increased to supply approximately 7·0 g of protein per kg. With two bananas a day and 120 cc

[1] The co-operation of Dr. Grace Goldsmith, Professor of Medicine, Tulane University School of Medicine, in arranging for the vitamin B_{12} determinations is gratefully acknowledged.

of orange juice the total calories can be readily brought to approximately 130 per kg. During the second and third week green and yellow vegetables are added to the diet, and by the third or fourth week meat, egg, cereals and bread can all be given. By the end of the first month the child should be receiving a varied and balanced diet supplying 5 to 6 g of protein per kg, 140 to 150 cal per kg, and containing all the necessary vitamins and minerals in physiological amounts. No vitamin supplements need be administered. An oral iron preparation supplying 60 to 120 mg of iron is introduced during the second to fourth week of treatment to meet the increased demand occasioned by rapid haematopoiesis (Fig. 4.5).

B. Correction of Electrolyte Disturbances

The treatment of kwashiorkor is greatly complicated by potassium depletion, which is reported to be a manifestation of the severe protein deficiency (Hansen and Brock, 1954; Metcoff *et al.*, 1956; Politzer and Wayburne, 1957; Senecal, 1958) and in most instances also by a serious fluid and electrolyte imbalance resulting from diarrhoea and occasionally from vomiting (Metcoff *et al.*, 1956; Gómez *et al.*, 1957*b*). Hansen and Brock (1954) consider that the potassium deficiency is a factor in the aetiopathogenesis of the oedema, while Thompson (1955) reports hypokalaemia only in patients with diarrhoea upon admission but finds that even in those cases without diarrhoea a subsequent potassium deficiency can develop if the child is given a diet high in protein without sufficient potassium to maintain a normal nitrogen/potassium retention ratio. Furthermore, serum potassium levels do not always reflect the basically intracellular deficiency of this electrolyte. Balance studies conducted by Hansen and Brock (1954) in South Africa, and tissue analysis carried out in Mexico (Metcoff *et al.*, 1956; Frenk *et al.*, 1957) demonstrate a deficiency of potassium in kwashiorkor; both determinations are much more revealing than the measurement of serum levels.

Finally, some of the clinical manifestations of acute kwashiorkor, such as the psychic changes, anorexia, vomiting, abdominal distention and weakness (Politzer and Wayburne, 1957; Thompson, 1955), may be explained, at least in part, by potassium deficiency.

In order to correct this disturbance, some authors recommend the routine oral administration of potassium at least in those cases in which a deficiency is suspected. Thompson (1955) recommends 1 g daily of potassium chloride during the first 10 days; similarly, Politzer and Wayburne (1957) employ a mixture of equal parts of potassium acetate, bitartrate and citrate and even recommend the intravenous administration of potassium chloride when there is evidence of hypokalaemia.

Senecal (1958) recommends the addition of 100 to 200 mg of potassium per kg per day to the therapeutic diet, preferably as citrate or acetate in order to avoid aggravating the acidosis resulting from a high protein diet.

We have obtained good results with the addition of 1 g of potassium chloride to the diet in those cases suffering from persistent diarrhoea or which have clinical manifestations suggesting a potassium deficiency; we do not prescribe it, however, until we are certain that diuresis is adequate. Appreciable amounts of this element should not be given parenterally except under careful laboratory control of serum levels and adequate facilities to follow electrocardiographic changes.

Serious disturbances in water and electrolyte balance have been recognized as important causes of mortality during the first forty-eight hours of hospitalization (Gómez *et al.*, 1957*b*). Frequently, these children enter the hospital severely dehydrated as a result of prolonged diarrhoea, and possibly also vomiting, even though the severity of the dehydration may be partially concealed by the oedema. Particularly detailed and valuable investigations of this problem have been carried out in the Children's Hospital of Mexico City (Metcoff *et al.*, 1956; Gómez *et al.*, 1957*b*; Frenk *et al.*, 1957; Gordillo *et al.*, 1957; Metcoff *et al.*, 1957). The results of these studies indicate that the electrolyte disturbances in malnourished children with diarrhoea are qualitatively different from those of well-nourished children with this symptom and much more difficult to correct.

Two fundamental characteristics are reported for the dehydrated and severely malnourished children—(1) hypotonicity of the extracellular fluid with an expansion of the aqueous intracellular phase independently of the volume of extracellular fluid; (2) an increase of intracellular sodium relative to the increased water content of this compartment and reduction of both the absolute and relative intracellular concentration of potassium. The specific cause of these alterations is at present unknown but they are usually reversible with treatment. Death sometimes occurs, however, as a direct consequence of the disproportionate expansion of intracellular at the expense of the extracellular fluid. In malnourished children there is a decrease of the filtration rate through the kidneys, considered by the Mexican workers to represent a defence mechanism for the maintenance of extracellular volume. The renal plasma flow is also decreased and this is interpreted as an adaptation to the cellular hypotonicity.

These alterations explain why many children do not respond to the measures usually employed to correct dehydration in a well-nourished child. The authors report the successful treatment of extremely severe cases with intravenous hypertonic saline for the purpose of relieving the intracellular oedema. However, as the authors state, before recommending general use of this potentially dangerous measure, additional studies and observations are necessary.

To combat this electrolytic imbalance, Brock *et al.* (1955) recommend the oral administration, or intravenous if necessary, of an electrolyte solution (such as Darrow's or Hartman's) with glucose, during the first twelve to twenty-four hours. When there is no clinical evidence of dehydration, we follow a similar practice.

If there is severe dehydration associated with diarrhoea and/or vomiting, we treat this condition and disregard the coexistent malnutrition and the presence of oedema. Usually treatment is initiated with the intravenous administration of the so-called 1–2–3 solution which contains 1 part of one-sixth molar sodium lactate, 2 parts of Ringer solution and 3 parts of 5 per cent glucose solution. This is a hypotonic solution, and according to the data obtained from studies carried out in Mexico, it should not be the method of choice. Nevertheless, in contrast to the abundant hypotonic urinary excretion reported by workers in Mexico, we have observed a marked oliguria in these children, and have found that both the dehydration and oliguria are considerably improved after the intravenous administration of hypotonic fluids in the amount of 40 to 50 cc per kg at a rate of 40 to 50 drops per minute. Once we have obtained sufficient diuresis, we continue with a solution richer in potassium (Darrow's) and, if necessary, with additional amounts of Ringer or normal saline solution in 5 per cent glucose, until the disorder has been corrected. If vomiting has been too severe and alkalosis is suspected, as may occasionally be the case, the sodium lactate is omitted from the treatment described.

Obviously, serial determinations of the child's ionogram can be of invaluable help in deciding the measures to be taken in the correction of the electrolytic imbalance. This is at present impossible, however, in the majority of hospitals in the underdeveloped areas of the world where kwashiorkor is a frequent problem. The indicated measures, which have been published in detail previously (Béhar, Viteri and Scrimshaw, 1957), have proved effective and easy to carry out even without laboratory facilities. However, we strongly urge further studies of the characteristics, mechanism of production and methods of correcting electrolytic disorders which are commonly present in the child with kwashiorkor and appear to be a frequent and baffling cause of death.

C. Role of Blood Transfusions

Blood transfusions have long been used in the treatment of kwashiorkor (Carvalho, 1947; Meneghello, 1949; Van der Sar, 1951; Gómez *et al.*, 1954*c*; Autret and Béhar, 1954; Waterlow and Vergara, 1956). Although in the past they have helped to compensate for inadequate initial therapy, they are rarely necessary if good dietary treatment is given. Only in the unusual case of severe secondary anaemia or circulatory collapse and shock from either toxic infectious processes or very severe dehydration, do we employ blood transfusions at present. In the latter they are not given until after initial treatment with appropriate electrolyte solutions. Small transfusions of from 10 to 20 cc per kg, which can be repeated if necessary, are preferable since greater amounts given at one time may cause circulatory embarrassment.

Blood transfusions are a costly and ineffectual means of administering protein and should not be used for this purpose; protein can be supplied in adequate quantities by dietary means and the expense of transfusions for this purpose is totally unjustified. The needlessness of blood transfusion emphasizes further the important fact that even severe kwashiorkor can be treated successfully in the small hospitals in rural areas with limited facilities and funds.

D. Use of Plasma and Protein Hydrolysates

Plasma should be used only when blood is not available for the treatment of the rare cases of circulatory collapse due to secondary complications. There is no justification for the use of either plasma or parenteral protein hydrolysates as a protein source, and there is evidence, from refeeding of prisoners after World War II, that the latter may aggravate liver damage in severe malnutrition.

E. Need for Antibiotics and Chemotherapy

Every sign or symptom of infection observed in a child with kwashiorkor should be treated promptly and energetically with antibiotics or chemotherapy, since infections interfere with the recovery of the child and may be more serious than they at first appear. Even when signs of infection are not detectable at the time of admission, we prefer to administer full therapeutic doses of penicillin during the first 10 days of hospitalization and find that this practice aids in the prevention of deaths that otherwise occur during the first week due to severe secondary infection. Broncho-pneumonia, for example, may develop asymptomatically without fever, leucocytosis and even without any respiratory sign or symptom. The seriousness of the problem is illustrated by the fact that 70 per cent of all autopsies of kwashiorkor deaths in Guatemala reveal a significant degree of broncho-pneumonia (Tejada, Béhar and Cofiño, 1956), and broncho-pneumonia is a major terminal cause of death wherever kwashiorkor occurs. For this reason the administration of either antibiotics or sulphonamides is widely employed as a routine preventive measure (Hansen, Howe and Brock, 1956; Waterlow and Vergara, 1956; Symonds and Mohammed, 1956).

No specific treatment need be given for diarrhoea since this is present upon admission in almost every child with kwashiorkor and usually disappears after a few days of adequate dietary treatment. When amoebae are identified in stool samples, however, specific therapy should be given promptly. Similarly, children in malaria regions should have their blood examined for malaria parasites and should be treated adequately if these are found. Although intestinal helminths are very commonly present, no effort should be made to eliminate them until the child is well recovered. They seldom interfere significantly with recovery and most antihelminthic drugs are dangerously toxic to severely malnourished children. Considerable numbers of intestinal helminths, particularly ascaris, are often spontaneously expelled coincidently with the initial dietary treatment.

F. General Hospital Care

Children suffering from kwashiorkor require special care and treatment during the initial phases of recovery. The attending staff must make sure that the child actually ingests the quantities of food ordered, even if it is necessary to resort to tube feeding. However, with patient and responsible personnel, gastric intubation can be avoided most of the time. In studies of the recovery of vitamin A absorption ability in kwashiorkor (Arroyave *et al.*, 1959), we have observed that children admitted to a general hospital ward took more than twice as long to recover this function than children under research care, even though identical orders for a therapeutic diet were written by the physician. Careful investigation revealed that the attending personnel in the general hospital did not have the time or patience to feed the children the prescribed diet.

In some hospitals, mothers are encouraged to stay in the hospital and help with the care of their children (Geber and Dean, 1956). This has the double advantage of ensuring individual attention for the child and teaching the mother correct feeding practices. For most mothers and hospitals this may be impractical, but frequent visits by the mother make possible careful explanation to her of the treatment given and the reasons why her child developed the disease. Since ignorance of proper feeding of young children is a major factor in the development of kwashiorkor, this type of instruction is often very effective. In follow-up visits to families with a child who has been treated for kwashiorkor, we sometimes find the former patient in superior physical condition to others in the neighbourhood because the parents have learned the importance of good nutrition.

The cross-infections common to a general hospital ward also greatly interfere with normal recovery and prolong hospitalization time. The treatment of kwashiorkor under conditions of semi-isolation instead of an open ward has been a major factor in reducing our usual hospitalization from 16–20 weeks to 10–14 weeks. The cost of separating children with kwashiorkor from each other and from those with general paediatric conditions is more than met by the saving due to the shorter hospital stay. More space, screens between beds, and more care in the washing of hands after attending other children with diarrhoea are helpful, and individual cubicles are desirable. These should be combined with hygienic measures on the part of personnel to limit cross-infections.

In severe cases with marked apathy and muscular hypotonicity, oedemas or skin exulcerations, frequent changes in position and cleanliness are particularly necessary in order to avoid decubitus ulcers or secondary infections of the cutaneous lesions.

It is also important to recognize that the children do react favourably to sympathy and kindness on the part of the personnel. Some children respond so remarkably to affectionate attention in the hospital as to suggest that its lack may have been a factor in the development of the syndrome as postulated by Geber and Dean (1956) for many African cases. Certainly it is particularly important that kwashiorkor cases be placed in the care of attendants who like children and are patient with them.

IV. FACTORS RESPONSIBLE FOR THE DEVELOPMENT OF CLINICAL CASES

Any discussion of the factors responsible for kwashiorkor must emphasize that clinical kwashiorkor *per se* is only an indication of the total extent of protein malnutrition among children in endemic areas. In most regions in which kwashiorkor is a public health problem, nearly all young children are affected by protein malnutrition, even though they may never develop the fully-fledged syndrome. Very often they do not even present sufficient obvious signs or symptoms to be considered ill (Scrimshaw *et al.*, 1955, 1957*a*), but their sub-optimal status is objectively revealed by retarded growth and development, which begins about the eighth month of life. The retardation is evident first in failure to register normal gains in weight and later in height as well as bone maturation, as compared with well-nourished children of the same age. This retardation is the result of inadequate supplementary feeding when the mother's milk, which previously had maintained the child in a good nutritional state, becomes insufficient to satisfy physiological requirements and later is withdrawn entirely as the result of weaning. Both growth and development may remain practically at a standstill until the child is three to five years old. After this, depending on the local circumstances, he receives relatively better nourishment which is more nearly that of the adult; at the same time, his requirements per kg of body weight gradually decrease.

Children suffering from sub-clinical protein deficiency tend to be apathetic, show marked muscular weakness and wasting and are slower to mature. They become ill easily and very often die of an infectious disease that is usually not fatal to well-nourished children. Even with very inadequate diets the physical examination may not reveal any signs of nutritional deficiency other than retardation of growth and maturation.

The problem of preventing kwashiorkor, therefore, consists not only in the elimination of the syndrome in its frank form, but also in the correction of the underlying malnutrition affecting the great majority of children in some areas; thus the presence of kwashiorkor must be considered only as the visible reminder of a grave and largely hidden problem.

While the prevention of kwashiorkor requires adequate food, which in turn involves economic factors, limited purchasing power is only one aspect and not usually the principal one. Diets consumed by school children and adults, even in the poorest communities, are usually not as deficient in relation to physiological requirements for protein as those consumed by pre-school children. In many regions of the world, the majority of these children are breast fed until they are at least one year old, and frequently, especially in the rural areas, until they are one and a half or two years old or even longer. In present circumstances, this prolonged breast feeding is advantageous for the child who after weaning receives a diet markedly deficient in protein, particularly in protein of animal origin. Supplementary feeding is introduced late to nursing infants, generally after the eighth or ninth month and often after the child is one year old. The foods employed in the supplementary feeding are the same foods given to the child after weaning. Unfortunately, the mother tends to consider that foods easily swallowed by the child are also easily digested. Accordingly, toward the end of breast feeding and after weaning, the child's diet is based primarily on starchy gruels, thin broths, breads, rice, noodles, a few vegetables and coffee. Although beans, for example, constitute a rich source of protein in the adult diet in Central America, small children are ordinarily given only the water in which these beans are cooked. When the family can afford meat, it is consumed only by the adults and older children for it is not considered appropriate for the small child.

The foregoing are merely examples of the great influence of ignorance on the prevalence of kwashiorkor. With local variations and in greater or lesser degree, poor feeding practices for the young child exist in all areas where kwashiorkor is prevalent (Williams, 1954; Jelliffe, 1955). Unfortunately, some prejudices against particular foods have a basis in experience and are accordingly difficult to combat. Prejudices against milk are an example. They exist in part because of the poor sanitary conditions under which milk has been available and its consequent association with diarrhoeal disease and even with death. Thus, when the mothers are told that cow's milk is a valuable food for the small child, they may still be reluctant to give it to their children, even when it is made available. Ignorance and lack of facilities for adequate preservation may also result in good milk supplies becoming unfit for consumption by the time they reach the child.

Prejudices such as the one described have particularly serious consequences when the child becomes ill. Feeding is restricted even more in the presence of any sickness and especially when the child has diarrhoea. The mothers believe that in order to correct the diarrhoea the child should be placed on a diet restricted largely to starchy gruels, rice-water or sugar-water. Such diets are sometimes prolonged for several weeks, since the child fails to improve, and the result is clinical kwashiorkor and death. Unfortunately, some physicians still recommend this type of diet in cases of diarrhoea in small children and thus help to perpetuate the belief and practice.

It is no coincidence that most kwashiorkor cases in Guatemala give a history of an episode of diarrhoea of apparently infectious origin shortly before the onset of the oedema, skin lesions and other signs of kwashiorkor (Scrimshaw *et al.*, 1957*a*). In addition to the worsening of the diet as the result of misguided therapeutic efforts, there is a direct contribution of the diarrhoea to protein malnutrition. Even with mild and transient diarrhoea and a relatively high protein intake of good quality, it has been shown experimentally that nitrogen retention in young children may actually become negative with this type of gastro-intestinal disturbance (Robinson *et al.*, 1957; Macy, 1958) and remain markedly reduced for a period of days thereafter. But the infectious diarrhoea affecting malnourished children in most technically underdeveloped areas is neither mild nor transient. It is sufficiently severe and frequent as to be a major primary cause of death among children under five years of age (Verhoestraete, 1956; Verhoestraete and Puffer, 1957). Preliminary studies in rural Guatemala, conducted by the Institute of Nutrition of Central America and

Panama (INCAP), indicate that at least 5 per cent of all children between one and four years of age have clinical diarrhoea at any given time; in two moderately poor, small highland towns, house-to-house visits every two weeks for twelve months revealed an average of five separate episodes of diarrhoea per year for children in the same age range. Prevalence studies carried out in four highland and four lowland towns over a two-year period suggest that much of the enteric infection is due to various strains of Shigella; at least as evidenced from even a single faecal examination by means of the rectal swab technique (Watt and Hardy, 1945; Hardy and Watt, 1948; Watt *et al.*, 1953; Hollister *et al.*, 1955). Shigellas were recovered in nearly 8 per cent of all children under ten years of age examined (Beck, Muñoz and Scrimshaw, 1957), while Salmonellas were present in less than 1 per cent. In most children from areas where kwashiorkor is endemic, there is also a very high prevalence of intestinal parasites of several species. While they do not seem to be factors of primary importance, intestinal parasites can have an adverse effect on protein absorption (Venkatachalam and Patwardhan, 1953).

Not only intestinal infections but also systemic ones can apparently have a markedly adverse effect on nitrogen retention. We were recently astonished to find that even during the prodromal stage of measles nitrogen retention was reduced in two children recovering from kwashiorkor. This would explain why there are children with histories of measles, chickenpox or other systemic infection which closely precedes the development of kwashiorkor. For children who are already basically malnourished, the added stress of infection, enteric or systemic, is often the factor determining the actual onset of acute kwashiorkor.

Kwashiorkor arises out of ignorance of proper feeding practices for the young child, a high prevalence of enteric infections due to poor sanitary practices, prejudices against the use of milk and other protein-containing foods of animal origin for young children, limitations in food production due to poor agricultural practices, and low purchasing power of the family as part of general poverty. All of these, with the possible exception of the last, are subject to direct attack by health workers, teachers and agriculturists.

The methods and opportunities for so doing are discussed in the sections which follow, and although they are presented with special reference to protein deficiency, they are generally applicable to the nutritional problems of children in technically underdeveloped areas. Techniques for the direct improvement of the economic status of countries or peoples are, however, considered to be beyond the scope of this review.

V. INCREASING PROTEIN SUPPLIES FOR HUMAN CONSUMPTION

The prevention of protein malnutrition requires greater availability and use of foods or combinations of foods whose protein is of good biological value. It is axiomatic that for good health and normal growth and development food must do more than satisfy hunger and provide energy; it must furnish protein containing the essential amino acids in the amounts and proportions required by the body, supplying also the other essential nutriments. It is appropriate, therefore, to examine ways in which the quantity and quality of protein for human consumption in technically underdeveloped areas may be increased.

A. Meat and Dairy Products

Products of animal origin are the major source of protein of high biological value in more technically developed countries. For young children cow's milk is of greatest importance. The capacities of technically underdeveloped areas to develop an animal industry without undue competition with food crops are often underestimated. Most such regions contain large areas which are suitable only for raising livestock and should be utilized for this purpose. Furthermore, farm animals, particularly ruminants, can thrive on foods and by-products which are not ordinarily suitable for human consumption. There have also been great technological advances in the feeding and management of livestock in tropical areas which should be applied. Some of these measures, such as the introduction of new grasses and improved management of grasslands, the control of ecto- and endoparasites, the maintenance of dry-season production through the use of silage and artificial feeding, and the use of proper mineral supplements, can revolutionize tropical agriculture and result in large increases in the availability of animal protein in areas in which kwashiorkor is now prevalent.

For example, in nearly all underdeveloped areas of the world, better management of cattle and the use of forages of high nutritional quality would significantly contribute to increase the production of animal proteins, particularly milk and milk products and meat. It has been shown in the American tropics that the production of animal products can be increased by the production and use of forages of good quality such as Desmodium (*Desmodium intortum*), kikuyu grass (*Pennisetum clandestinum*), quinamul (*Ipomonea sagittata*), ramie (*Boehmeria nivea*) and others (Squibb *et al.*, 1952; Squibb *et al.*, 1954; Bressani, Elías and Jarquín, 1959).

The production of another important animal protein source, poultry and eggs, could also be greatly increased through better feeding, management and selection of the birds. That this can be done even with locally compounded all-vegetable rations has been demonstrated. For example, good-quality forages (Squibb, Guzmán and Scrimshaw, 1953), palm-nut oil meals such as corozo, mbocayá palm and African palm (Squibb and Wyld, 1952; Squibb, Aguirre and Bressani, 1958) can be used successfully in poultry rations. These by-products of the oil industry cannot be used directly by humans because of their high fibre content which is uneconomical to remove.

B. Fish and Other Sea Food

Most countries have an opportunity to secure additional quantities of animal protein from fish and other sea food. The food potential of various products of the sea has been discussed recently by Weiss (1953), who has presented an impressive series of illustrations of types of highly nutritious foodstuffs which could be harvested from the sea in large quantities. He emphasizes that the food reserves of the sea molluscs, crustaceans (and even seaweeds) as well as fish deserve careful research to determine the best means of utilizing them. In addition to marine fisheries, the culture of fish, in natural or artificial fish-ponds, is already widely practised in the orient and can be adapted to most tropical regions.

The overall world shortage of protein of good quality has already stimulated studies on the nutritive value of derived products such as fish flour. Great uniformity has been observed in the amino acid composition of the protein of fish, the amino acid proportions of which are very similar to those of casein (Jaffé *et al.*, 1957). Fish proteins, like other animal proteins, are excellent sources of lysine, methionine and tryptophan, amino acids usually deficient in the cereal proteins which are the staple foods in underdeveloped areas (Flores and Reh, 1955*a*, *b*, *c*, 1955*d*; F.A.O., 1956; Sebrell and Hand, 1957). On the other hand, the biological value of the protein in derived processed fish products may differ. Bender and Haizelden (1957) studied twenty-seven fish meals and deodorized fish flours intended for human consumption and found net protein utilizations ranging from 18 to 80 per cent, digestibilities from 47 to 97 per cent, and biological values from 36 to 82 per cent. This and other studies (Cravioto *et al.*, 1955; Carpenter *et al.*, 1957) demonstrate that it cannot be assumed that a fish flour is a good protein source for human use until biological trials are carried out.

C. Legumes

The relatively high protein content and good protein quality for a single vegetable source, the soybean, has been extensively demonstrated and reviewed (Payne and Stuart, 1944; Cahill, Schroeder and Smith, 1944). In some areas soya is already a protein source of major importance to the human population, and wherever it is feasible to introduce or increase the production and consumption of soya and soya products, the problem of providing adequate protein supplies is greatly simplified. It should be noted, however, that it is not always easy to secure its acceptance by populations not accustomed to its use, and that the agronomic details of growing it have not been worked out for many of the regions in which protein malnutrition is a serious problem. For these areas it represents a potential long-range rather than an immediately applicable contribution to the solution of the problem.

Another promising protein source is peanut meal. Although it has the present disadvantage of high cost for many needy regions, its nutritive value alone and in combination with other foodstuffs has been well demonstrated (Sure, 1948*a*; Arthur, 1951; Holemans, Lambrechts and Martin, 1956). It is regarded as a practical component of vegetable mixtures for child-feeding in some areas and is under test in West Africa (Senecal, 1958). In South Africa dehydrated cowpea flour is commercially available as a protein source for supplementary feeding, particularly for school lunches (Hansen, 1958). The amino acid composition of a number of other tropical legumes has been studied (Vijayaraghavan and Srinivasan, 1953; Baptist, 1954; Jelliffe *et al.*, 1956). In general, these plant protein sources have a fair amino acid composition and their use as foodstuffs should be increased in areas where diets are deficient in protein.

D. Oil Seed Meals

In addition to the introduction of protein-rich plants, such as soybean, peanuts, and legumes, the press-cakes of oil seeds can be utilized for human feeding. This requires special processing, as is the case with the low-fibre, low-gossypol content cottonseed meal flour now available in the United States. Because of the economic importance of cottonseed meal to the cotton industry as a by-product and to the livestock industry as a protein supplement, cottonseed products as foodstuffs have received considerable attention and reliable information is now available as to their elaboration for use in foods destined for human consumption.

Other oil seeds which are being tested as possible protein concentrates for use in child-feeding, are rape seed (*Brassica napus*), sunflower seed (*Helianthus annuus*) and safflower seed (*Carthamus tinctorius*) (Fekete and Korpaczy, 1955; Klain *et al.*, 1956; Hale and Brown, 1957; Petersen *et al.*, 1957). Rape seed and sunflower seed oil meals are high in fibre and low in lysine (Klain *et al.*, 1956). However, Fekete and Korpaczy (1955) have described a specially prepared sunflower seed oil meal with a biological value surpassing that of soya. Decorticated safflower seed oil meal has been shown by Petersen *et al.* (1957) to replace satisfactorily part of the soybean oil meal in poultry rations for both growth and egg production. When substances toxic to animals occur in seeds, detoxified products can be prepared by special chemical treatment. For example, Ambekar and Dole (1957) have recently described a practical method for detoxifying castor seed cake for use in animal feeding, thus making available a protein-rich material used before only as a fertilizer. Thus, all the materials described above could, by the proper cultivation, management, and processing, be developed into useful products for the feeding of animals in order to increase animal protein production, and in combination with other foods for the feeding of humans.

E. Other Seeds

In the last few years reports have appeared in the literature on the biological value of certain seed proteins, which may be useful either alone or in combination with other sources of vegetable protein. Sure (1955) found buckwheat flour (*Fagopyrum esculentum*) when given to rats at the 8 per cent protein level to have the highest biological value of any known plant source of protein. The biological value of buckwheat protein for rats was 92·3 per cent of that of skimmed milk and 81·4 per cent of that of whole egg.

Quinua seed (*Chenopodium quinoa*, Willd), used for food in some South American countries has been shown by Quirós-Pérez and Elvehjem (1957) to have an excellent biological value as judged by the growth and lipotropic responses of weanling white rats. Under the experimental conditions used, at least seven essential amino acids had to be added to quinua to obtain slightly better weight gains than with quinua alone. The authors showed that the addition of 3 per cent casein to quinua, giving a total dietary protein of 12·42 per cent, produced the excellent growth of 36·7 g per rat per week and a normal amount of liver fat. This study confirmed a previous report by White *et al.* (1955), who showed with both young rats and depleted adult rats that, at equal levels of protein intake (6 or 9 per cent), the proteins of quinua produced gains equal or superior to those of milk protein, and that quinua supplemented with milk protein did not produce better gains than quinua alone.

F. Nuts and Palm Kernels

Dante Costa and De Paula Fonseca (1951) carried out research on the growth-promoting value of Brazil nut, black beans and milk, finding that the rat-growth-promoting value of the Brazil nut was 92 per cent of that of milk. If production can be increased and the cost of the Brazil nut decreased, this material could be used for child-feeding alone or in combination with other protein sources.

In the tropics there are other sources of vegetable proteins which, with further processing, could find use in preparations for the feeding of children. Important among these are the palm nut oil meals such as corozo, the African palm and the mbocayá palm. These nut oil meals have been tested on chicks by Squibb and co-workers and their amino acid composition determined (Squibb and Wyld, 1952; Squibb, Aguirre and Bressani, 1958). In recent years large-scale plantings of the African palm (*Elais guineensis*) in Central America have made available increased quantities of palm oil meal (Reif, 1951). Another palm, of the genus *Acrocomia*, grows in abundance from Central America to Argentina. The species *Acrocomia totai*, mbocayá palm, is of economic importance to Paraguay, where the fruit is eaten by both man and animals (Bertoni, 1941; Markley, 1955). Their biggest disadvantage as oil meals is their large crude fibre content, but it should be possible to correct this by proper processing.

G. Leaf Proteins

Attention has been focused for several years on the utilization of leaf protein for livestock feeding, and, possibly, for man. Several reports in the literature indicate that leaf proteins are relatively good supplements for cereal diets (Sur and Subrahmanyan, 1954; Sur, 1955). Kamath and Sohonie (1956) showed that the amino acid content of leaf protein, while inferior to casein, is sufficiently good to be a useful potential supplement to cereal diets. The amino acid composition of vegetable leaf proteins as well as the biological values of several preparations have been reported by Armstrong and Thomas (1950), Davies and Evans (1952) and Kelley and Baum (1953). The values varied from 55 to 71 per cent with very high digestibilities ranging from 76 to 93 per cent.

Leaf protein preparations have been made by expressing the juice from green crops, and coagulating it to obtain a product which, upon drying, has 30 to 60 per cent crude protein and less than 5 per cent crude fibre (Armstrong and Thomas, 1950; Cowlishaw *et al.*, 1956*a*; 1956*b*). However, the results of feeding this product have thus far proved disappointing.

Biological values of alfalfa protein have been found to range from 55 to 65 per cent (Armstrong and Thomas, 1950; Klosterman *et al.*, 1951) and both biological assays and chemical analyses have shown that methionine is a limiting factor (Klosterman *et al.*, 1951; Steward *et al.*, 1951). Processing methods still limit the feasibility of these leaf protein concentrates;

however, a successful product could be of practical importance for child-feeding.

H. Yeasts

Yeasts have received particular attention as protein supplements to both human and animal foods. The yeast *Torulopsis utilis*, which is preferred to brewer's or baker's yeast because of the greater economy of manufacture and freedom from bitterness, has received special attention (Owen and Johnson, 1955). Since the gross composition of the yeasts can be considerably varied by environmental conditions during production, strains of relatively high protein content can be produced if desired. Examples of this variability in yeasts have been given by Steinberg and Ordal (1954), who studied the effect of fermentation conditions on the rate of fat production by *Rhodotorula gracilis*.

I. Algae

The artificial culturing of unicellular photosynthetic organisms such as chlorella has been enthusiastically advocated by many investigators as a potential food *Nutrition Reviews*, 1955; Hundley, Ing and Krauss, 1956; *Nutrition Reviews*, 1958). Yields of cultured algae are large, and the ease with which their content of protein, fat and carbohydrate can be increased or changed by relatively slight manipulations of the culture conditions could make possible the production of a variety of food types from this single source. As yet, very few studies have been conducted on the value of algae as the major source of protein in animal diets, although the few which have been reported have indicated that up to 20 per cent of dried chlorella in the diet was beneficial for chicks and acceptable to human beings (*Nutrition Reviews*, 1958; Combs, 1952).

VI. PRINCIPLES OF PREVENTION

A. Use of Educational Techniques

Wherever kwashiorkor occurs, cultural factors, such as ignorance of the nutritional needs of the child and ways of satisfying them, prejudices or taboos against desirable foods and poor sanitary practices, combine with economic and agricultural limitations to determine the prevalence of the syndrome.

In preventing protein malnutrition in children, educational programmes can play an important role. These should involve all educational and income levels, with greatest emphasis among the low socio-economic group, who are the most affected. Appropriate teaching of the basic concepts of hygiene, including nutrition, should form part of the general educational programme and be included in campaigns against the illiteracy and ignorance which so greatly retard sound progress and economic development in technically underdeveloped areas. Co-ordinated efforts need to be carried out through schools, health centres, agricultural extension agencies, community development projects and such other means of diffusion of knowledge and contact with local people as may be available.

Basic principles of nutrition and general hygiene should be included in the curriculum of future teachers. Special orientation should be given to those persons who will be teaching in rural areas. These principles should be incorporated as an integral part of the general knowledge imparted by primary schools, and the child inculcated with concepts that will eventually influence family and community practices.

It is particularly important that social workers, nurses and doctors working in health centres, especially in the maternal and child health programmes, have adequate and practical knowledge of nutrition, and apply and transmit this knowledge as part of their health education activities and other applied programmes. Agricultural extension workers, home economists and home demonstration agents can also make a valuable contribution to the diffusion of the concepts of good nutrition.

As an example of what may be achieved when mothers are brought to a recognition of the importance of administering adequate diets to their children, our observations on our own hospital-treated cases of kwashiorkor may be cited. When these children return to their homes, after recovery and discharge from the hospital, the majority continue in good nutritional condition because the mothers have been convinced, through talks prior to the discharge of the patient, that a deficient diet was the principal cause of the disease. Most of these mothers have proved capable of administering a more nourishing diet to their children without any alteration in the economic condition of the family.

Unfortunately, in most underdeveloped areas there is a lack of personnel trained in nutrition to fill even the minimum needs required for initiating and supervising educational programmes. The training of qualified persons should, therefore, be a prime objective of organizations responsible for, or interested in, combating these serious nutritional problems. This must include the preparation of suitable teaching material in nutrition adapted to the local situation.

Nutritional education programmes should consider existing food habits and prejudices of the population, and employ to the fullest extent those sources of food which are locally available, or whose production can be readily increased or developed. Very frequently, personnel in charge of advising as to correct feeding habits, including physicians, make the mistake of recommending foods or cooking techniques which give excellent results in other circumstances, but which are impractical because they ignore local economic and cultural realities.

As will be discussed separately, supplementary feeding programmes should serve educational functions and they may frequently be major instruments for developing more desirable food habits.

All of the above educational activities are of importance, and require the co-ordinated efforts of several agencies working in an area. Personnel in the field of health, education, agriculture and welfare should co-operate in nutrition programmes designed to prevent kwashiorkor. Such co-operation, however, is often difficult to achieve because of the failure to realize the gravity and importance of malnutrition in areas in which kwashiorkor occurs. For the best results, it is essential that project leaders and professional personnel recognize the importance of the problem before undertaking popular education campaigns.

B. Improving Dietary Protein

1. Increased Use of Animal Protein in Mixed Diets

When diets contain predominantly protein of high biological value, it is relatively easy to ingest quantities adequate to meet protein needs. As protein quality drops, the amount of food which must be consumed to meet protein needs increases to the point at which monotonous diets containing an unbalanced protein (*e.g.* corn or millet diets) cannot be consumed in sufficient quantities to make up for the poor quality of their protein. The prevention of protein malnutrition for people consuming such foods requires an improvement in the biological value of the protein in the diet.

The classical method of so doing is to increase the proportion of protein of animal origin. This is the basis for various milk distribution and milk conservation programmes. Increased consumption of meat, eggs, cheese and fish can be similarly effective. Animal products are particularly good supplements to the protein of cereals so that the resulting increase in biological value has benefits beyond the protein content of the animal products themselves. This is due in part to the fact that they supply adequate lysine, which is a limiting amino acid in cereal proteins. For example, it has been demonstrated that neither wheat flour supplemented with milk and meat nor a wheat cereal product combined with 30 per cent milk powder are further improved by supplementation with lysine (Sarett, 1956). When animal proteins supplement corn diets, they supply important quantities of tryptophan as well as lysine (Cravioto *et al.*, 1955). In addition to recent amino acid studies with cereals there are, of course, numerous demonstrations of the improvement in protein nutrition which result from adding animal protein foods to predominantly vegetable diets (Costamaillere and Ballester, 1956; Carpenter *et al.*, 1957; Sure *et al.*, 1957).

2. Complementary Combinations of Vegetable Proteins

In many areas, however, sufficient animal protein is not available nor likely to be in the foreseeable future. Fortunately there are other means of improving dietary protein. The approach which appears to have the greatest immediate practicality, and on which work is most advanced, is the improvement of the protein content of diets by combining protein sources of vegetable origin to improve the total amino acid pattern of the diet.

Desikachar, Sankaran and Subrahmanyan (1956) have demonstrated by biological trials on rats the improvement in protein value obtained by adding soya or Bengal gram to mixed local diets based on rice. Phansalkar and Patwardhan (1956) have shown that the egg-replacement and biological values of proteins from vegetables were higher when the protein was derived from mixtures of Indian cereals and legumes than when derived from a single cereal grain such as wheat.

Several combinations of cereal grains and legumes with a high nutritive value have been described by Tongur and Orlova (1956). The best mixture tested contained 60 per cent buckwheat, 20 per cent soya and 16 per cent rice, and proved to be better than casein when tested in rats.

Mangay, Pearson and Darby (1957) showed that millet (*Setaria italica*) will correct the niacin deficiency induced in the rat by a 9 per cent casein and 40 per cent corn diet. The authors also showed that the addition of 1 per cent lysine to a diet of 40 per cent corn and 40 per cent millet improved growth considerably, but produced no response when added to a diet of 80 per cent corn and 10 per cent millet unless niacin and/or tryptophan were also added. Millet, therefore, improved the tryptophan but not the lysine deficiency of corn. Other studies have shown that corn and other cereal proteins can be improved biologically by adding yeast, soybean flour, or peanut meal (Sure, 1948*a*, *b*). Both corn and wheat flour can be improved by adding buckwheat flour as shown by Chen and Wang (1937), Orru (1940), Sure (1955), and Koyanagi, Ota and Takanohashi (1956).

3. Prepared Vegetable Protein Mixtures for Child Feeding

It is clear from the preceding section that many different combinations of vegetable proteins can be devised which are of high nutritive value, and that protein quality can be improved by this means wherever animal protein is costly or in short supply. It is also quite feasible to prepare combinations of vegetable protein sources in a form suitable for the supplementary and mixed feeding of infants and young children. In order to do this the following should be taken into consideration—

(*a*) The amino acid composition of the individual ingredients and of the final product.

(*b*) The possible presence of toxic or interfering factors.

(*c*) The need for obtaining exact specifications for each of the components.

(*d*) The necessity of avoiding processes that damage the quality of the protein.

(*e*) The desirability of using products of local origin.

(*f*) The fact that the final product must be inexpensive and easily preserved.

(*g*) The requirement that it may be easily used in the home as an infant food by mothers of low-income families.

(*h*) The demand that it must not run counter to the existing dietary habits and prejudices.

Promising mixtures should be analysed for their nutritive value as finally prepared. They should then be submitted to careful biological testing in animals and later in children before they are recommended for general use. Suitable criteria are listed in the report of the Princeton Conference on Human Protein Requirements and their Fulfilment in Practice (Waterlow and Stephen, 1957).

Although the primary objective in developing such mixtures is the provision of an inexpensive supplementary source of protein whose quality is better than that in existing diets, care should be taken to ensure an adequate content of the vitamins and minerals which are likely to be deficient in the local diets. Otherwise, the beneficial results from improved protein intake may be negated by deficiencies of other nutriments, and the product fail in its purpose of improving human health. Taking account of these considerations, and encouraged by the success of Gómez *et al.* (1952) and Dean (1953) in treating malnourished children with soya preparations, the Institute of Nutrition of Central America and Panama has developed INCAP Vegetable Mixture 8 made up of 50 per cent dried corn masa, 35 per cent sesame meal, 9 per cent cottonseed press-cake, 3 per cent torula yeast and 3 per cent kikuyu-leaf meal. This mixture has proved to be a good protein source for children recovering from kwashiorkor and for the rehabilitation of undernourished children (Scrimshaw *et al.*, 1957*a*, *b*; Béhar *et al.*, 1958). A still cheaper preparation, Mixture 9, omitting the sesame oil meal, is now being tested. This formula, which consists of 28 per cent dried corn masa, 28 per cent ground sorghum, 38 per cent cottonseed press-cake, 3 per cent torula yeast and 3 per cent kikuyu-leaf meal is scheduled for field use in Central America in the near future.

The Indian Council of Medical Research (Subrahmanyan, Patwardhan and Moorjani, 1955) has reviewed work carried out in India and China on the preparation, testing and use of milk substitutes for child-feeding in areas where milk production is inadequate, and concluded that simple preparations from soybean, peanuts, cashew nuts, coconut, or legumes can be helpful in supplementing poor cereal diets. These workers have also described the development, testing and economic aspects of a multipurpose food composed of 25 per cent Bengal gram grits and 75 per cent peanut cake grits fortified with calcium phosphate, thiamine, riboflavin and vitamins A and D in suitable proportions. The multipurpose food was tested as a supplement to poor cereal diets for undernourished children and in the treatment of nutritional oedema, and found effective.

Senecal (1958) has reported a mixture of millet and peanut press-cake to give good results in the treatment of kwashiorkor. A vegetable milk prepared from peanuts has been tested by Holemans, Lambrechts and Martin (1956) and found to be a good supplement as judged by both biochemical analyses and clinical indices. Hansen (1958) has had good success in treating kwashiorkor and in demonstrating satisfactory nitrogen retention in children using a mixture containing 33 per cent whole ground corn (mealie meal), 33 per cent corn germ and 33 per cent green cowpea flour (*Pisum arvense*).

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4. Addition of Synthetic Amino Acids to Vegetable Diets

Improvement of poor-quality protein or of amino acid deficiencies in food protein can also be achieved by the addition of the deficient amino acids. In underdeveloped areas the amount of animal protein consumed is low and there is a corresponding increase in consumption of cereal grains, which contain protein deficient in several amino acids. For this reason Flodin (1953, 1956) concludes that cereal grains are the favourable vehicles for amino acid supplementation.

Scrimshaw *et al.* (1958) and Bressani *et al.* (1958) have shown that a significant improvement in nitrogen retention can be obtained upon addition of tryptophan, lysine and isoleucine to corn masa flour. Mosqueda-Suarez (1955) found that the addition of 0·2 per cent tryptophan to a de-germed corn product, "arepa", increased the rate of weight gain in rats. The addition of lysine alone also increased weight gain, but not as much as that obtained with tryptophan; with the addition of both amino acids, the rate of increase in growth was highly significant.

Several recent studies (Westerman, Hays and Schoneweis, 1957; Westerman, Kannarr and Rohrbough, 1957) have once again demonstrated the finding of Osborne and Mendel (1914) that the addition of lysine to wheat products results in an improvement in their protein quality. That the addition of lysine not only improves the growth rate of rats but also prevents the development of fatty livers where cereal diets are fed at a 5·4 per cent protein level has been shown by Deshpande, Harper and Elvehjem (1957).

Other vegetable proteins have also been successfully supplemented with synthetic amino acids. Demonstrations of the beneficial effect of supplementing most animal feeds with methionine and lysine have been recently reviewed by Rosenberg (1957). Cowlishaw *et al.* (1956*a*, *b*), have shown that concentrates from the proteins of leaves, as feed for chicks, are improved by the addition of lysine, but not by methionine. Kik (1956*a*, *b*) demonstrated that the proteins of rice and rice products are improved by the addition of 0·2 per cent lysine and 0·2 per cent DL-threonine and that the addition of 0·5 per cent DL-methionine, 0·5 per cent DL-threonine and 0·4 per cent L-lysine to barley resulted in a significant increase in the protein efficiency ratio. The same author has also shown that supplementation with 0·5 per cent each of DL-threonine and DL-methionine improved peanut flour as measured by weight gain in rats and protein efficiency ratio.

Examples of the experimental evidence for the biological effects of amino acid supplementation are cited because of their promise for the future. At the present time, however, knowledge of amino acid requirements and interrelationships are incomplete and the costs of synthetic amino acids, other than methionine and possibly lysine, too high to make amino acid supplementation a practical procedure for improving protein quality of human diets.

5. Selection of More Nutritive Varieties of Basic Food Crops

Another method of improving vegetable proteins deserves mention. Improved varieties of some basic food crops of higher nutritive value can be developed by selective breeding. Some of the factors affecting the amino acid composition of soybean have been studied by Krober (1956), who reported significant differences in methionine concentration among fourteen varieties of soybeans. The author concluded that it is practical through selection to increase the methionine content of soybean. The factors influencing the methionine, lysine and tryptophan content of twenty-five varieties of beans (*Phaseolus vulgaris*) were studied by Tandon *et al.* (1957), who reported that the overall differences in nitrogen and tryptophan content among varieties and between localities were highly significant. This means that through selection of varieties for localities, nutritionally better beans could be developed. Other studies on beans which have appeared recently also show the effects of environmental and genetic factors on the nutritive value and suggest the possibilities for breeding more nutritious varieties (Lantz, Gough and Campbell, 1958).

Cereal grains are in general the most important staple foods in underdeveloped areas (F.A.O., 1956; Sebrell and Hand, 1957) and for this reason more attention should be given to possibilities of improving their protein quality. Corn is such an important staple food in many parts of the world that numerous studies have been directed toward its biological value. Hogan *et al.* (1955) have shown that although the biological value of high-protein corn (16·1 per cent) was inferior to that of the low-protein corn (7·3 per cent), the former was superior per unit weight in its ability to satisfy protein requirements. Similarly, Reussner and Thiessen (1957) have shown that two high-oil-protein corns fed *ad libitum* to rats give better growth and protein efficiency than ordinary corn even though inferior on an equal nitrogen basis. Similar results have been reported by other investigators in pigs (Dobbins *et al.*, 1950), rats and chicks (Mitchell, Hamilton and Beadles, 1952; Sauberlich, Chang and Salmon, 1953*a*). The amino acid composition of corn and factors affecting it have also been extensively studied and the results, in general, confirm the possibilities of selecting more nutritious varieties (Miller, Aurand and Flach, 1950; Sauberlich, Chang and Salmon, 1953*b*; Wolfe and Fowden, 1957; Bressani and Mertz, 1958). Other cereal grains have also been investigated so as to find out their deficiencies in order to improve them by genetic means, and for the better complementation with other food proteins (Frey, Hall and Shekleton, 1955; Baptist and Perera, 1956; Weber *et al.*, 1957; Gunthardt and McGinnis, 1957; Adrian and Sayerse, 1957).

6. Improvement of Protein Quality of Foods by Processing

Finally, improvement in nutritive value of their protein can result from cooking, roasting or other processing of foods. An interesting and classical example is the lime treatment which corn for human consumption receives in the Latin-American countries (Bressani and Scrimshaw, 1958). Several investigators have shown that this treatment gives a product of better nutritional qualities than the raw material as judged by rat and pig growth studies. (Squibb *et al.*, 1955; Kodicek *et al.*, 1956; Pearson *et al.*, 1957). Beans and other legume seeds also gain in nutritive value from cooking or roasting (N.R.C., 1950; Siener, 1950; Carpenter, 1958). Care should be taken, however, to determine the optimum treatment conditions to obtain a product with the desired characteristics; over-treatment may have serious adverse effects on nutritive value.

C. Instituting Supplementary Feeding Programmes

The permanent correction of nutritional deficiencies in a population requires measures leading to improved food production, education and public health. These are inherently difficult and long-range measures, while the direct distribution of supplementary food to vulnerable groups is a method of combating malnutrition which is in theory capable of immediate application. It has been widely recommended and frequently attempted as both an emergency and a transitional measure for getting more and better food to those in greatest need. School feeding programmes have also been adopted on a semi-permanent basis in many of the more highly developed countries as part of educational activities in nutrition.

Unfortunately, while supplementary feeding programmes are well adapted to the nutritional improvement of individuals in captive populations as in school and public institutions, frequently the bulk of persons in nutritional need in an underdeveloped country cannot be reached through existing public channels. For example, the prevention of kwashiorkor requires that children shall receive supplements of good-quality protein long before they reach school age since the requirements for protein, per unit of body weight, are high, and the customary diets shall be least adequate in this age group. Supplementary feeding programmes for pre-school children can be effectively organized only with a great deal of effort and the use of relatively numerous and well-trained auxiliary personnel. Although great need exists, in rural areas, they are least practical where the population is scattered.

Nursing mothers and, to a lesser extent, women during pregnancy also merit special protection from nutritional deficiency because of their higher requirements during these physiological periods. Attention to them is also justified on the basis of the possible adverse influences of nutritional deficiency in the mother on the health of the child. To the extent to which countries have the human and material resources to organize effective programmes for the distribution of food to these vulnerable groups, the assistance of U.N.I.C.E.F. and other governmental and non-governmental agencies in helping to make available suitable food for supplementary feeding programmes, at little or no cost, is of incalculable value.

Needless to say, such programmes should provide the necessary elements for a good diet, and, to be safe and effective, should not overlook any of the major deficiencies. Fortunately, the dried skimmed milk widely available for this purpose provides protein of excellent quality in a concentrated and inexpensive form, as well as abundant riboflavin and calcium. Thus, with the exception of vitamin A, it supplies the nutriments most lacking in many areas. Although skimmed milk is lacking in fats and fat-soluble vitamins, its use presents no problem as long as attention is given to supplying a supplementary source of vitamin A when this nutriment is found to be critically low in the basal diet.

U.N.I.C.E.F. has given invaluable world-wide support to supplementary feeding programmes in areas of nutritional need, particularly through the distribution of powdered milk, and where needed, vitamin A concentrates. A primary objective of these programmes has been to stimulate the local consumption of milk and then to co-operate with F.A.O. in assisting countries to improve milk production and conservation. Particularly good progress has been achieved in countries where powdered-milk plants have been successfully established and a marked increase in the production and utilization of milk and milk products observed as a consequence. In areas in which these efforts alone will not suffice to ensure adequate protein supplies for infant and child feeding, similar programmes for the production and distribution of suitable vegetable mixtures are contemplated.

Thus far, little has been said concerning the use of supplementary feeding programmes for improving the nutrition of school children. Although there are some areas in which this has importance as a health measure, in most regions correction of nutritional deficiencies through supplementary feeding would require concentration on the groups previously mentioned—pre-school children, lactating mothers and pregnant women. The more important opportunity presented by school feeding programmes is an educational one. Children can be taught to eat a greater variety of foods, and the school snack or meal can be made the basis of a nutrition education programme involving parents as well as children. To neglect the educational aspects of the school feeding programmes, as is so widely the case at present, is a serious mistake.

The development of school gardens and small animal-raising projects in connection with school feeding programmes offers a further opportunity to provide instruction in nutritional principles, as well as permitting the introduction of measures to improve the agricultural production of protective foods.

D. Development of Nutritional Rehabilitation Centres

Much more frequent than frank kwashiorkor is the border-line or sub-clinical case of protein malnutrition with a varying degree of growth retardation, apathy, mild skin and mucuous membrane lesions, muscular wasting, weakness and slight oedema. The term "pre-kwashiorkor" has been used to describe this condition, which characterizes large numbers of pre-school children in areas in which kwashiorkor occurs.

Generally, when seen in clinics and health centres, these "pre-kwashiorkor" children are not considered ill enough to merit hospitalization, and it is customary to attempt to treat them as out-patient cases, especially when hospital services are already overcrowded with more severe cases. In these circumstances, the ordinary treatment too often consists of a hurried prescription for a proprietary product or a general admonition to feed the child better, without considering either the economic limitations of the family or the failure of the mother to understand the instructions. Lack of time, interest or full comprehension of the problem on the part of the physician or nurse, often results in failure to emphasize proper feeding and how it may be attained. Even when a recommended dietary supplement is purchased the mother may be unprepared to overcome the child's anorexia or resistance to a new food. The child thus inexorably develops the severe form of the disease and eventually requires costly hospitalization or else may die in the meantime of an intercurrent infection. The final cost in loss of life or prolonged hospitalization is high.

In order to care for these children the establishment of "recovery centres" has been suggested. These are low-cost day-care centres requiring less personnel and expense than hospital facilities and organized to meet local conditions and needs, where the children can receive adequate food throughout the day to improve their nutritional status. The centres may give the best results if some participation in the preparation and administration of food can be arranged for the mothers. Such institutions can also make possible earlier discharge of hospitalized children by accepting them in the recovery phase when the only further treatment needed is an adequate diet.

The "recovery centres" can perform a very important function in the prevention of kwashiorkor through both the direct improvement of the child's diet and the education of the mother. They can also greatly help the hospitals by reducing the number of cases that reach the stage of requiring hospitalization and by permitting an earlier dismissal of the treated cases without the danger of relapse. Obviously the care of children in such a centre after a period of hospitalization for the treatment of kwashiorkor is not only advisable for them but it is also far less expensive.

E. Environmental Sanitation Procedures

There is increasing recognition of the extent to which diarrhoea of infectious origin and other infectious diseases act synergistically with poor dietary habits to result in kwashiorkor and other nutritional deficiencies. In addition, episodes of dysentery and other infectious diseases may prove fatal in malnourished subjects while they would not have serious consequences for well-nourished individuals.

The high frequency with which infections appear in the recent medical histories of children hospitalized with kwashiorkor has already been mentioned. Not only do the majority of Guatemalan children hospitalized for kwashiorkor, for example, give a history of diarrhoea with fever, but other illnesses such as measles and whooping-cough sometimes appear to precipitate this syndrome. Unfortunately, environmental sanitation is likely to be poor in precisely those areas in which feeding practices for young children are grossly inadequate. In rural Guatemalan towns, where kwashiorkor is a major cause of death, almost 8 per cent of all children under ten years reveal Shigella organisms following the culture of a single rectal swab from each child (Beck, Muñoz and Scrimshaw, 1957). Since a single examination detects only part of the infection present, true Shigella prevalence among these children may be somewhat higher. There is also a possibility that other micro-organisms, not normally pathogenic, may become so when the child is grossly debilitated by malnutrition.

In areas in which kwashiorkor is of public health importance, intestinal parasites are usually very common and constitute a further burden on the malnourished child. Although there is some direct evidence that moderate to severe infestation with *Ascaris lumbricoides* interferes with the digestion and absorption of protein (Venkatachalam and Patwardhan, 1953), we feel that the role of intestinal parasites in the development of the syndrome has sometimes been overestimated and overstated by professional as well as lay persons.

There is a general tendency to attribute the majority of deaths among young children to Ascaris and other intestinal parasites instead of to the malnutrition, diarrhoea and other infectious diseases which are primarily responsible for the high mortality in children in underdeveloped areas. In Central America this has the further harmful effect of encouraging the giving of drastic purgatives to rid the child of "worms" with a resulting aggravation of the diarrhoeal disease and the already poor nutritional status. Unfortunately, the efficacy of this treatment is demonstrated to lay minds by the Ascaris commonly excreted in diarrhoeal stools and expelled, in still larger numbers, when purgatives and vermifuges are given.

It should be abundantly clear that in most technically underdeveloped areas the problems of nutrition and infection are closely related, particularly for young children. Progress in reducing enteric infection and infestation through the improvement of water supplies and disposal of excreta and by the introduction of other sanitary measures, will help to decrease deaths from malnutrition just as improving nutrition will lower mortality from infectious diarrhoea.

While improved environmental sanitation will not correct the underlying protein malnutrition which limits the growth and maturation of very large numbers of children in underdeveloped areas, it will allow more of them to survive the critical pre-school years. If they live to school age, cultural factors will usually result in an improvement in their diets. In addition, sanitary measures may contribute to the improvement of the efficiency and working capacity of the parents and thus enable the family to improve their nutritional status.

VII. MAGNITUDE OF THE PROBLEM

Published studies and the experience of health workers in most of the technically underdeveloped countries indicate that child deaths from malnutrition, including kwashiorkor, are exceedingly common. Owing to the way in which the *International Classification of Diseases, Injuries and Causes of Death* is compiled, however, the official vital statistics of the country and the cumulative reports published by W.H.O. fail to reveal the magnitude of the problem. Furthermore, the principal sign of underlying protein malnutrition in a population, slowing of growth and maturation, is regarded as normal for these areas and indeed often described as a racial characteristic. Finally, for children dying of an intercurrent infection, which would not have been fatal in a well-nourished child, there is no record or even good means of evaluating the role of malnutrition in the death.

As a consequence, the magnitude of the protein malnutrition problem from the standpoint of both morbidity and mortality is usually grossly underestimated. This leads to a disproportionate investment of time and money on other, more obvious or better reported problems. The matter is not a simple one since infections of all kinds, particularly enteric, are major determinants of the final appearance of clinical kwashiorkor. In these circumstances programmes for the improvement of environmental sanitation have an added significance. It should be evident, however, that no amount of infectious disease control, or eradication, will eliminate protein malnutrition in the young child except as it indirectly results in an improvement in the productivity and economic well-being of the population. The elimination of protein malnutrition in the young child requires extensive health education efforts and the availability of cheap and effective protein-rich foods.

The difficulties in interpreting the magnitude of the problem from vital statistics are well illustrated by an investigation of the causes of death in children under fifteen years of age in four rural communities in the highland area of Guatemala (Béhar, Ascoli and Scrimshaw, 1958). This study revealed that the death rate was 19·8 per 1,000 population in these communities and for children of one to four years of age 50·3. The infant death rate was 136·8 per 1,000 live births. As determined by questioning the parents, usually within forty-eight hours after the death occurred, of the 222 deaths, 49 were attributed to "*Congenital Malformations and Diseases Peculiar to Early Infancy*", 42 to "*Diseases of the Respiratory System*", 37 to "*Diseases of the Digestive System*" (principally infectious diarrhoea), 27 to "*Infective and Parasitic Diseases*", 43 to "*Other Specified Causes*" (almost all of these kwashiorkor), 17 to "*Ill-Defined or Unknown*", while 7 could not be investigated. The important point is that, in contrast to our classification given above, only one of these deaths, the only case in the entire series that died in a hospital and was medically certified, was classified as due to nutritional deficiency in the official statistics, while 58 were listed officially as dying from intestinal parasites—"worms," "worm attack," "worm fever," etc.—and even though Ascaris infestation in the Guatemalan highland is widespread, it is impossible to conceive that Ascaris *per se* are responsible for these many deaths.

Persons concerned with preventive programmes in areas in which hospital cases and knowledge of the population make it evident that kwashiorkor is a serious public health problem, will doubtless find it desirable to make similar studies in their own areas. Such studies are useful for the proper interpretation of the official vital statistics and helpful in focusing the attention of health and other government authorities on the magnitude of the problem. Studies of differences in the growth and maturation among different socio-economic groups and of morbidity from diarrhoeal disease are also likely to prove revealing and helpful in defining the problem.

VIII. ROLE OF GOVERNMENTAL AND NON-GOVERNMENTAL AGENCIES

It should be apparent from the discussion of factors responsible for the development of clinical cases of kwashiorkor, that the task of its prevention within a country cannot be left to specialized nutrition personnel nor to any single programme or agency. Governmental departments, whose job is to work with people, and non-governmental welfare agencies should be made to understand the magnitude of the problem and should contribute to its solution.

It is obvious that agricultural agencies will help by working toward a greater availability of animal and plant sources of protein for human consumption. Health agencies will assist both by disseminating information as to desirable feeding practices for young children—through health education, maternal and child health, and health centre programmes—and also through programmes to improve environmental sanitation and reduce the spread of infectious disease. The training of schoolteachers to include principles of nutrition in the curriculum as well as in their programmes with parents is also an important part of a determined national effort to abolish kwashiorkor.

Supplementary feeding programmes are usually maintained by a variety of agencies of both governmental and private nature within a country. To the extent to which these programmes can reach preschool children and nursing mothers, they will contribute to reducing the magnitude of the problem. The value of rehabilitation centres should also be recognized and established as a vital link between outpatient and hospital care of malnutrition cases. The hospitals can do a great deal by educating the parents of their kwashiorkor patients as to the cause and cure of the disease in a way that will help to avoid recurrences and benefit other children in the family.

The health department should maintain liaison with the economic and industrial development plans of a country to be sure that these do not conflict with health objectives. For example, governments should not encourage the production of cassava flour in a country where cassava is not now in general use, for it is almost certain that the product will be used for infant feeding with unfortunate consequences. In some countries the leadership of a national nutrition council, integrated by representatives from all of the governmental, and perhaps from the major non-governmental agencies, concerned with matters directly influencing nutrition policy or administering programmes relating to the improvement of the nutritional status of the population may be desirable. In others this leadership may well be provided by the Nutrition Section of the Health Department or by a National Institute of Nutrition. The prevention of kwashiorkor is such an enormous job that, without comprehension of the problem and co-operation at all levels, progress will be slower than would otherwise be the case and thousands of additional children will die needlessly from kwashiorkor.

IX. CONTRIBUTION OF INTERNATIONAL AGENCIES AND PROGRAMMES

Just as the national ministries and agencies must co-ordinate their efforts to combat malnutrition and to eliminate kwashiorkor, so should the International Agencies co-operate in the common effort and encourage national elements to do so. While countries will naturally look to W.H.O. for guidance in the medical aspects of kwashiorkor, supplementary feeding programmes for this vulnerable group and the improvement of environmental sanitation, F.A.O. should be prepared to give technical assistance in problems relating to food production and surveys of the dietary habits of population. Both agencies, together with U.N.E.S.C.O., are likely to be involved in educational efforts, and U.N.I.C.E.F. has been, and will continue to be, a major resource for the provision of food supplements in areas in which protein is inadequate, as well as for supplies and materials for the combat of infectious diseases.

The problem of preventing kwashiorkor and other forms of protein malnutrition is so large and important, that each of the specialized agencies of the United Nations mentioned has a responsibility in this area. It is to be hoped that the future will see a growing realization of these obligations and of their material and human resources to help meet them. Valuable assistance can also be rendered by the various bilateral technical assistance programmes between countries.

X. SUMMARY

The underlying cause of kwashiorkor is a relatively severe deficiency of protein, and treatment consists primarily in giving the child a diet rich in protein of good quality, and, as soon as initial anorexia is overcome, ensuring that the diet contains all the other essential nutriments in physiological amounts. Since children have often suffered considerable diarrhoea before admission, it is frequently necessary to give special attention to restoring electrolyte balance and it is best to give penicillin until the acute danger of broncho-pneumonia is past.

The disease occurs where diets of young children fail to contain sufficient protein, especially in the months following weaning, and is, therefore, highly susceptible to stress factors. The most important of these, diarrhoea of infectious origin, is exceedingly common in most areas where kwashiorkor is endemic, and precedes the development of clinical signs in a

large proportion of cases. Other stress factors are the common contagious diseases.

Technically underdeveloped areas in general do have adequate potential protein sources which have not been exploited. Where animal protein production is inadequate, mixtures of vegetable proteins, with a high biological value, can be prepared for the supplementary and mixed feeding of infants and young children. To a considerable extent, the problem is also one of ignorance and lack of proper feeding habits rather than inability of the parents to supply protein to the child.

The prevention of kwashiorkor requires understanding of the problem on the part of officials and other personnel in the fields of health, education and agriculture, as well as their active co-operation in the development and application of prophylactic measures. Similarly, the technical agencies of the United Nations W.H.O., F.A.O., U.N.I.C.E.F. and U.N.E.S.C.O. can be of major assistance to countries in various aspects of the problem.

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