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Chapter 42

PROTEIN-ENERGY MALNUTRITION

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Protein-energy malnutrition (PEM) results when the body's needs for protein, energy fuels, or both cannot be satisfied by the diet. It includes a wide spectrum of clinical manifestations conditioned by the relative intensity of protein or energy deficit, the severity and duration of the deficiencies, the age of the host, the cause of the deficiency, and the association with other nutritional or infectious diseases. Its severity ranges from weight loss or growth retardation to distinct clinical syndromes, frequently associated with deficiencies of minerals and vitamins.

Dietary energy and protein deficiencies usually occur together, but sometimes one predominates and, if severe enough, may lead to the clinical syndrome of *kwashiorkor* (predominant protein deficiency) or *marasmus* (mainly energy deficiency). *Marasmic kwashiorkor* is a combination of chronic energy deficiency and chronic or acute protein deficit. It is difficult to recognize which deficit predominates in milder forms of the disease.

The origin of PEM can be primary, when it is the result of inadequate food intake, or secondary, when it is the result of other diseases that lead to low food ingestion, inadequate nutrient absorption or utilization, increased nutritional requirements, and/or increased nutrient losses. Its onset can be relatively fast, as in starvation due to abrupt withholding of food, or gradual. This chapter discusses primary PEM of a relatively chronic onset, where the metabolic alterations and clinical characteristics of protein and/or energy deficits predominate. PEM secondary to other diseases and the metabolic and clinical manifestations of starvation and of specific vitamin and mineral deficiencies are described in other chapters.

HISTORICAL BACKGROUND

It has long been recognized that inadequate food intake produces weight loss and growth retardation and, when severe and prolonged, leads to body wasting and emaciation. It took much longer to understand the nature of the edematous forms of PEM, probably because they could be found among children who were not starving and in families in good socioeconomic position. Although the disease was possibly mentioned by Hippocrates[1], one of the earliest descriptions of edematous PEM, or of something resembling it, was written in Yucatan, Mexico by Patrón-Correa

In 1908.[2] The disease was called "culebrilla" ("snake-like") because of the serpentine areas of skin hyper- and hypopigmentation. The dermatologic signs were further described with undue attention in later publications from Asia,[3,4] Africa,[5,6] and tropical America,[7,8] leading to the initial beliefs that the disease was caused by tropical parasites or a vitamin deficiency. The distinction of PEM from pellagra and other vitamin deficiencies and the absence of a causal relationship with parasites were suggested by various authors in the late 1920s and 1930s. The real nature of the disease received more attention, however, after Cicely Williams published in 1933 an extended note of a report she had written one year earlier in the Gold Coast.[9] In another publication, two years later, she referred to the disease by its local name, "kwashiorkor," used by the Ga tribe in the Gold Coast (now Ghana) for "the sickness the older child gets when the next baby is born."[10] This native term already suggested that the disease could be due to ignorance or inability to provide good foods to a child during the weaning period.

Several pediatricians who worked in tropical countries described various aspects of the disease in the 1930s and showed that it could be cured by feeding milk or other high-protein food, sometimes in combination with blood transfusions.[11,12] In the 1940s researchers showed that the concentration of serum proteins was low in most patients. Thus, the association of the disease with dietary protein intake became increasingly more evident. Hegsted and co-workers pointed out that the quality of dietary proteins could also affect serum protein concentration.[13] Nevertheless, it was not until the 1950s that the nature and importance of this disease gained worldwide recognition, partly owing to publications such as those of Brock and Autret,[14] Autret and Béhar,[11] and Trowell, Davies, and Dean.[12] By then, more than 40 names had been given to this clinical syndrome.[12] Some of them, such as "sÍndrome policarencial de la infancia" (infantile pluricarential syndrome), indicated that young children were mainly affected and that a deficit of various nutrients was involved. Others, such as "Mehlnahrschaden" ("damage by cereal flours"), "starch edema," and "sugar babies" indicated that it was caused by the intake of foods with high carbohydrate and low protein contents. Today, the more comprehensive term of "protein-energy (or protein-calorie) malnutrition"[15] is universally accepted, and its severe forms are most often called "marasmus," "kwashiorkor," and "marasmic kwashiorkor." The term "malnutrition" is usually used in lay language for PEM.

Studies done in the last 25 years have shown that marasmus and kwashiorkor have distinct metabolic features, that some manifestations, such as anemia and reduced physical activity, are due to adaptive mechanisms, that the immune response of severely malnourished patients is impaired, and that physical and emotional stimulation are important elements in treating malnourished children. These findings are the basis of current therapeutic measures.

ETIOLOGY AND EPIDEMIOLOGY

Protein-energy malnutrition is the most important nutritional disease in the developing countries because of its high prevalence and its relationship with child mortality rates, impaired physical growth, and inadequate social and economic development. Associated deleterious effects on mental growth and maturation have been demonstrated in experimental animals and they seem to occur in humans, but it has not been possible to disassociate completely the nutritional factors from other environmental conditions, nor to ascertain the irreversibility of the nutritional mental damage. PEM occurs more frequently when infections impose additional demands or induce greater losses of nutrients and when living conditions demand greater energy expenditure, as in heavy physical work.

Magnitude of the Problem

The global magnitude of PEM is difficult to estimate with precision because mild and moderate malnutrition usually is not recorded, and many patients with kwashiorkor or marasmus do not receive medical attention. Rough estimates made by the United Nations' Food and Agriculture Organization[16] and the World Bank,[17] based on the chronic consumption of food in amounts that provide less than the minimum energy to lead a sedentary life (i.e., 1.2 times basal energy expenditure), indicate that between 800 million and one billion persons have some degree of PEM. This may be a conservative estimate, as an energy intake of 1.2 times basal expenditure will still limit the functional performance and optimal development of most growing children and of adults with energy-intensive life-styles.[18–20]

As PEM mainly affects infants and preschool children, another estimate of its magnitude is based on considering it the main cause of growth retardation. The World Health Organization estimates that around 300 million children have growth retardation related to malnutrition.[21] If one uses weight deficit for a given age as indicator of present or past growth impairment, in many developing countries 20 to 75% of all children under 5 years of age have suffered from PEM.[22] An anal-

ysis of 25 different surveys in Asia, Africa, and Latin America indicated that about 3% (range: 0.5 to 20%) had severe PEM and about 20% (range: 4 to 46%) had a moderate form of the disease.[22] These figures increase markedly during severe food shortages, as in wars or droughts.

Most malnourished persons live in developing countries, about 30% each in Africa and the Far East, and 15% each in Latin America and the Near East.[16] The current differences between countries with different degrees of development will probably become wider, as projections for food demands in 1985, compared with 1970, show increases of 26% for developed countries and 75% for developing countries.[23] The situation is even more serious for the latter, since the distribution of food is usually unequal between more and less affluent groups in those societies.

Causes of PEM

Primary PEM results from insufficient food intake or from the ingestion of foods with proteins of poor nutritional quality. These inadequate intakes are almost always linked to conditions such as poverty, ignorance, infectious diseases, and low food availability. Therefore, social, economic, biologic, and environmental factors must be considered as underlying causes of PEM.

Social and Economic Factors. Poverty almost always accompanies PEM. As its consequence there is low food availability for lack of means to produce or buy foods, overcrowded and unsanitary living conditions, and improper child care.

Ignorance, by itself or associated with poverty, is a frequent cause of PEM in some families or societies, leading to poor infant- and child-rearing practices, misconceptions about the use of certain foods, inadequate feeding conducts during illnesses, and improper food distribution within the family members.[24,25] A decline in the practice and duration of breastfeeding, combined with inadequate weaning practices when breast milk is withdrawn or when it can no longer provide sufficient dietary energy and protein to the infant, is associated with growing rates of infantile PEM.

Social problems such as child abuse, maternal deprivation, abandonment of the elderly, alcoholism, and drug addiction can result in PEM. Cultural and social practices that impose food taboos, some food and diet fads, particularly popular among adolescents and women,[26] and the migration from traditional rural settings to urban slums can also contribute to or precipitate the appearance of PEM.

Biologic Factors. Maternal malnutrition prior to and/or during pregnancy is more likely to produce an underweight newborn baby.[27] This intrauterine malnutrition can be compounded after birth by insufficient food to satisfy the infant's needs for catch-up growth, resulting in PEM.

Infectious diseases are major contributing and precipitating factors in PEM. Diarrheal disease, measles, and respiratory and other infections frequently result in negative protein and energy balance due to anorexia (reduced food intake), vomiting, decreased absorption (increased nutrient losses), and catabolic processes (increased requirements and metabolic losses).[28–32] Intestinal parasites apparently have little or no effect unless the infection is extensive or causes acute diarrhea.[33,34]

Diets with low concentrations of proteins and energy, as occur with overdiluted milk formulas or bulky vegetable foods that have low nutrient densities, can lead to PEM in young children whose gastric capacity does not allow the ingestion of large amounts of food. Foods with low protein quality (i.e., low contents of one or more essential amino acids) will be poorly utilized, and imbalanced diets can produce anorexia.[35] Moreover, foods poor in protein and rich in carbohydrates are particularly prone to produce kwashiorkor.

Environmental Factors. Overcrowded and/or unsanitary living conditions lead to frequent infections with deleterious nutritional consequences. This is an especially important cause of PEM among weanlings who develop severe or frequent episodes of diarrhea.[36]

Agricultural patterns, climatic conditions, and man-made catastrophes, such as wars and forced migrations, that lead to cyclic, sudden, or prolonged food scarcities can cause PEM among whole populations. Post-harvest losses of food due to bad storage conditions and inadequate food distribution systems contribute to PEM, even after periods of agricultural plenty.

Age of the Host

PEM can affect all age groups but it is more frequent among infants, especially those born prematurely or weighing less than 2,500 g, and among preschool children. This is because dietary protein and energy requirements of young children are high per unit of body weight, they cannot obtain food by their own means and, when living under poor hygienic conditions, they frequently become ill with diarrhea and other infections.[37,38] Most infants from poor families in developing countries who are weaned prematurely from the breast or who are breast-fed for a prolonged time without adequate complementary feeding practices become malnourished for lack of adequate energy and protein intake. The chronic intake of

insufficient food can result in marasmus, which is the most common form of severe PEM before one year of age. The edematous forms of the disease are more frequent after 18 months of age and typically occur in children who are fed diets consisting of starchy gruels, diluted cereal-based beverages, and vegetable foods that are rich in carbohydrates but almost devoid of proteins of good nutritional quality (i.e., lacking one or more essential amino acids). Children who consume large amounts of such diets can develop kwashiorkor. Most often, the severe protein deficit is associated with chronic dietary energy deficit and results in a combined form of marasmic kwashiorkor. The appearance of edema is frequently preceded or accompanied by acute diarrhea or other infectious disease.

Older children usually have milder forms of PEM because they can cope better with social and food availability constraints. Infections and other precipitating factors become less severe, and early survival may imply a natural selection of the more fit.

Pregnant and lactating women are also vulnerable to PEM because the increases in their nutritional requirements may not be accompanied by equivalent increments in food intake due to economic or cultural factors, nausea in early pregnancy, and gastric discomfort as pregnancy advances. Energy deficiency with or without proportional protein deficit predominates in this age group. However, the consequences of the dietary deficiencies usually have a greater impact on the growth, nutritional status, and survival rates of their fetuses, newborn babies, and infants.

The elderly who are unable to care properly for themselves due to physical or mental deterioration tend to suffer from PEM. Gastrointestinal alterations can be an important contributing factor. Their energy requirements fall as a consequence of reduced physical activity and reductions in maintenance energy metabolism, but their protein needs do not diminish at the same rate.[39] Consequently, protein deficiency may predominate in this age group.

Adolescents, men, and nonpregnant, nonlactating women usually have lowest prevalence and the mildest forms of the disease because of the greater opportunities to obtain food, and the cultural and social practices that protect the productive members of the family. Nevertheless, many weight-losing diets and food fads can predispose them to, or actually produce some degree of, PEM.

PATHOPHYSIOLOGY AND ADAPTIVE RESPONSES

PEM develops gradually over many days or months. This process allows a series of metabolic and behavioral adjustments that result in decreased nutrient demands and a nutritional equilibrium compatible with a lower level of cellular nutrient availability. If the supply of nutrients becomes persistently lower than that to which the body can adapt, death supervenes. Metabolic equilibrium can also be disrupted during the progression of the disease or as a result of inadequate therapeutic measures. Therefore, the following characteristics of PEM must be considered:

1. PEM induces a metabolically dynamic, changing state to which the affected person adapts to survive in a compensated manner.
2. The cost of this adaptation includes functional limitations and decreased interactions with the physical and social environment.
3. Harmonic changes in the metabolism of proteins, energy, and other nutrients allow a better adaptation to current nutritional conditions.
4. Metabolic adjustments are more stable when PEM develops slowly, as in chronic mild-moderate cases or in marasmus, than more acutely, as in kwashiorkor of rapid onset.
5. Severe protein and energy deficiencies and sudden additional metabolic stress, such as dehydration, overloading with dietary proteins or energy, and acute infections, can cause decompensation with functional derangement and even death.

Energy Mobilization and Expenditure

A decrease in energy intake is quickly followed by a decrease in energy expenditure, accounting for shorter periods of play and physical activity in children[40–42] and for longer rest periods and less physical work in adults.[43] When the decrease in energy expenditure cannot compensate for the insufficient intake, body fat is mobilized with a decrease in adiposity and weight loss.[44] Lean body mass diminishes at a slower rate, mainly as a consequence of muscle protein catabolism with increased efflux of amino acids, primarily alanine, that contribute to the energy sources. As the cumulative energy deficit becomes more severe, subcutaneous fat is markedly reduced, and protein catabolism leads to muscular wasting. Visceral protein is preserved longer, especially in the marasmic patients.

In marasmus, these alterations in body composition lead initially to increased basal oxygen consumption (i.e., basal metabolic rate) per unit body weight, and it decreases in more sereve stages.[45,46] In kwashiorkor, the severe dietary protein deficit leads to an earlier visceral depletion of amino acids that affects visceral cell function

and reduces oxygen consumption; therefore, basal energy expenditure decreases per unit of lean or total body mass.

Blood glucose concentration remains normal, mainly at the expense of gluconeogenic amino acids and fats, and it falls in severe PEM or when complicated by serious infections or fasting.

Protein Breakdown and Synthesis

The poor availability of dietary amino acids decreases protein synthesis in viscera and muscles. This is followed by increased muscle protein catabolism resulting in modified composition of the free amino acid pool and increased amino acid availability for viscera. A marked recycling of amino acids and a reduction in urea synthesis and excretion occur. In the steady state, the amount of free amino acids entering the body pool from dietary and tissue proteins is equal to the amount leaving it. The latter is represented by the amino acids synthesized into body protein and the amount of amino acid nitrogen that is excreted. On a normal protein intake, 25% of the amino acids leaving the total body pool are excreted as nitrogenous compounds and 75% are recycled or reutilized for protein synthesis. This latter fraction may rise to 90 to 95% when protein intake is reduced.[47,48] Therefore, the adaptive change is not so much a reduction of total nitrogen or amino acid turnover, but an increase in the proportion turned over that is used for synthesis and a corresponding reduction in the proportion of nitrogen that is excreted.

At the intracellular level there are changes in the activity of enzymes involved in the adaptive adjustments of energy and protein metabolism.[49-52] Table 42–1 shows some of the changes observed in leukocytes, muscle, and liver cells. These enzymatic changes result in energy mobilization from reserve depots (mainly fat), and in the provision of amino acids by muscle cells and their optimal utilization by viscera. Consequently, the synthesis, catabolism, and breakdown of proteins and specific amino acids differ in the various tissues and organs.

The half-life of some proteins increases. The rate of albumin synthesis decreases, but after a time lag of a few days the rate of breakdown also falls.[53] In addition to its increased half-life, a shift of albumin from the extravascular to the intravascular pool assists in maintaining adequate levels of circulating albumin in the face of reduced synthesis. Muscle breakdown also supplies amino acids to the liver for the synthesis of albumin, lipoproteins, and other serum proteins. When the adaptive mechanisms fail, the concentration of serum proteins, and especially albumin, decreases. The ensuing reduction in intravascular oncotic pressure and outflow of water into the extravascular space contribute to the development of the edema of kwashiorkor.

These adaptations lead to the sparing of body protein and the preservation of essential protein-dependent functions. The gradual and inevitable loss of body protein as a result of long-term dietary protein deficit is primarily from skeletal muscle. Some visceral protein is lost in the early development of PEM but then becomes stable until the nonessential tissue proteins are depleted; the loss of visceral protein then increases, and death may be imminent unless nutritional therapy is successfully instituted.

Endocrine Changes

Endocrine changes may not be wholly explained by the circulating levels of hormones, because their secretion rates and half-lives and the cellular responses to hormonal stimulation may also be altered in PEM.[54] There are contradicting reports concerning many endocrine functions in malnutrition, probably because of differences in analytical techniques, type and severity of PEM, and conditions and timing of the studies.[54-56] Table 42–2 summarizes the most consistent changes reported in severe PEM. The functional capacities of the hypothalamic-pituitary axis and adrenal medulla are preserved, thus allowing en-

Table 42–1. Selected Enzyme Activity Changes in Protein-Energy Malnutrition*†

Cells	*Enzymes*	*Change in Activity*
Muscle and leukocytes	aldolase	decrease
	dehydrogenases	decrease
	pyruvic kinase	decrease
	aminotransferases	increase
Liver	phenylalanine hydroxylase	decrease
	urea cycle enzymes	decrease
	valine aminotransferase	decrease
	amino acid activating enzymes	increase

*Changes favor energy mobilization, muscle protein breakdown, and liver protein synthesis.
†Adapted from Viteri, F.E.[52]

Table 42–2. Summary of Selected Hormonal Changes and Their Main Metabolic Effects Usually Seen in Severe PEM

Hormone	Influenced in PEM by	Hormonal Activity in: Energy Deficit	Hormonal Activity in: Protein Deficit	Metabolic Effects of Changes in PEM
Insulin	Low food intake (↓ glucose) (↓ amino acids)	Decreased	Decreased	↓ muscle protein synthesis ↓ lipogenesis ↓ growth
Growth hormone	Low protein intake (↓ amino acids) Reduced somatomedin synthesis	Normal or moderately increased	Increased	↑ visceral protein synthesis ↓ urea synthesis ↑ lipolysis
Somatomedins	Low protein intake?	Variable	Decreased	↓ muscle and cartilage protein synthesis ↓ collagen synthesis ↓ lipolysis ↓ growth ↑ production of growth hormone
Epinephrine	Stress of food deficiency, infections (↓ glucose)	Normal but can increase	Normal but can increase	↑ lipolysis ↑ glycogenolysis inhibits insulin secretion
Glucocorticoids	Stress of hunger Fever (↓ glucose)	Increased	Normal or moderately increased	↑ muscle protein catabolism ↑ visceral protein turnover ↑ lipolysis ↑ gluconeogenesis
Aldosterone	↓ blood volume ↑ extracellular K ? ↓ serum Na ?	Normal	Increased	↑ sodium retention and ↑ water retention contribute to appearance of edema
Thyroid hormones	?	T4 normal or decreased; T3 decreased	T4 usually decreased; T3 decreased	↓ glucose oxidation ↓ basal energy expenditure ↑ reverse T3
Gonadotropins	Low protein intake? Low energy intake?	Decreased	Decreased	delayed menarche

↓ = low or reduced ↑ = high or increased

docrine and metabolic responses to stress conditions.[57]

Hormones play important roles in the adaptive processes of energy and protein metabolism in severe PEM.[58] These can be summarized as follows: (1) The decreased food intake tends to reduce plasma concentrations of glucose and free amino acids which, in turn, reduce insulin secretion and increase epinephrine release; the latter further reduces insulin secretion. (2) The low plasma amino acid levels, seen mainly in kwashiorkor, also stimulate the secretion of human growth hormone; the low plasma somatomedin activity, also seen mainly in kwashiorkor, contributes to the high circulating levels of growth hormone, due to the absence of the feedback inhibition postulated for somatomedins.[59,60] (3)The increased levels of growth hormone and epinephrine influence the reduction of urea synthesis, thereby favoring amino acid recycling.[48,61] (4) The stress induced by the low food intake and further amplified by fever, water, and electrolyte losses, and other manifestations of the infections that frequently accompany PEM, also stimulates epinephrine release and corticosteroid secretion, more so in marasmus than in kwashiorkor, probably because of the greater severity in energy deficit that characterizes marasmus.[62,63] (5) Resistance to the peripheral action of insulin increases,[64] probably due to the increase in plasma free fatty acid concentration resulting from the lipolytic activity of growth hormone, glucocorticoids, and epinephrine. (6) The plasma concentrations of T_3 and T_4 decrease, by mechanisms that are not clearly defined. The iodination of tyrosine and monodeiodination of T_4 are probably involved, as the reduction of T_3 (3,5,3′-triiodothyronine) is accompanied by an increase in the circulating levels of the metabolically inactive reverse-T_3 (3,5,5′-triiodothyronine).[65] (7) The secretion of hormones involved in nonvital, growth-related functions, such as gonadotropins, decreases.[66]

All these changes, illustrated in Figure 42–1,

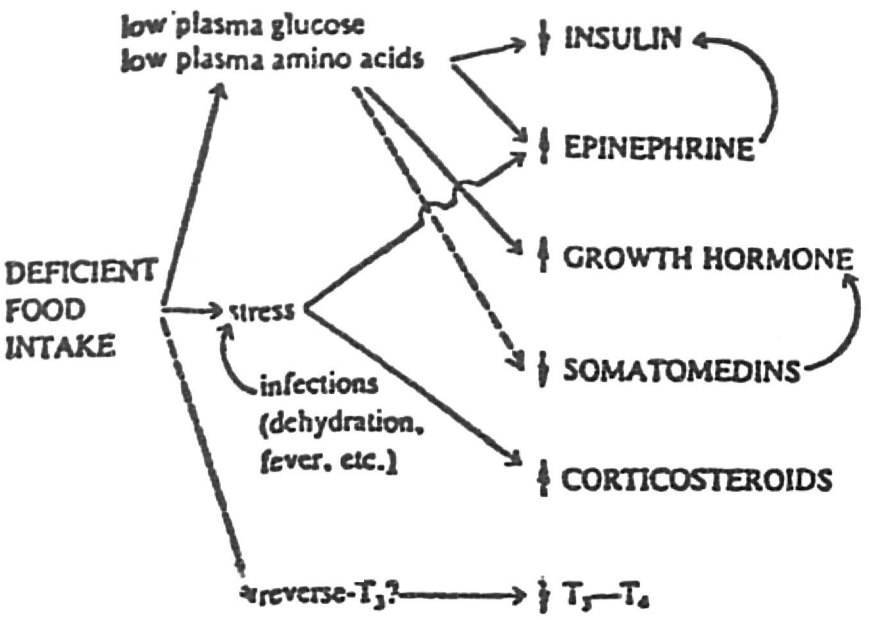

Fig. 42–1. Endocrine adaptive functions in severe PEM related to energy and protein metabolism. (From Torun, B., Viteri, F.E.,[149] with permission of McGraw Hill Book Co.)

contribute to the maintenance of energy homeostasis through increased glycolysis and lipolysis; increased amino acid mobilization; decreased storage of glycogen, fats and proteins; and decreased energy expenditure. Amino acids are spared for the synthesis of proteins that are essential for survival through preservation of visceral protein, growth retardation, and enhanced breakdown of muscle protein. The latter increases the availability and turnover of amino acids in viscera, particularly liver. In addition to being energy fuels and producing ketone bodies that can be used by the brain as energy sources, the increase in circulating fatty acids also reduces the peripheral actions of insulin.

Hematology and Oxygen Transport

The reduction in hemoglobin concentration and red cell mass that almost always accompanies severe PEM is an adaptive phenomenon related to tissue oxygen needs.[46,67] Figure 42–2 illustrates the proposed responses. The reduction in lean body mass and the lower physical activity of malnourished patients lead to lower oxygen demands. The simultaneous decrease in dietary availability of amino acids results in reduced hematopoietic activity, which spares amino acids for synthesis of other more necessary body proteins. As long as the tissue's needs for oxygen are satisfied by the existing capacity for oxygen transport, this should be considered an adaptive response and not a "functional" anemia (i.e., with tissue hypoxia). [illegible], lean body mass, and physical activity begin improving with dietary treatment, there is a rise in oxygen demands calling for accelerated hematopoiesis. If iron, folic acid, and vitamin B_{12} are not available in sufficient amounts, functional anemia with tissue hypoxia will develop.

Figure 42–3 shows that the administration of hematinics to a severely malnourished patient will not induce a hematopoietic response until dietary treatment produces an increase in lean body mass. Figure 42–4 shows that the reticulocyte response is related to the amount of protein intake when erythropoetic substances are not limiting.[58]

The severely malnourished patient may have relatively high body iron stores[68] and retains the ability to produce erythropoietin and reticulocytes in response to acute hypoxia. Nevertheless, these patients are prone to develop functional, severe anemia if there is a superimposed dietary iron or folic acid deficiency, or a chronic blood loss, as in hookworm infection.

Other Physiologic and Metabolic Changes

Not all pathophysiologic changes lead to advantageous adjustments. Certain functions are affected and some nutrient reserves decrease, making the malnourished individual more susceptible to injuries that a well-nourished individual can withstand with little repercussion.

Cardiovascular and Renal Functions. Cardiac work decreases, as does functional reserve, and central circulation takes precedence over peripheral circulation.[69–71] Cardiovascular reflexes are altered, leading to postural hypotension and diminished venous return. In severe PEM, peripheral circulatory failure comparable to hypovolemic shock may occur. Hemodynamic compensation occurs primarily from tachycardia rather than from increased stroke volume. Renal plasma flow and glomerular filtration rates may be reduced as a consequence of the decreased cardiac output, but water clearance and the ability to concentrate and acidify urine appear unimpaired.[72–74]

The Immune System. The major defects seen in severe PEM seem to involve T-lymphocytes and the complement system.[75,76] A marked depletion of lymphocytes from the thymus and atrophy of the gland occur. In addition, cells from the T-lymphocyte regions of the spleen and lymph nodes are depleted, probably owing to decreases in thymic factors.[77,78] The production of several complement components, the functional activity of the complement system assessed by both the classic and alternative pathways, and the opsonic activity of serum are depressed in severe PEM.[76,79] These deficiencies may explain the high susceptibility of severely malnourished patients to gram-negative bacterial sepsis. Phagocytosis, chemo-

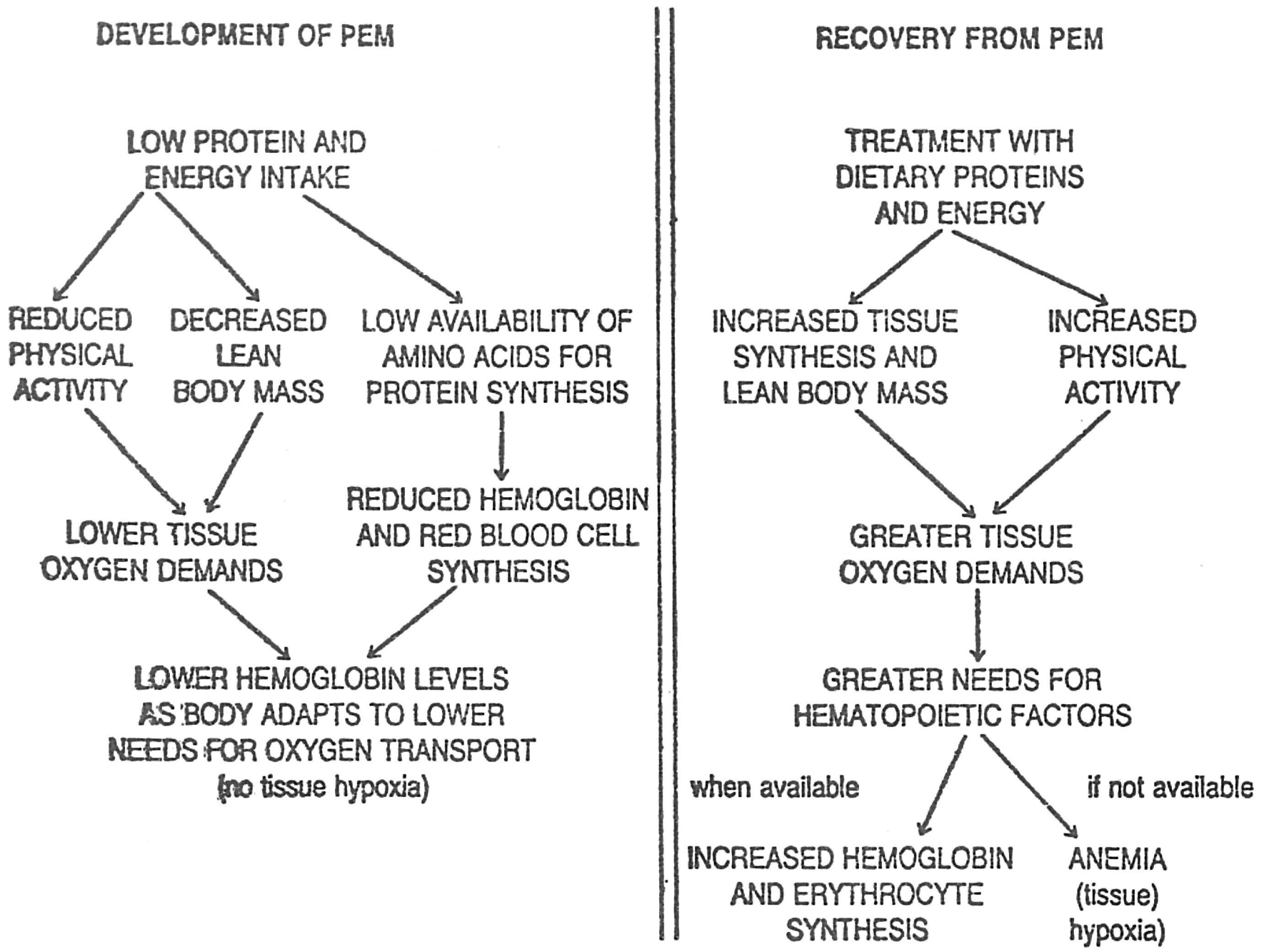

Fig. 42–2. Proposed hematologic responses in protein-energy malnutrition and during its treatment.

taxis, and intracellular killing are also impaired, partly due to the defects in opsonic and complement functional activities. The B-lymphocyte areas of spleen and lymph nodes and the circulating levels of B cells and immunoglobulins are relatively normal, but there may be defects in antibody production, such as secretory IgA.

The overall consequences of all these alterations in severe PEM are a greater predisposition to infections and to severe complications of otherwise less important infectious diseases. The defects in immune functions disappear with nutritional rehabilitation, except perhaps when they are due to intrauterine malnutrition.[80]

Potassium and Sodium. Total body potassium decreases in PEM because of the reduction in muscle proteins and loss of intracellular potassium. The low insulin action and diminished intracellular energy substrates reduce the availability of ATP and phosphocreatine.[81] This process probably alters the cellular exchange of sodium and potassium, leading to potassium loss and increased intracellular sodium.[82] Water accompanies the sodium influx, and although total body intracellular water is decreased because of losses in lean body mass, there may be intracellular overhydration. These alterations in cell electrolytes and energy sources may explain, at least in part, the increased fatigability and reduced strength of skeletal muscle.[83]

Gastrointestinal Functions. Impaired intestinal absorption of lipids and disaccharides and a decreased rate of glucose absorption occur in severe protein deficiency. The greater the protein deficit, the greater the functional impairment. A decrease in gastric, pancreatic, and bile production is also observed, with normal to low enzyme and conjugated bile acid concentrations.[84–86] These alterations further impair the absorptive functions. Nevertheless, the ingestion of nutrients in high, therapeutic amounts usually allows for their uptake in sufficient quantity to permit nutritional recovery.[87] Malnourished persons, however, are prone to have diarrhea because of these alterations and possibly also because of irregular intestinal motility and gastrointestinal bacterial overgrowth. Diarrhea aggravates the malabsorption and can further impair nutritional status. Malabsorption disappears with nutritional recovery, unless there is an underlying food or nutrient intolerance unrelated to primary PEM.

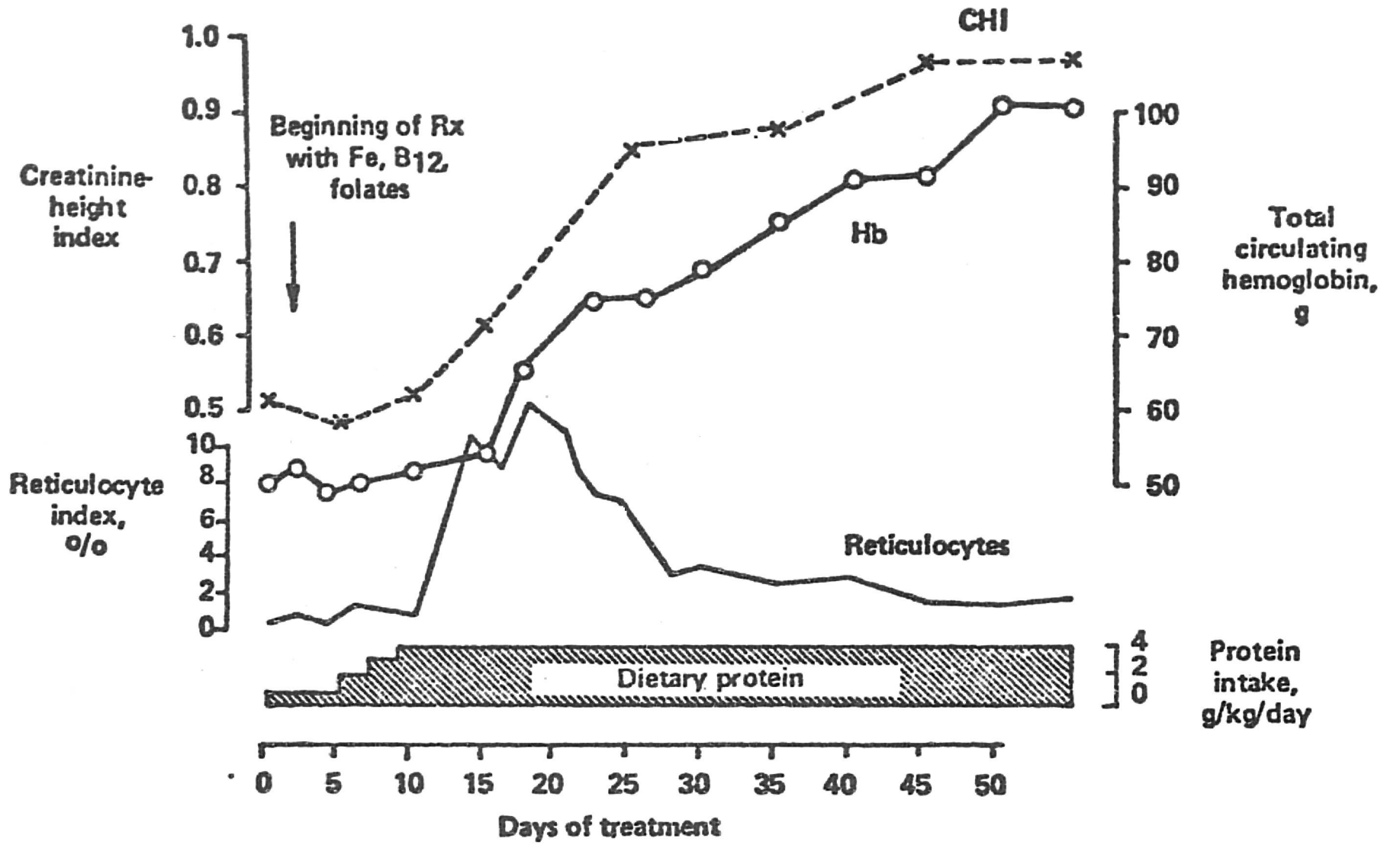

Fig. 42–3. Hematologic response of a child with severe protein-energy malnutrition. Treatment with iron, folic acid, and vitamin B_{12} began on day 2; dietary energy and proteins were increased gradually to 150 kcal and 4 g protein/kg/day on day 9. There was no reticulocyte or hemoglobin response until lean body mass, assessed by the creatinine-height index, began increasing.

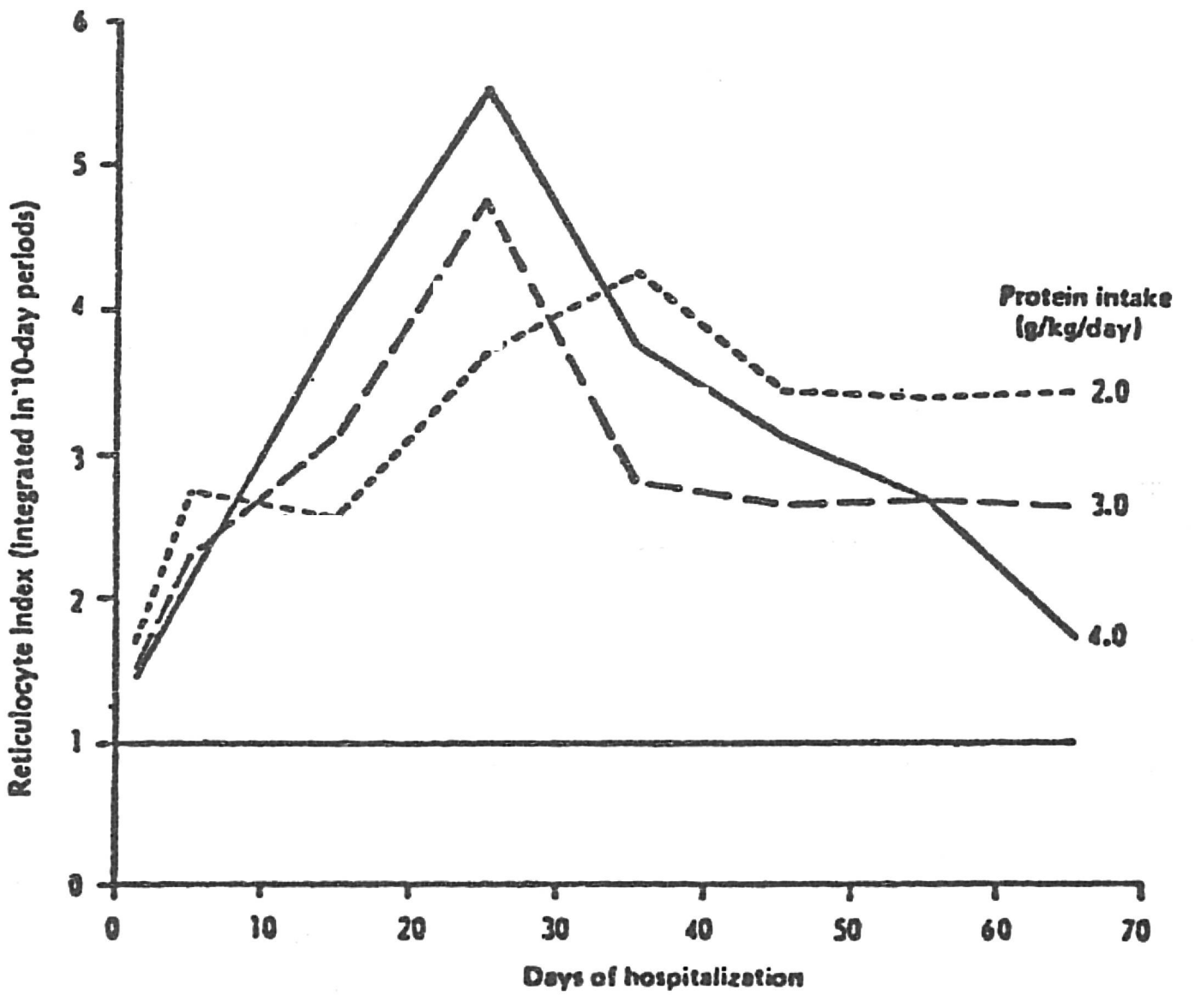

Fig. 42–4. Reticulocyte response of children treated for severe PEM with different amounts of dietary proteins, and adequate amounts of dietary energy and hematinics. (From Viteri, F.E.,[58] with permission of Raven Press.)

Central and Peripheral Nervous System. Individuals with severe PEM may have decreased brain growth, nerve myelination, neurotransmitter production, and velocity of nervous conduction, although the long-term functional implications of these alterations have not been clearly demonstrated. Neither have their causes and mechanisms been fully elucidated. The explanations proposed include reduced number of nervous cells when PEM occurs in utero or before six months of age, small cell size when it occurs at a later age, alterations in brain catecholamine production, defects in lipid metabolism, and decreased content of potassium in the brain.[88–93]

METABOLIC FACTORS LEADING TO MARASMUS AND KWASHIORKOR

The concept that marasmus or kwashiorkor is the end result of either severe energy or protein deficiency[94,95] is too simplistic.[58,96] Other factors such as overloading a severely malnourished person with carbohydrates, or metabolic changes induced by infections, may cause or contribute to the appearance of kwashiorkor with its characteristic edema, hypoalbuminemia, and enlarged fatty liver. Some investigators have postulated that the evolution of PEM into either kwashiorkor or marasmus may be partly related to differences in adrenocortical response, whereby a greater response preserves visceral proteins more efficiently and leads to the better-adapted syndrome of marasmus.[97,98] Most probably, both endogenous and exogenous factors play a role in the development of marasmic or edematous PEM.[58,99,100] This might explain, at least in part, the fact that marasmus, kwashiorkor, and marasmic-kwashiorkor predominate in different parts of the world.

When there is a severe lack of food, endocrine adjustments mobilize fatty acids from adipose tissue and amino acids from muscle tissue, plasma protein concentration remains normal, and hepatic gluconeogenesis is enhanced.[101] An increase in carbohydrate intake when protein intake is very low can produce a breakdown of those adjustments, as follows: (1) Carbohydrate intake induces insulin release and a reduction in the production of epinephrine and cortisol.[102,103] (2) Lipolysis decreases and the action of insulin is enhanced due to the suppression of the inhibitory effects of free fatty acids on the peripheral action of insulin.[104] (3) Muscle protein breakdown is reduced and the body pool of free amino acids decreases. The decreased [illegible]ly of muscle amino acids to the other organs results in less visceral protein synthesis.[105–107] (4) The decreased synthesis of plasma proteins in the liver, particularly albumin, reduces intravascular oncotic pressure. Plasma water decreases and accumulates in extravascular tissues, tissue pressure rises, and cardiac output diminishes. As a consequence, perfusion pressure in the kidney is reduced with a fall in glomerular filtration, a rise in sodium retention, and juxtaglomerular ischemia. The latter results in more renin production, increased aldosterone, and further enhancement of sodium and water retention.[108–110] The ensuing dilution of plasma proteins further reduces oncotic pressure, more water goes into the extravascular space, and clinical edema appears or increases. (5) Increased hepatic fatty acid synthesis from the excess carbohydrate, impaired lipolysis, and reduced production of apo-beta-lipoproteins for lipid transport lead to fatty infiltration of the liver and hepatomegaly.

Infections in undernourished children also can precipitate the onset of kwashiorkor. The process by which this occurs has not been satisfactorily explained, but the following mechanisms may be involved: (1) Infections might divert the meager amino acid pool to the production of globulins and acute phase reactant proteins (AP), instead of albumin and transport proteins.[111–113] (2) The increase of APs that are proteinase inhibitors, such as alpha-1-antitrypsin and alpha-1-antichymotrypsin, may impair muscle protein breakdown.[114] (3) An impaired production and utilization of ketone bodies for energy during infections might lead to the use of more amino acids for gluconeogenesis.[115] (4) Protein catabolism and nitrogen losses are enhanced by many viral and febrile infections, probably through increased epinephrine and cortisol actions.[116,117] Regardless of the mechanisms involved, protein losses during severe infections can amount to as much as 2% of muscle protein per day.[118]

Disruption of Adaptation

When the supply for tissue and cell energy can no longer be maintained by patients with severe energy deficiency, a serious decompensation occurs with hypoglycemia, hypothermia, impaired circulatory and renal functions, acidosis, coma, and death. These events can occur within a period of a few hours. Metabolic decompensation due to severe protein deficiency, in addition to the changes discussed in the onset of kwashiorkor, may include hemorrhagic diathesis and jaundice due to failure by the liver to synthesize several clotting factors and transport proteins; various degrees of renal failure with acidosis, and water and sodium retention; decreased cardiac work, pulmonary congestion, and increased susceptibility to pulmonary infections; coma, and death.

A high-carbohydrate, low-protein diet is not the only iatrogenic cause of serious metabolic disrup-

tion in patients who have or are prone to develop edematous PEM. The abrupt administration of too much protein to patients with edematous PEM can also have serious, life-threatening consequences. When such patients have been eating minute amounts of protein or none at all, and they are suddenly fed large amounts of proteins or given large transfusions of plasma or blood, they may experience a rapid increase in intravascular protein concentration and entry of extracellular fluid into the vascular compartment leading to cardiovascular insufficiency and pulmonary edema. In fact, a premature introduction of high-energy or high-protein diet to a severely malnourished patient may be fatal.[119,120]

DIAGNOSIS

The clinical, biochemical, and physiologic characteristics of PEM vary according to the severity of the disease, the patient's age, the presence of other nutritional deficits and infections, and the predominance of energy or protein deficiency.

Classification of PEM

The classifications shown in Table 42–3 are important for the diagnosis and treatment of PEM, and for the application and evaluation of public health measures. Intensity is determined mainly by anthropometry, since other clinical findings and biochemical indexes usually do not show changes unless the disease is well advanced. More accurate measurements, such as assessment of body composition, are not practical or feasible in most of the settings where PEM occurs, and the so-called functional indicators[121] are not as yet well standardized or may be too complex to measure routinely.

Classification of the disease as acute, chronic, or acute with a chronic background is also done by anthropometry to assess current nutritional status and degree of growth retardation in children. Dietary history is useful, especially in adults, as are dietary surveys in population groups. The relative contributions of dietary protein and energy deficits in the mild and moderate forms of PEM are assessed mainly by the individual's dietary history or the population's dietary habits and food availability. Clinical characteristics and biochemical data confirm the diagnosis in severe PEM.

Table 42–3. Classification of PEM According to Intensity of Disease, its Duration, and Predominant Nutrient Deficiency

Intensity	*Duration*	*Main Deficit*
Mild	Acute	Energy
Moderate	Chronic	Protein
Severe	Both	Both

Anthropometric Measurements. The choice of anthropometric measurements depends on their simplicity, accuracy, and sensitivity; on the availability of measuring instruments; and on the existence of reference standards for comparison.

In order to allow international comparisons, it is sensible to use the same standard of reference for various populations. International or universal standards based on reliable anthropometric data can be used because: (1) Most children have similar growth potentials, regardless of ethnic background.[122,123] (2) The relationship of various anthropometric measurements, especially weight and height, is relatively constant in normal, healthy individuals of all age groups.[20] (3) The reference standards are merely for purposes of comparison and do not necessarily represent an ideal or a target. (4) The interpretation of the comparison (i.e., the values that separate "normal" from "deficient" and further divide the latter into "mild," "moderate," and "severe" forms) is a matter of judgment that comes into play when deciding whether the expected normal value for a given population should be 100%, 90%, or other proportion of the standard. Setting different cut-off points relative to a single standard is more practical than constructing local standards which, in a country with heterogeneous population groups, may pose the same problem as a "foreign" commonly used reference. At present, the World Health Organization recommends the data from the United States National Center for Health Statistics (NCHS)[124] as reference for weight and height.

The best anthropometric assessment of nutritional status and PEM is based on measurements of weight and height or length, and records of age, to calculate two indexes: *weight for height*, as an index of current nutritional status, and *height for age*, as an index of past nutritional history. Deficient height for age may represent a short period of growth failure at an early age or a longer period at a later age. Waterlow suggested the terms *wasting* for a deficit in weight for height, and *stunting* for a deficit in height for age.[125] Patients may then fall into four categories: (1) normal, (2) wasted but not stunted (suffering from acute PEM), (3) wasted and stunted (suffering from acute and chronic PEM), and (4) stunted but not wasted (past PEM with present adequate nutrition, or "nutritional dwarfs"). The intensity of wasting and stunting can be graded by calculating weight as percentage of the reference median weight for height, and

height as percentage of the reference median height for age, as follows:

$$\text{\% wt for ht (or ht for age)} = \frac{\text{observed weight (or height)}}{\text{reference wt for patient's ht (or reference ht for patient's age)}} \times 100$$

The grading shown in Table 42–4 is suggested for most countries, although some might find it convenient to use different cut-off points for specific groups. For example, the normal height for age in populations that are genetically short could be less than 95% of the reference. Some authors advocate the use of centiles or standard deviations from the mean, instead of percent deviations from the median. Although there may be a statistical advantage for the former, percent deviations are easier to understand by the general public, and to calculate by field workers. Color-coded charts and graphs have been devised to simplify the measurements and their interpretation.[126–128]

For adolescents and adults, weight for height alone is usually used to assess nutritional status, and the use of the *body mass index* (or Quetelet's index), weight/height^2, has been advocated as being independent of the person's height.[20]

The Gomez classification has probably been the most widely used index for children.[129] It classifies PEM into three grades based on *weight for age:* grade I = 90 to 75% of reference; grade II = 74 to 60%; grade III = less than 60% The use of this index does not differentiate between a truly underweight child (current PEM) and one who is short in stature but well proportioned in weight (past PEM); furthermore, the information about chronologic age is not always reliable. However, it is useful in public health and epidemiologic studies, as it indicates the proportion of children in a population group who at some time in their lives had malnutrition.

Other anthropometric indexes have been used, such as the developmental quotient for weight or height (weight-age or height-age divided by the chronologic age),[130] mid-arm circumference in absolute terms[131] or relative to height (QUAC-stick)[132] or weight, and ratio of arm circumference to head circumference.[133]

Mild and Moderate PEM

The main clinical feature of mild and moderate PEM is weight loss. A decrease in subcutaneous adipose tissue may become apparent. When PEM is chronic, children show growth retardation in terms of weight (wasting) and height (stunting). Groups of populations in whom PEM is highly prevalent or "endemic" show slow weight gains, as illustrated in Figure 42–5.

Physical activity and energy expenditure of children decrease.[40–42] Other functional indicators of immunocompetence, gastrointestinal functions, and behavior may be altered, but their assessment is not yet practical for diagnostic purpose.[19,46,58,76,121] Nonspecific manifestations include more sedentary behavior, frequent episodes of diarrhea, and apathy, lack of liveliness, and short attention spans.

In adults, mild to moderate PEM results in leanness with reduction in subcutaneous tissue. The most common change in body composition is a reduction of adiposity below the average 12 and 20% expected in normal, well-nourished men and women, respectively. Capacity for prolonged physical work is reduced, but this change is usually apparent only in persons engaged in intense, energy-demanding, occupations.[18,43] Malnourished women have a higher probability of giving birth to infants with low birth weights.[134] As in children, there may be other functional alterations not yet well characterized.

Biochemical information is not consistent in mild and moderate PEM. Laboratory data related to low protein intakes may include low urinary excretion of creatinine, leading to a low creatinine-height index in children,[135] low urinary urea nitrogen and hydroxyproline excretions, altered plasma patterns of free amino acids with a decrease in branched-chain essential amino acids, slight decreases in serum transferrin and albumin, and reduced number of circulating lymphocytes.

Table 42–4. Classification of Intensity of Current ("Wasting") and Past or Chronic ("Stunting") PEM Based on Weight for Height, and Height for Age*

	Normal	*Mild*	*Moderate*	*Severe*
Weight for height (deficit = wasting)	90–110†	80–89	70–79	<70, or with edema
Height for age (deficit = stunting)	95–105	90–94	85–89	<85

*Adapted from Waterlow, J.C.[125]
†Percentage relative to the median NCHS standards.[124]

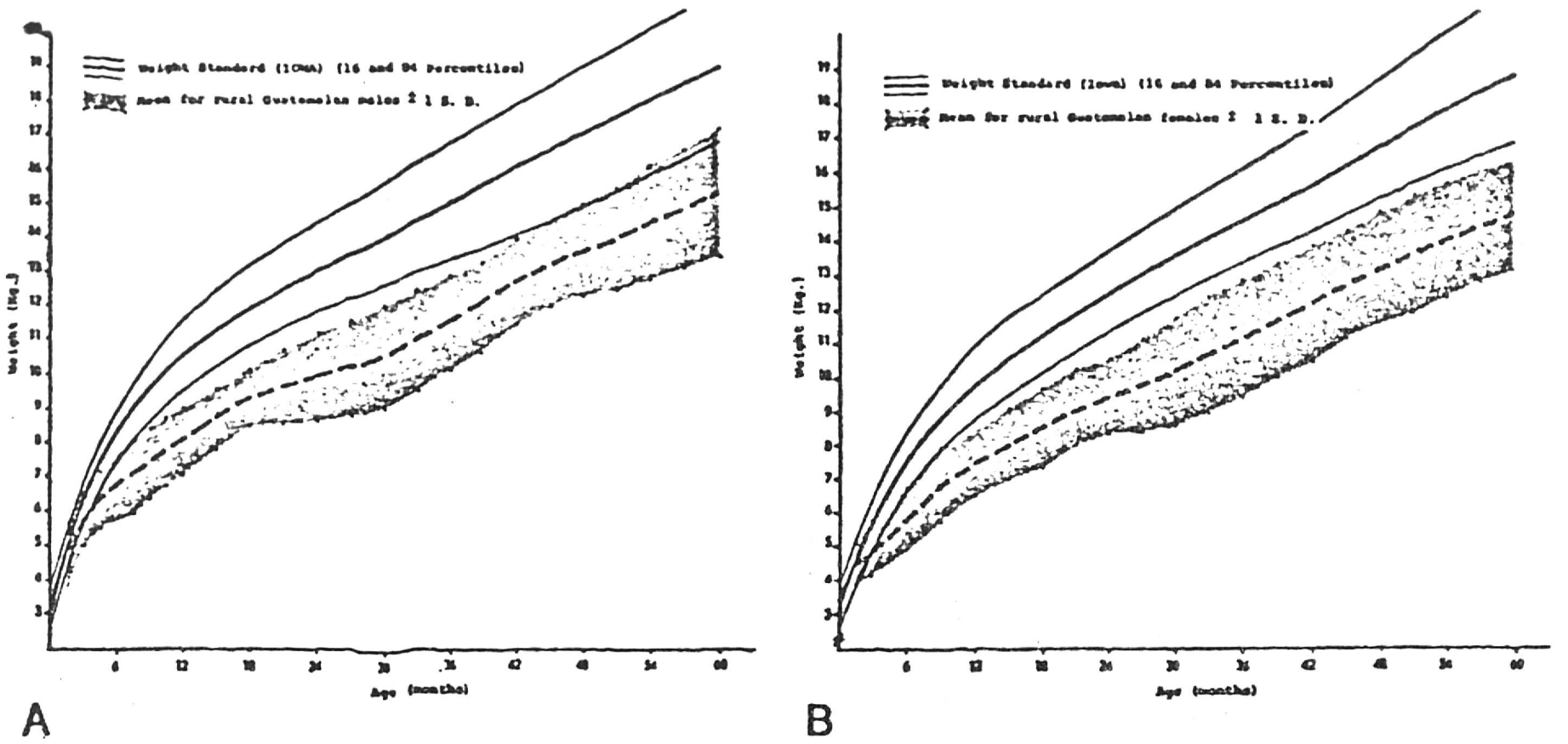

Fig. 42–5. Pattern of weight gain, from birth to 5 years, in 431 boys and 436 girls from low-income families in rural Guatemala. (From INCAP,[150] with permission.)

Severe PEM

The diagnosis is principally based on dietary history and clinical features. Marasmus is usually associated with severe food shortage, prolonged [illegible]ation, or infrequent feeding of infants, and kwashiorkor with poor protein intakes. Chronic or recurrent diarrhea and infections are common features.

Marasmus. Generalized muscular wasting and absence of subcutaneous fat give the patient with severe, nonedematous PEM a "skin and bones" appearance (Figs. 42–6 and 42–7). Marasmic patients frequently have 60% or less of the weight expected for their height, and children have marked retardation in longitudinal growth. The hair is sparse, thin, and dry, without its normal sheen, and usually of a dull brown or reddish color; it is easily pulled out without causing pain. The skin is dry, thin, with little elasticity, and wrinkles easily. Patients are apathetic but usually aware and with a look of anxiety on their face. These features and the sunken cheeks caused by disappearance of the Bichat fat pads, which are among the last subcutaneous adipose depots to disappear, give the marasmic child's face the appearance of a monkey's or an old person's.

Some patients are anorexic while others are ravenously hungry, but they seldom tolerate large amounts of food [illegible]. Constipation is frequent but diarrhea may be present. There is marked weakness and children frequently cannot stand without help. Heart rate, blood pressure, and body temperature may be low. Hypothermia of 35°C or less can occur, especially after fasting for 8 or more hours, and is often accompanied by hypoglycemia. The viscera are usually small. Abdominal distention may be present. The lymph nodes are easily palpable.

Differential diagnosis must be made from the secondary PEM of body-wasting diseases; dietary history plays an important role.

Common complicating features are acute gastroenteritis, dehydration, respiratory infections, and eye lesions due to hypovitaminosis A. Systemic infections can be present without an appropriate febrile response, tachycardia, or leukocytosis. These infections lead to septic shock or intravascular clotting with high mortality rates.

Kwashiorkor. The predominant feature is soft, pitting, painless edema, usually in the feet and legs, but extending to the perineum, upper extremities, and face in severe cases (Fig. 42–8). Most patients have skin lesions, often confused with pellagra, in the areas of edema, continuous pressure (e.g., buttocks and back), or frequent irritation (e.g., perineum and thighs). The skin may be erythematous, and it glistens in the edematous regions with zones of dryness, hyperkeratosis, and hyperpigmentation, which tend to become confluent. The epidermis peels off in large scales, exposing underlying tissues that are easily infected. Subcutaneous fat is preserved, and there may be some muscle wasting. Weight deficit, after accounting for the weight of edema, is usually not as severe as in marasmus. Height may be normal or retarded, depending on the chronicity of the current episode and on past nutritional history.

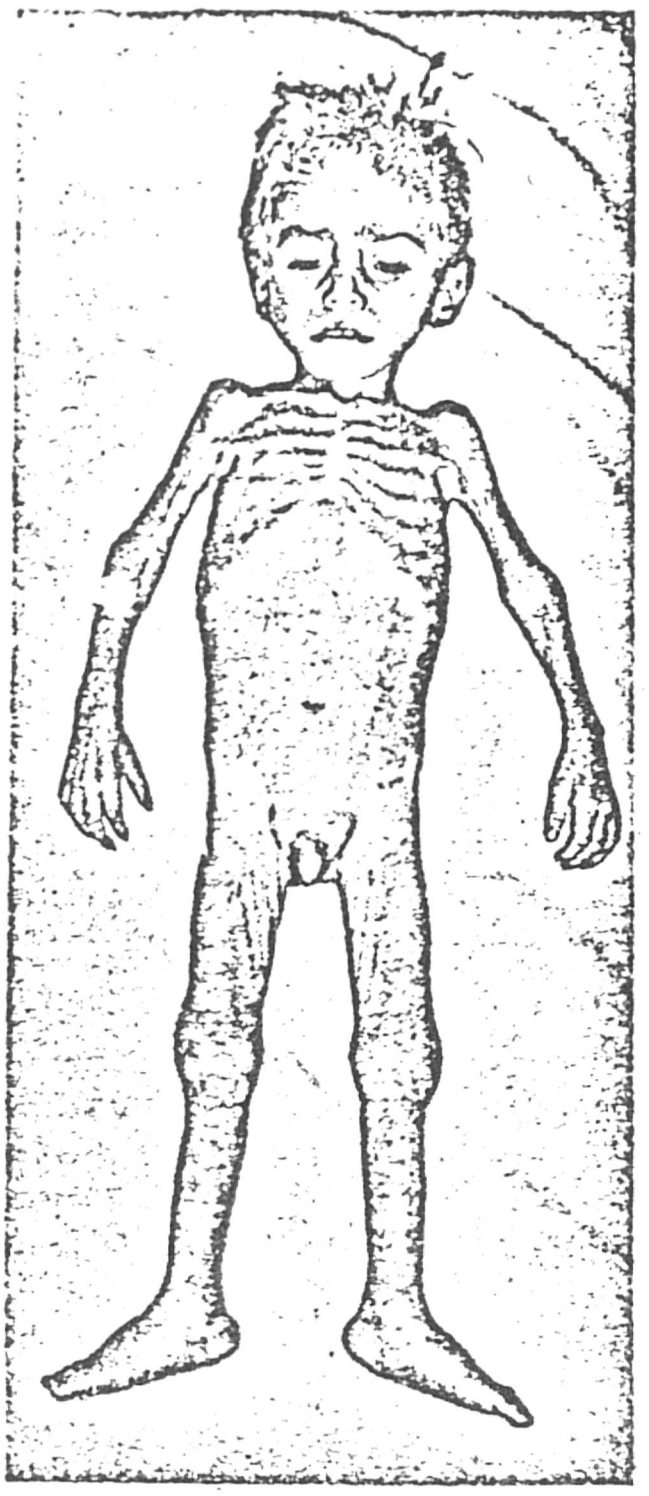

Fig. 42–6. Marasmus in a 21-month-old child. (From Viteri, F.E.,[58] with permission of Raven Press.)

The hair is dry, brittle, without its normal sheen, and can be pulled out easily without pain. Curly hair becomes straight, and the pigmentation usually changes to dull brown, red, or even yellowish-white. Alternating periods of poor and relatively good protein intake can produce alternating bands of depigmented and normal hair, which have been termed the "flag sign."

The patients may be pale, with cold and cyanotic extremities. They are apathetic and irritable, cry easily, and have an expression of misery and sadness. Anorexia, sometimes necessitating nasogastric tube feeding, postprandial vomiting, and diarrhea are common. These conditions improve without specific gastrointestinal treatment as nutritional recovery progresses. Hepatomegaly with a soft, round edge caused by severe fatty infiltration is usually present. The abdomen is frequently protruding because of distended stomach and intestinal loops. Peristalsis is irregular. Muscle tone and strength are greatly reduced and tachycardia is common. Both hypothermia and hypoglycemia can occur after short periods of fasting.

Differential diagnosis must be made from other causes of edema and hypoproteinemia, and from secondary PEM due to impairment in protein absorption or metabolism.

The same complications occur as in marasmus, but diarrhea and respiratory and skin infections are more frequent and severe. Serious, fatal infections may occur, frequently without fever, tachycardia, respiratory distress, or appropriate leukocytosis. The most common causes of death are pulmonary edema with bronchopneumonia, septicemia, gastroenteritis, and water and electrolyte imbalances.

Marasmic Kwashiorkor. This form of edematous PEM combines clinical characteristics of kwashiorkor and marasmus. The main features are the edema of kwashiorkor, with or without its skin lesions, and the muscle wasting and decreased subcutaneous fat of marasmus (Fig. 42–9 and 42–10). When edema disappears during early treatment, the patient's appearance resembles that of marasmus. Biochemical features of both marasmus and kwashiorkor are seen, but the alterations of severe protein deficiency usually predominate.

Biochemical and Histopathologic Features of Severe PEM

The most common biochemical findings are the following: serum concentrations of total proteins, and especially albumin, are markedly reduced in edematous PEM, and normal or moderately low in marasmus; hemoglobin and hematocrit are usually low, more so in kwashiorkor than in marasmus; the ratio of nonessential to essential amino acids in plasma is elevated in kwashiorkor and usually normal in marasmus; serum levels of free fatty acids are elevated, particularly in kwashiorkor; blood glucose level is normal or low, especially after fasting 8 to 12 hours; urinary excretions of creatinine, hydroxyproline, 3-methylhistidine, and urea nitrogen are low. Edematous children have markedly reduced urinary creatinine excretions in relation to their height, leading to a low creatinine-height index,[135] whereas marasmic children may have a normal or somewhat low index.

Plasma levels of other nutrients vary and tend to be moderately low. They do not necessarily reflect the body stores. For example, serum iron and retinol may be normal with almost depleted body stores, or in kwashiorkor they may be relatively low with adequate stores because of alterations in

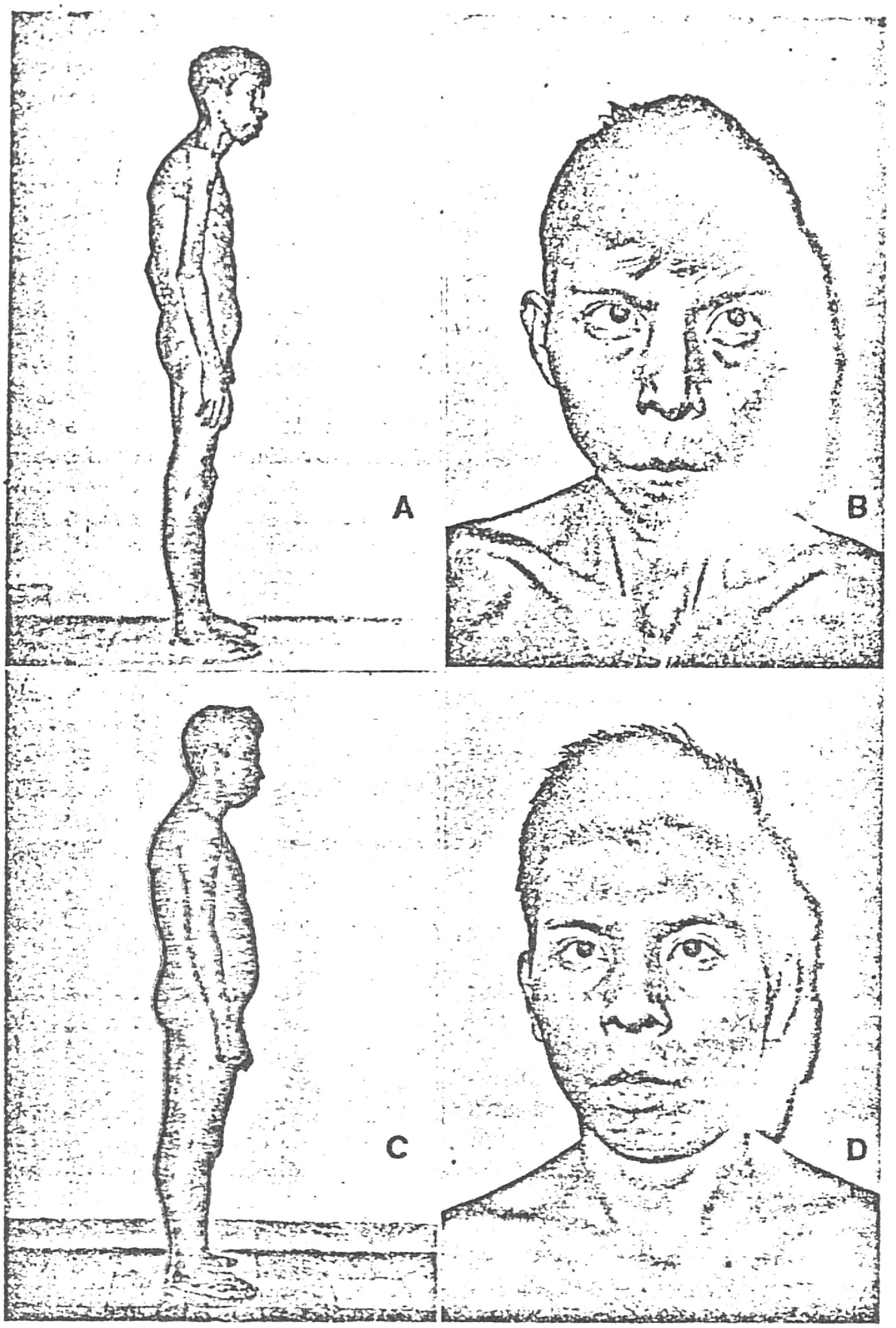

Fig. 42–7. *A,B,* Marasmic PEM in a 29-year-old man. *C,D,* Patient after three months of treatment.

the transport proteins, transferrin, and retinol-binding protein.

Many other biochemical changes have been described in severe PEM; some of them were discussed in the section on "Pathophysiology and Adaptive Responses." Others are listed in Table 42–5. Although they have little practical importance in diagnosing the disease, they allow a better understanding of the pathophysiologic modifications.

Body protein decreases at a slow rate, most of it from muscle, and the greater loss of adipose tissue results in a relative increase of total body water (i.e., per unit of body mass), mainly as intracellular water. In severe protein deficiency (kwashiorkor) extracellular water also increases. The intracellular concentrations of potassium and magnesium decrease and that of sodium increases, although the serum concentrations of electrolytes do not necessarily reflect these alterations.[81]

Table 42–5. Additional Selected Biochemical Changes Observed in Severe PEM§

	Marasmus	*Edematous PEM*
Body composition		
Total body water	High	High
Extracellular water	High	Higher
Total body potassium	Low	Lower
Total body protein	Low	Low
Serum or plasma		
Transport proteins*	Normal or low	Low
Branched-chain amino acids	Normal or low	Low
Tyrosine/phenylalanine ratio	Normal or low	Low
Enzymes (in general)†	Normal	Low
Transaminases	Normal or high	High
Liver		
Fatty infiltration	Absent	Severe
Glycogen	Normal or low	Normal or low
Urea cycle and other enzymes‡	Low	Lower
Amino acid synthesizing enzymes	High	Not as high

*For example, transferrin, ceruloplasmin, retinol-, cortisol-, and thyroxine-binding proteins, α- and β-lipoproteins.
†For example, amylase, pseudocholinesterase, alkaline phosphatase.
‡For example, xanthine oxidase, glycolic acid oxidase, cholinesterase.
§From Torun, B., Viteri, F.E.,[149] with permission of McGraw-Hill Book Co.

Histopathologic studies show nonspecific atrophy, mainly in tissues with greater cell turnover rates, such as intestinal mucosa, red bone marrow, and testicular epithelium; intestinal villi are flattened and enterocytes lose their columnar appearance.[136] In marasmus there is generalized atrophy of skeletal muscle. The skin changes consist of dermal atrophy, ecchymosis, ulcerations, and hyperkeratotic desquamation, seen primarily in areas subjected to irritation and not necessarily restricted to exposed areas, as in the case of pellagra. The liver in individuals with kwashiorkor is enlarged with fatty infiltration; periportal fat appears first and advances centripetally as severity increases. Other histologic analyses, special staining techniques, and electron microscopy reveal more alterations, not all of which result specifically from primary protein-energy malnutrition. All do reflect generalized atrophy, however. Lesions due to superimposed infections and other nutrient deficiencies often are evident macroscopically and upon histopathologic examination. These changes usually revert to normal with nutritional recovery, although some residual lesions may persist for some time.

PROGNOSIS AND RISK OF MORTALITY

Treatment of mild and moderate PEM corrects the acute signs of the disease, but children's catch-up growth in height may take a long time or might never be achieved. It has been suggested that many children who have suffered from severe or moderate PEM are not normal even when they have recovered fully.[137] These children have been deprived not only of food but also of opportunities for development, and they have missed the critical periods for harmonic physical, mental, and social maturation. Weight for height can be restored easily, but the child may remain stunted, and a small body size may influence his maximal working capacity as an adult. Many severely malnourished children appear to have residual behavioral and mental problems in terms of creativity and social interaction. However, the causal roles of malnutrition and a poor living environment are difficult to disassociate, and there is no irrefutable evidence that the damage cannot be corrected in a good, stimulating environment.

Anthropometric characteristics are associated with mortality rates, as in the classification of severe PEM into first, second, or third degrees, based on weight for age.[129] A higher mortality rate is associated with the more intense anthropometric deficits but not with mild or moderate deficiencies.[138] Mortality rates in severe PEM can be as high as 40%; the immediate causes of death are usually infections. Table 42–6 lists the characteristics that generally indicate a poor prognosis. Mortality rate can decrease to 10% or less with the prevention and adequate treatment of infections and other complications, together with adequate dietary therapy.

TREATMENT

Severe PEM

Patients with uncomplicated PEM should be treated outside the hospital whenever possible. Hospitalization increases the risk of cross-infec-

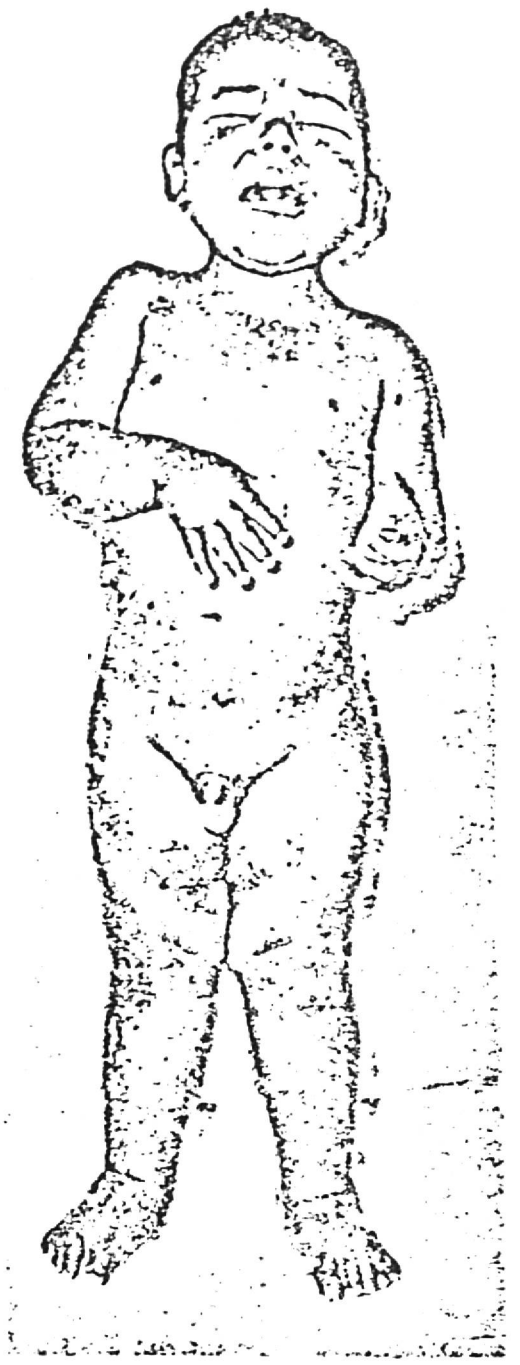

Fig. 42–8. Kwashiorkor in a 36-month-old child. Note that subcutaneous tissues were preserved in the trunk and face.

tions, and the unfamiliar setting may increase apathy and anorexia in children, making feeding more difficult. When hospitalization is necessary, treatment strategy can be divided into three stages: (1) resolving life-threatening conditions, (2) restoring nutritional status without disrupting homeostasis, and (3) ensuring nutritional rehabilitation.

Resolving Life-Threatening Conditions. Nutritional rehabilitation can be delayed until life-threatening conditions are solved. The most frequent are:

1. *Fluid and electrolyte disturbances.* The assessment of dehydration is not easy in severe PEM, as classic signs of dehydration, such as sunken eyeballs and decreased skin turgor, are frequently found in well-hydrated patients, while hypovolemia may coexist with subcutaneous edema. Useful signs are low urinary output, weak and rapid pulse, low blood pressure, and a declining state of consciousness. The therapeutic approach differs from that in well-nourished patients because of water and electrolyte peculiarities of severe PEM, namely: (1) hypo-osmolality with moderate hyponatremia, frequently with intracellular sodium excess; (2) intracellular potassium depletion, usually without hypokalemia; (3) mild-to-moderate metabolic acidosis, which decreases or disappears when the patient receives dietary or parenteral energy, and electrolyte balance is reestablished; (4) high tolerance to hypocalcemia, partly because the acidosis produces a relative increment in ionized calcium and partly because hypoproteinemia makes less protein available to bind calcium ions; and (5) decreased body magnesium, with or without hypomagnesemia.

Fluid repletion should allow a diuresis of at least 200 ml in 24 hrs in children and 500 ml in adults, or a micturition every 2 to 3 hrs. Whenever possible, oral or nasogastric rehydration should be used. Initially, 10 ml/kg/hr can be given every 1 to 2 hrs, and the volume should be modified according to patient response. Patients who are urinating should receive about 6 meq K, 2 to 3 meq Na, 2 to 3 meq Ca, and 20 to 30 kcal/day/kg of body weight. This can be accomplished by dissolving in 1 L of water, 3 g KCl, 1 g table salt (NaCl), 2 g $CaCl.6H_2O$ (or 4 g calcium gluconate), and 50 g glucose or sucrose (sugar). Potassium should be withheld when there is no diuresis. Additional fluids must be given to compensate for the losses of diarrhea and vomiting, providing about 35 meq Na and 30 meq K per Kg of excreta (i.e., 2 g table salt and 2 g KCl/L). Dietary formula with calcium should be started as early as possible, if necessary alternating with the electrolyte solution; this can usually be 4 to 6 hrs after beginning the oral rehydration therapy. Total K intake can be raised to 8 to 10 meq/kg/day.

Intravenous fluids must be used in severe dehydration with hypovolemia, impending shock, frequent vomiting, and persistent abdominal distention. Hypo-osmolar solutions (200 to 280 mOsm/L) must be used. K (when urinating) and Na should not exceed 6 and 3 meq/kg/day, respectively, and glucose must provide 15 to 30 kcal/kg/day. During the first hour, 10 to 30 ml/kg are infused, depending on the patient's condition. Subsequent volumes are calculated at 2- to 4-hr intervals. Additional losses through diarrhea and vomiting must be compensated with about 3 meq Na, 3 meq K, 6 meq Cl, and 15 kcal/100 g (i.e., 20 ml isotonic saline, 2 ml of 10% KCl, and 78 ml of 5% dextrose/100 g excreta). An increase in pulse and respiratory rate with weight gain after accounting for weight of excreta, pulmonary rales, and appearance or exacerbation of edema indi-

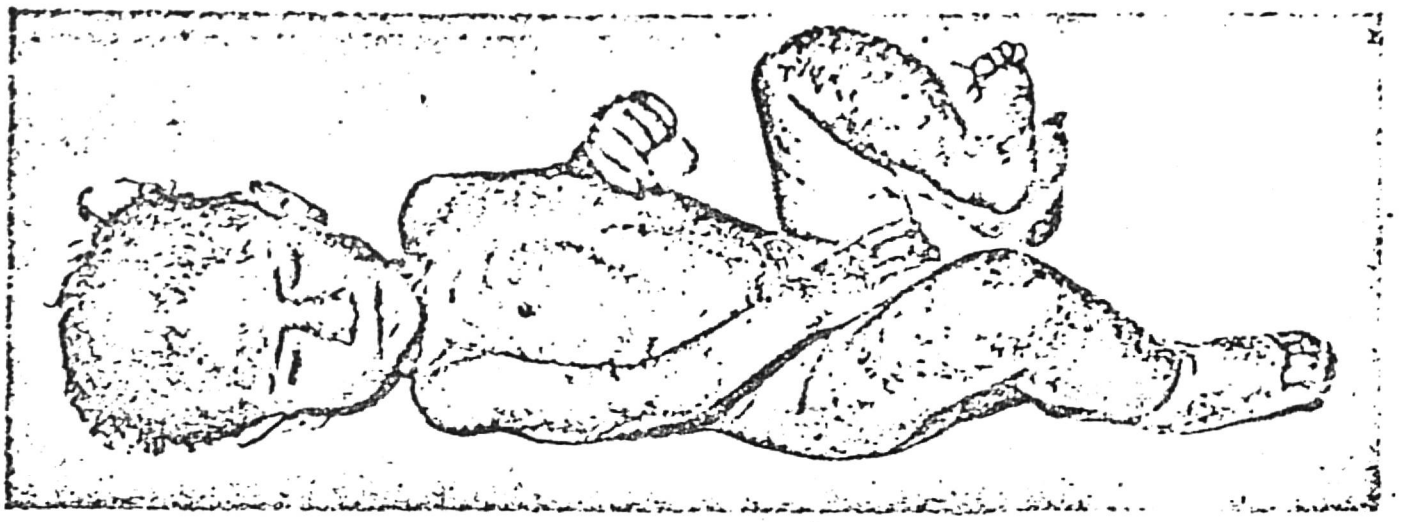

Fig. 42–9. Marasmic kwashiorkor in a 22-month-old child. Note the edema in the lower part of the body, the emaciated upper part, and the skin lesions. (From Torun, B., Viteri, F.E.,[149] with permission of McGraw-Hill Book Co.)

cates overhydration. An increase in pulse and respiratory rate with weight loss, low urine output, and continuing losses from diarrhea and vomiting suggests insufficient fluid therapy.

Some clinicians advocate the routine use of solutions containing lactate or bicarbonate. However, the mild metabolic acidosis of malnutrition usually disappears with energy intake. Therefore, treatment for acidosis should be withheld unless blood pH is below 7.25, urinary pH is below 5, or clinical signs of severe acidosis are present.

Small increases (0.5 to 1 g/dl) in plasma protein concentration help to prevent a rapid exit of water from the intravascular compartment in patients with severe hypoproteinemia (less than 3 g/dl), anuria, and signs of hypovolemia or impending circulatory collapse. This can be achieved by administering plasma intravenously, 10 ml/kg in 1 to 2 hrs, followed by 20 ml/kg/hr of a mixture of two parts of 5% dextrose and one part of isotonic saline, for 1 or 2 hrs. If diuresis does not improve, the dose of plasma can be repeated. Further treatment for circulatory collapse is similar to that of well-nourished patients.

Hypocalcemia may occur secondary to magnesium deficiency. When the patient has symptoms of hypocalcemia and serum magnesium determinations are not available, it is essential not only to give calcium infusion but also to give magnesium intravenously or intramuscularly. When the serum concentration of calcium rises to normal level or, in the absence of laboratory data, when the symptoms of hypocalcemia disappear, calcium infusion may be discontinued. Intramuscular or oral magnesium supplementation should follow the initial parenteral magnesium until the patient is repleted with this ion as indicated by maintenance of serum and urine magnesium concentrations. When there are no laboratory facilities to monitor Mg concentrations, a general therapeutic guideline is to give magnesium intramuscularly as a 50% solution of magnesium sulfate in doses of 0.5, 1, and 1.5 ml, respectively, for patients who weigh less than 7, between 7 and 10, and more than 10 kg. The dose can be repeated every 12 hours until there is no recurrence of the hypocalcemic symptoms and oral magnesium supplementation of 0.5 to 1 meq Mg/kg/day can be given, as described later. Certain antibiotics, such as amphotericin, can cause loss of magnesium and potassium into the urine, increasing the need for both ions.

2. *Infections.* Malnourished patients are particularly prone to infections. Although these are often severe and life-threatening, paradoxically, clinical manifestations may be mild and the classic signs of fever, tachycardia, and leukocytosis absent. Antigen-antibody reactions are often impaired and skin tests, such as tuberculin, often give falsely negative results.

Antibiotics should not be used prophylactically, but when an infection is suspected appropriate antibiotic therapy must be started immediately, even before obtaining the results of microbiologic cultures. The choice of drug will vary with the suspected etiologic agent, the severity of the disease, and the local pattern of drug resistance. When septicemia is suspected, a broad-spectrum antibiotic or a combination, such as ampicillin and gentamicin, is usually given intravenously. Other supportive treatment may also be necessary, as for respiratory distress, hypothermia, and hypoglycemia.

Repeated transfusions of fresh frozen human plasma, 10 ml/kg during the first 3 to 4 days of treatment, accelerate the recovery of impaired complement hemolytic activity in patients with edematous PEM.[79,139] Although this might reduce serious infections complications, clinical evidence is still lacking about the advantages of this treatment.

Clinicians should be aware that gastrointestinal,

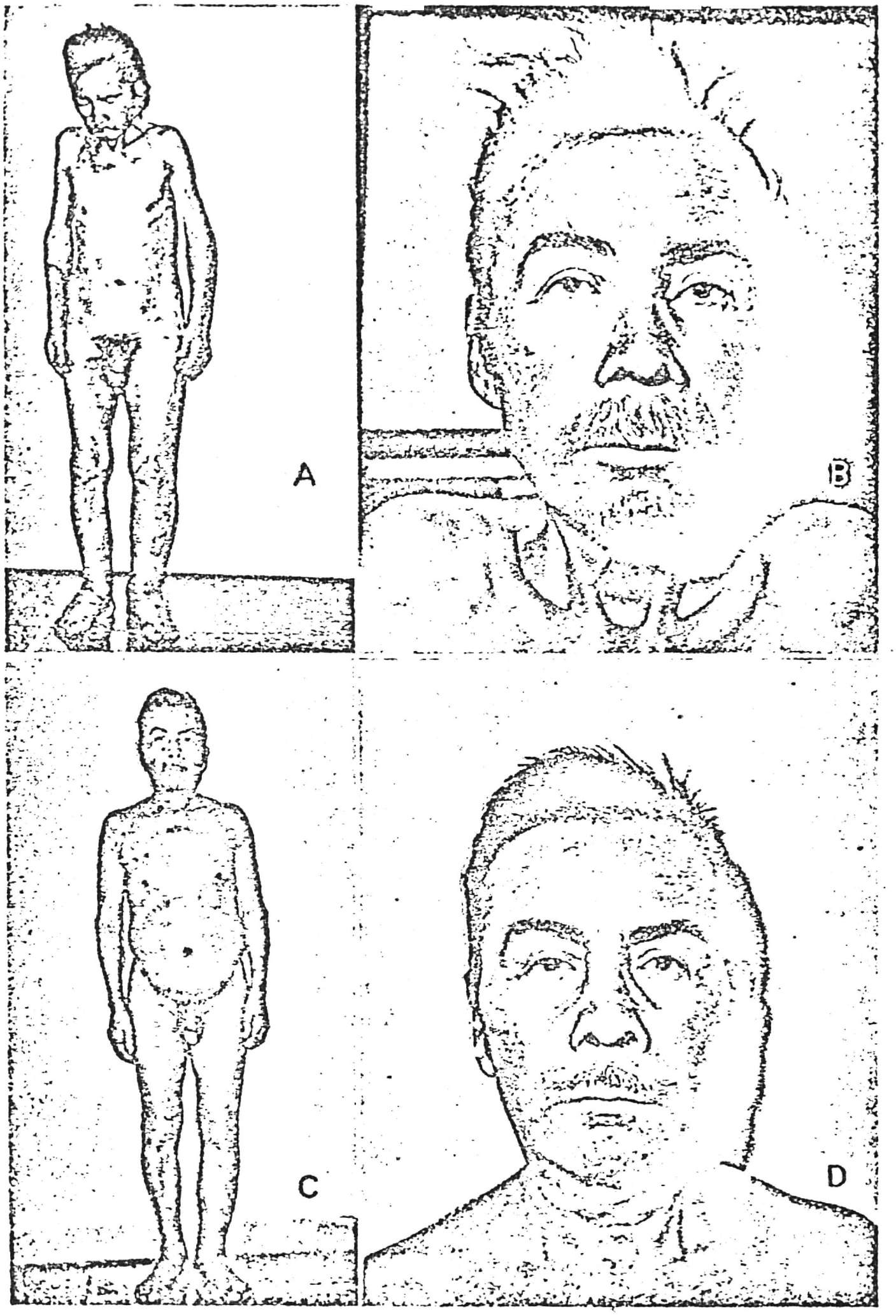

Fig. 42–10. *A,B,* Edematous PEM in a 46-year-old man. *C,D,* Patient after three months of treatment.

hepatic, and renal alterations that might accompany severe PEM could potentiate the toxic effects of a drug. Treatment for intestinal parasites is rarely urgent and can be deferred until nutritional rehabilitation is underway. This delay decreases the risks of potential toxicity, including the possibility of absorbing drugs normally not absorbed by a healthy intestine.

3. *Hemodynamic alterations.* Cardiac failure may develop during or after administration of intravenous fluids, or shortly after the introduction of high-protein and high-energy feedings, leading to pulmonary edema and frequent secondary pulmonary infection. These alterations may be the result of impaired cardiac function, sudden expansion of the intravascular fluid volume, severe anemia, or impaired membrane function. Diuretics such as furosemide (10 mg intravenously or

Table 42–6. Characteristics that Indicate Poor Prognosis in Patients with PEM

—Age less than 6 months.
—Deficit in weight for height greater than 30%, or in weight for age greater than 40%.
—Stupor or coma.
—Infections, particularly bronchopneumonia or measles.
—Petechiae or hemorrhagic tendencies (purpura is usually associated with septicemia or a viral infection).
—Dehydration and electrolyte disturbances, particularly hyponatremia, hypokalemia, and severe acidosis.
—Severe tachycardia, signs of heart failure, or respiratory difficulty.
—Total serum proteins below 3 g/dl.
—Severe anemia with clinical signs of hypoxia.
—Clinical jaundice, increased serum bilirubin, and/or frankly elevated transaminases.
—Extensive exudative or exfoliative cutaneous lesions, or deep decubitus ulcerations.
—Hypoglycemia or hypothermia.

intramuscularly, repeated as necessary) should be given, as well as other supportive measures. Many clinicians advocate the use of digoxin (0.03 mg/kg intravenously, every 6 to 8 hrs). *The use of diuretics merely to accelerate the disappearance of edema in kwashiorkor is contraindicated.*

4. *Severe anemia.* Blood transfusions should be given *only in cases of severe anemia* with less than 4 g hemoglobin/dl, or with signs of hypoxia or impending cardiac failure. Whole blood (10 ml/kg) can be used in marasmic patients, but it is better to use packed red blood cells (6 ml/kg) in patients with edematous PEM. The transfusion should be given slowly, over 2 to 3 hrs, and repeated if necessary after 8 to 24 hrs. The routine use of blood transfusions endangers the patient. Hemoglobin levels will improve with proper dietary treatment supplemented with hematinics.

5. *Hypothermia and hypoglycemia.* Body temperature below 35.5°C and plasma glucose concentration below 60 mg/dl can be due to either impaired thermoregulatory mechanisms, reduced fuel substrate availability, or severe infection. Asymptomatic hypoglycemia can be prevented or treated by the frequent feeding of small volumes of glucose-containing diets and solutions. Severe symptomatic hypoglycemia must be treated intravenously with 10 to 20 ml of 50% glucose solution followed by oral administration of 25 to 50 ml of 5% glucose solution at 2-hr intervals for 24 to 48 hrs.

Body temperature usually rises in the hypothermic patient with frequent feedings of glucose-containing diets or solutions. Body temperature must be closely monitored when external heat sources are used to reduce the loss of body heat, as these patients may rapidly become hyperthermic. It is best to keep the seminude patients in an ambient temperature of 30 to 33° C.

6. *Severe vitamin A deficiency.* Severe PEM is often associated with vitamin A deficiency. A large dose of vitamin A should be given on admission, since ocular lesions can develop as a result of increased demands for retinol when adequate protein and energy feeding begins. Water-miscible vitamin A should be given orally or intramuscularly on the first day, at a dose of 50,000 to 100,000 IU for infants and preschool children, or 100,000 to 200,000 IU for older children and adults, followed by 5,000 IU orally each day for the duration of treatment. The initial dose should be repeated two more days in symptomatic patients. Corneal ulcerations should be treated with ophthalmic drops of 1% atropine solution and antibiotic ointments or drops until the ulceration heals.

Homeostatic Restoration of Nutritional Status. The next objective of therapy is to replace nutrient tissue deficits as rapidly and safely as possible. Based on the premise that the patient is adapted to the malnourished state, nutritional treatment must be gradual to avoid disrupting his metabolic equilibrium. Various regimens provide a diet that meets daily maintenance requirements for a few days, followed by increases in nutrient delivery. Table 42–7 shows a therapeutic schedule for children, based on the experience of INCAP. The only difference between kwashiorkor and marasmus is that the latter often requires larger amounts of dietary energy, which can be provided by adding vegetable oil to increase the diet's energy density. Diets with as much as 60 to 75% of the energy from fats are usually well tolerated; there may be some steatorrhea without profuse diarrhea, and 85 to 92% of the fat is absorbed.[87] The intervals for the dietary increments in Table 42–7 can be lengthened to 3 to 5 days in severely malnourished children, especially those with plasma protein less than 3 g/dl or serious metabolic disturbances.

It is best to begin with a liquid formula fed orally or by nasogastric tube, divided equally into 5 to 12 feedings per day, depending on the patient's age and general condition. This frequent feeding of small volumes prevents vomiting and the development of hypoglycemia and hypothermia. For older children and adults with good appetite, the liquid formula can be partly substituted with solid foods that have a high density of good-quality, easily digestible nutrients.

Intravenous alimentation is rarely justified in primary PEM and can increase mortality rates.[140]

The diet must be supplemented to provide 8 to

Table 42–7. Dietary Therapeutic Regimen Based on Milk Formulas, for Infants and Preschool Children with Severe PEM*

Days From Beginning of Treatment	*Protein (g)*	*Energy (kcal)*	*Milk† oz. (g)*	*Sugar (g)*	*Oil‡ (g)*	*Water§ (ml)*
1	0.8–1	70–90	1 (3)	15	– –	70 (100)
3	1.5–2	105–115	2 (6)	20	– [1]	40 (100)
5	2.5–3	125–135	3 (9)	20	– [2]	10 (100)
7	3.5–4.5	145–160	4.5 (14)	20	– [3]	– (120)
Marasmus**						
12	—	175	—	—	2 [5]	—
..	—	200	—	—	5 [8]	—
22	—	220	—	—	7 [10]	—
etc.	3.5–4.5	"	4.5 (14)	20	"	– (120)

*Amounts are per kg body weight per day. The formulas must be supplemented with adequate amounts of vitamins, minerals, and electrolytes. Additional water must be given to provide at least 1 ml of total fluids per kcal in the diet.

†Amounts on the left are fluid ounces of whole fluid milk with 3% fat. Amounts in parentheses are g of dry, powdered milk.

‡IMPORTANT: When one is using powdered skim milk, vegetable oil must be added as indicated inside the brackets.

§Amounts on the left are added to fluid milk, amounts in parentheses to powdered milk.

**Marasmic patients may require more dietary energy. Two to three ml of vegetable oil per kg per day should be added at five-day intervals until the rate of weight gain becomes adequate.

10 meq K, 3 to 5 meq Na, 5 to 8 meq Ca, and 1 to 2 meq Mg/Kg of body weight per day. This can be accomplished by adding 0.3 g KCl and 0.1 g NaCl/kg to milk formulas, or by adding appropriate amounts of the mineral mixture shown in Table 42–8 to most other diets. Additional supplements should include daily doses of 60 to 120 mg elemental iron, 10 mg elemental zinc, 0.3 mg folic acid, 5,000 IU vitamin A, and other vitamins and trace elements in the doses provided by most commercial preparations.

The protein source must be of high biologic value and easily digested. Cow's milk is frequently available, but some clinicians worry about the possibility of lactose malabsorption in severe PEM. Cow's milk usually is well tolerated and assimilated by severely malnourished children and can be safely advocated.[141,142] Eggs, meat, fish, soy isolates, and some vegetable-protein mixtures are also sources of good protein. Most vegetable mixtures have protein digestibilities that are 10 to 20% lower than those of animal proteins, making it necessary to feed larger amounts, and their bulk might pose a problem in feeding small children.

The attitude of the person who feeds the patient and the appearance, color, and flavor of the foods are important to overcome the patient's lack of appetite.

The initial response to diet is either no change in weight or a decrease due to loss of edema, accompanied by large diuresis (Fig. 42–11). After 7 to 15 days, there is a period of rapid weight gain or "catch-up." The rate of catch-up usually is slower in marasmus than in kwashiorkor. In children, this initial rate of weight gain generally is 10 to 15 times that of a normal child of the same age, and it can be as high as 20 to 25 times greater. Some patients only show a four- or fivefold increase in catch-up. Most often this is associated with insufficient energy intakes (e.g., due to formula inadequately prepared, insufficient amounts of formula given at each feeding, too few feedings per day, anorexia, or lack of patience of the person who feeds the child) or with overt or asymptomatic infections, such as urinary infections and tuberculosis.

Table 42–8. Mineral Mixture to Complement Liquid Formulas*

Salt	*Amount (g)*	*1 g mixture provides (meq)*	
KCl	44	K^+	8.5
NaCl	9	Na^+	3.5
Na_2HPO_4	7	Ca^{2+}	1.4
$CaCO_3$	5	Mg^{2+}	0.6
$MgSO_4 \cdot 7H_2O$	5	HPO_4^{2+}	1.2

*From Torun, B., Viteri, F.E.,[119] with permission of Rev. Col. Med.

Ensuring Nutritional Rehabilitation. This last stage of treatment may begin in the hospital and continue on an outpatient basis, but the patient must continue to eat adequate amounts of protein, energy, and other nutrients, especially when traditional foods are introduced into the diet. Emotional and physical stimulation must be provided, and persistent diarrhea, intestinal parasites, and other minor complications must be treated. Children should be vaccinated during this period as well.

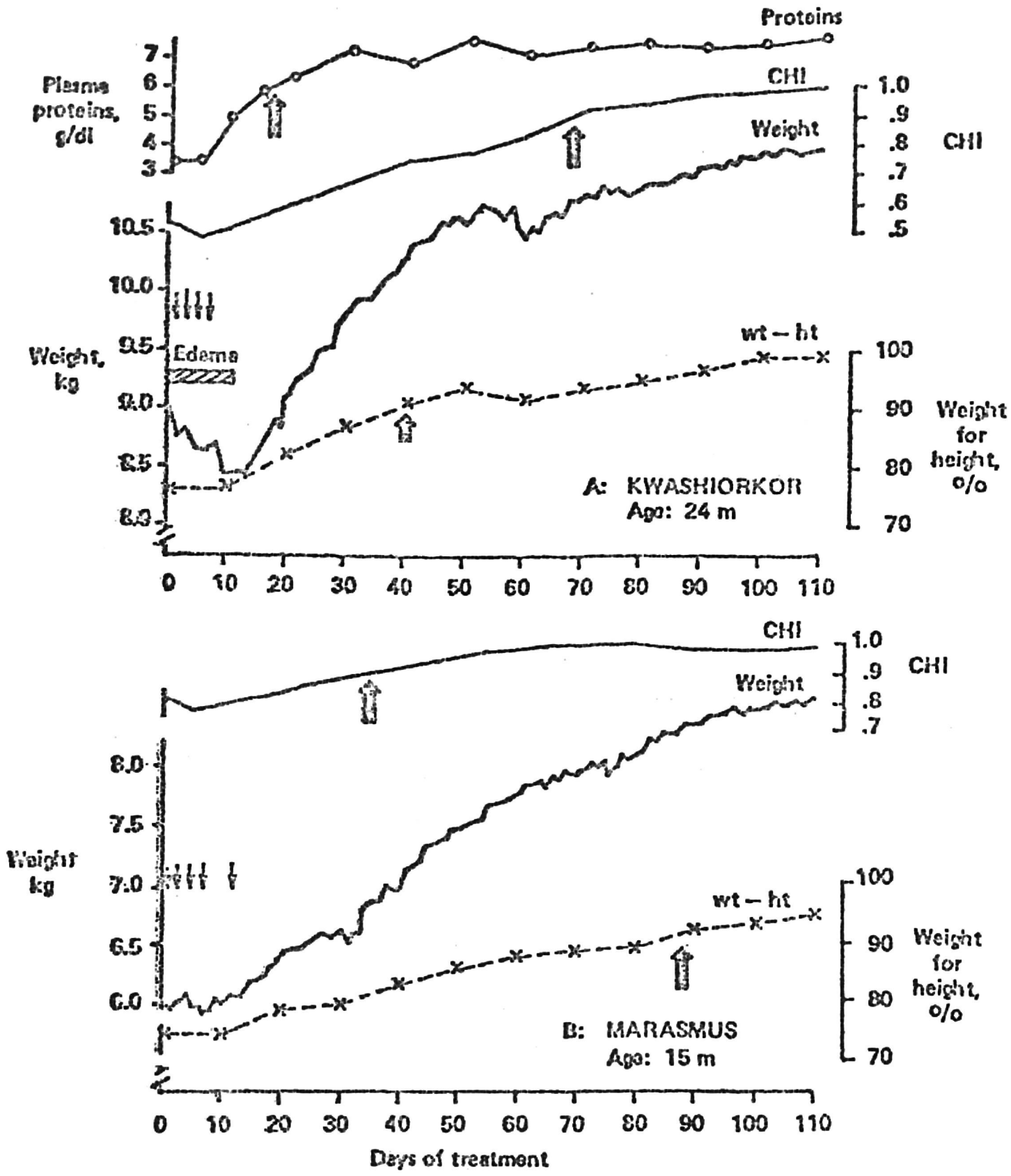

Fig. 42–11. Weight gain and improvement in weight-for-height, creatinine-height index (CHI), and plasma protein concentration of two children treated at INCAP for kwashiorkor *(A)* and marasmus *(B)*. The thin arrows (↓) indicate gradual increments in dietary proteins and energy, as described in Table 42–7. The thick arrows (↑) indicate the day when the lower limit of normal values was reached. The marasmic child had normal plasma protein concentration on admission. Weight-for-height was calculated for child A on admission after correcting for the weight of edema. Dietary energy was reduced on days 60 and 80 for child A, and on day 100 for child B.

1. *Introduction of traditional foods.* Other foods, especially those available at home, are gradually introduced into the diet in a combination with the high-energy, high-protein formula. This step should be taken when edema has disappeared, the skin lesions are notably improved, the patient becomes active and interacts with the environment, the appetite is restored, and adequate rates of catch-up growth have been achieved in children. A daily minimum intake of 3 to 4 g of protein and 120 to 150 kcal/kg of body weight (or more in marasmus) must be ensured. To achieve this, the energy density of solid foods must be increased with oil or fat, and protein density and quality must be high, using animal proteins, soybean protein preparations, and good vegetable protein mixtures. Local traditional foods can be used in appropriate combinations[143–145] *in addition to the liquid formula*, as in the following examples: (1) One part of a dry pulse or its flour (e.g., black beans, soybeans, kidney beans, cowpeas) and three parts of a dry cereal or flour (e.g., corn, rice, wheat) may be used; fat or oil should be added to the mashed or strained pulse during or after cooking in amounts equal to the weight of the dry pulse or flour, and to the cereal prep-

arations in amounts of 10 to 30 ml oil/100 g dry cereal product, depending on the type of preparation. (2) Four parts of dry rice and one part of fresh fish may be used; fat or oil should be added in amounts equal to 20 to 40% of the dry weights. The food can be served as separate dishes or it can be mashed or blended and fed as paps to infants and young children.

2. *Emotional and physical stimulation.* The malnourished child needs affection and tender care from the beginning of treatment. This requires patience and understanding by the hospital staff and the relatives. Involvement of parents or relatives is usually very helpful. Hospitals should be brightly colored, cheerful, with audible stimulation such as music. As soon as the child can move without assistance and is willing to interact with the staff and other children, he must be encouraged to explore, to play, and to participate in activities that involve body movements. Relatively small increments in physical activity and energy expenditure during the course of nutritional rehabilitation result in faster longitudinal growth and accretion of lean body tissues.[146] Parents should be encouraged to stimulate and teach their children by playing and talking. Toys and play materials can often be made from discarded local articles. Adult patients should exercise regularly with gradual increments in cardiorespiratory workload.

3. *Persistent diarrhea and other health problems.* Mild diarrhea does not interfere with nutritional rehabilitation as long as fluid and electrolyte intakes maintain satisfactory hydration. This condition often disappears without specific treatment as nutritional status improves.[147] However, persistent diarrhea can contribute to the development of a new episode of PEM and should be treated. Treatment is undertaken by determining the underlying cause of diarrhea, usually intestinal infections, excessive bacterial flora in the upper gut that ferment food substrates and deconjugate bile salts, intestinal parasites (particularly amebiasis, giardiasis, and trichuriasis), and intolerance to food components. Among the latter, lactose, milk protein, and gluten have often been held responsible. However, the apparent high prevalence of lactose malabsorption and intolerance in PEM is often founded on inadequate diagnostic procedures (e.g., intolerance to 2 g lactose/kg in aqueous solution, rather than to the 7 to 15 g lactose contained in a milk meal.)[85] When food intolerance is suspected, the diet should be modified, taking care to preserve its nutritional quality and density. Before a patient is deemed intolerant to a given food, it should be reintroduced into the diet to confirm the diagnosis, and adequate diagnostic tests should be done.

4. *Criteria for recovery.* The most practical criterion is weight gain. A patient should be discharged from in-hospital or outpatient treatment when he has no edema and reaches a body weight equal to or near that expected for his height. As shown in Figure 42–11, however, weight-for-height does not necessarily indicate protein repletion, and it is best to use it in conjunction with body composition indices. If urine can be collected for 24 to 72 hours in children, the creatinine-height index (CHI) can be used as an indicator of body protein repletion. An increase in plasma protein or albumin concentration indicates a good response but not full recovery (see Fig. 42–11).

A premature termination of treatment increases the risk of a recurrence of malnutrition. As a general guideline, when body composition cannot be assessed, dietary therapy should continue for one month after the patient admitted with edematous PEM reaches an adequate weight-for-height without edema and his clinical and overall performances are adequate, or for 15 days after the marasmic patient reaches that weight. The minimum normal limits should be 92% of the weight expected for height and, especially in children, a creatinine-height index of 0.9. Some patients, however, do not reach those values because they are in the lower end of the normal distribution curve. If they continue growing at a normal rate and have no functional impairments, treatment can be terminated after one month of adequate dietary intake and weight-for-height and CHI stabilization. Specific treatment of other nutritional problems (e.g., iron deficiency) sometimes must be prolonged beyond discharge for PEM.

When discharged, patients or their parents must be taught about the causes of PEM, emphasizing rational and nutritious use of household foods, personal and environmental hygiene, appropriate immunizations, and early treatment of diarrhea and other diseases.

Mild and Moderate PEM

The less severe forms of PEM should be treated in an ambulatory setting, supplementing the home diet with easily digested foods that contain proteins of high biologic value and a high energy density. In some instances, therapy can be achieved merely by instructing the adult patient about adequate eating habits and a better use of food resources, or by instructing mothers in improved child-feeding practices and in more nutritious culinary habits. It is almost always nec-

essary, however, to provide both nutritious food supplements and instructions for their use.

The quantity of food supplements will vary depending upon the degree of malnutrition and the relative deficit of proteins and energy. As a general guideline, the goal should be to provide a total intake, including the home diet, of at least twice the protein and 1.5 times the energy requirements. For preschool children, this would signify a daily intake of about 2 to 2.5 g of high-quality protein and 120 to 150 kcal/kg of body weight, and for infants under 1 year, about 3.5 g protein and 150/kcal/kg/day.

The ingestion of the food supplement by the malnourished person must be ensured. This is more likely to occur if it is appetizing to both the child and the mother, if it is ready-made or easy to prepare, if additional amounts are provided to feed the siblings, and if it does not have an important commercial value outside the home that would make it easy and profitable for the family to sell the item for cash. A substitution effect on the home diet (i.e., a decrease in the usual food intake) is almost unavoidable, but it can be reduced by using low-bulk supplements with high-protein and -energy densities. Special attention should be given to avoid a decrease in breast-feeding. The supplements for breast-fed infants should be paps or solid foods that will not quench the infant's thirst and thus not change the infant's demand nor the mother's attitude toward lactation.

Adequate amounts of vitamins and minerals must be assured, although mild deficiencies can be overcome by the micronutrients in the food or by use of fortified vehicles such as iron-enriched bread or sugar fortified with retinol.

PREVENTION AND CONTROL OF PEM

Poverty, ignorance, frequent infections, cultural customs, cyclic climatic conditions, and natural and man-made disasters are among the main causes of PEM. Therefore, its control and prevention require multisectorial approaches that include food production and distribution, preventive medicine, education, social development, and economic improvement. At a national or regional level, control and prevention can only be achieved through short- and long-term political commitments, and effective actions to enforce the measures to eradicate the underlying causes of malnutrition.

Nevertheless, the physician, nutritionist, public health worker, and educator *can* and *must* play an active role in the prevention of PEM, even though aimed at smaller population groups or individuals. Their efforts may have to be diverted toward those with higher risk to develop PEM. A profile of risk factors is then useful. The most likely victims are children under 2 years of age from low socioeconomic strata whose parents have misconceptions concerning the use of foods, who come from broken or unstable families, whose families have a high prevalence of alcoholism, who live under poor sanitary conditions in urban slums or in rural areas frequently subject to droughts or floods, and whose families have societal beliefs that prohibit the use of many nutritious foods.

Special attention must be given to the availability and rational use of foods that optimize nutrient utilization, the control or reduction of infections, and health and nutrition education programs for the individual, the family, and the community.

Food Availability

Animal foods are the best protein sources but they tend to be expensive, unavailable, or prohibited by religious practices. Under such circumstances, the staple vegetable foods can be complemented with other vegetable foods combined in culturally acceptable ways to permit a good essential amino acid complementation and to improve the biologic value of dietary protein. For example, corn and black bean combinations that provide proteins in a proportion of about 60:40, equivalent to about three parts of dry corn and one part of dry beans, have an excellent amino acid composition and permit adequate growth and function.[148] The same is true of a series of other combinations of grains and pulses.[143–145] The relatively low nitrogen digestibility of these vegetable sources must be considered in recommending the amounts to be eaten. Energy density can be increased by adding fats or carbohydrates.

It is often necessary to convince parents about the safety of using foods which, in some cultures, are fed only to adults and older children. This is especially true of foods to complement mother's milk or to wean infants from the breast. Trials at INCAP have shown that it is feasible to feed paps based on black beans *(Phaseolus vulgaris)*, a cereal, and vegetable oil to babies as young as 3 months of age without intestinal discomfort and without decreasing breast milk intakes. Breast-fed infants from populations at risk of PEM should start receiving at 4 months of age paps prepared by mashing boiled rice, cooked corn products (e.g., tamale, tortilla), or bread soaked in about 50% water. At 6 months of age, one part of a cooked pulse (e.g., kidney beans, soybeans, chick peas) should be added for every three parts of rice, corn, or bread to provide a better protein mixture.

If the child is underweight, one teaspoon of vegetable oil or two teaspoons of sugar can be added to every 2 to 3 ounces of pap. Infants who are fully weaned or only occasionally breast-fed must receive energy- and protein-rich amounts of staples and, ideally, of animal foods to satisfy their nutritional needs and to allow adequate growth.

Reduction of Morbidity Rates

This is a logical consequence of the interactions of nutrition with infection. Since young children are at a greater risk of malnutrition, high priority must be given to immunizations, sanitary measures to reduce fecal contamination, and early oral rehydration and feeding of children with diarrhea.

Education

The presence of a malnourished child in a family suggests that other members of the household might also be at risk of malnutrition. Therefore, nutritional and health education must not be restricted to the rehabilitation of the index case, but to prevention of nutritional deterioration of other family members, especially siblings and pregnant and lactating women. Similarly, a high prevalence of children with malnutrition or growth retardation indicates that the entire community is at some risk of impaired nutrition. Consequently, education programs must be devised for community leaders, civic action groups, and the community as a whole. Such programs must emphasize promotion of breast-feeding, appropriate use of weaning foods, nutritional alternatives using traditional foods, personal and environmental hygiene, feeding practices during illness and convalescence, and early treatment of diarrhea and other diseases. Personal and communal involvement should be pursued through commitments to apply the recommendations. Toward this aim, it is important that all educational programs incorporate the people's own assessment of their nutritional problems and their feelings toward personal participation to contribute to the solution.

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