63

Protein-Energy Malnutrition

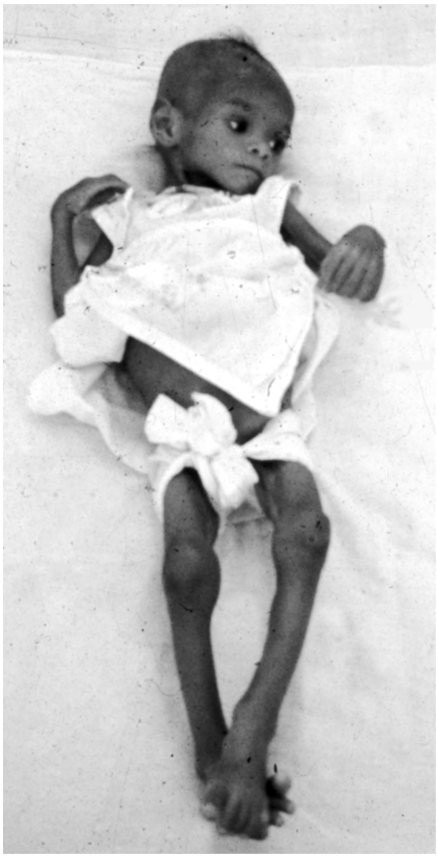
Naomi K. Fukagawa

Introduction

Protein-energy malnutrition (PEM) is not limited to the severe cases seen in developing countries. Individuals with varying degrees of malnutrition are seen in both inpatient and outpatient settings in the U.S., and all ages may be affected. By definition, PEM results from inadequate intakes of protein, energy fuels, or both. Deficiencies of protein and energy usually occur together but when one predominates and the deficit is severe, kwashiorkor (primarily protein deficiency) or marasmus (predominantly energy deficiency) ensues (Color Figure 63.1*). However, in many cases, it is difficult to recognize which deficit predominates.

Marasmus means wasting. Marasmus results from an overall deficiency of both protein and kcalories, and is characterized by emaciation. Kwashiorkor, a term first used by Williams in 1933,[1] refers to an inadequate protein intake with a fair or normal intake of energy. The classic finding in kwashiorkor is edema, which often masks the degree of wasting. However, because individuals often present with a mixed picture of marasmus and kwashiorkor, the term protein calorie malnutrition was suggested by Jelliffe to include the entire spectrum of undernutrition.[2] In 1973, the World Health Organization (WHO) renamed it PEM.[3] Table 63.1 summarizes the classification of PEM based on standard measures. The best anthropometric measure in children is based on measurements of weight and height or length, and records of age to calculate the two indices: weight for height as an index of current nutritional status, and height for age as an index of past nutritional history. The body mass index (BMI, or Quetelet's index), defined as weight in kg divided by the square of height in meters, is often used for adolescents and adults. Women have more body fat than men at all three cutoff points, but this is an intrinsic biological phenomenon so the same BMI cutoffs may be used for both sexes.

Weight loss is the main feature of mild and moderate PEM, with a decrease in subcutaneous fat. Physical activity and energy expenditure also decline.[4,5] Other functional indicators such as immunocompetence, gastrointestinal function, or behavior may be altered.[6,7] In adults, capacity for prolonged physical work is reduced, but this is usually apparent only in those engaged in intense, energy-demanding jobs. Malnourished women have a higher probability of giving birth to low birth-weight infants.[8] The diagnosis of



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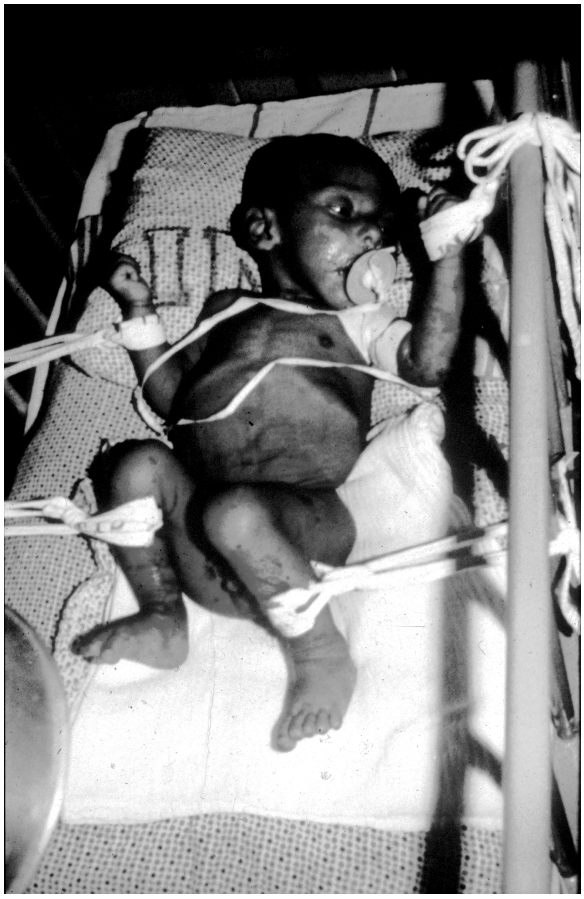

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FIGURE 63.1
(See Color Figure 63.1) 1. Kwashiorkor in a child. 2. Marasmic infant. Photographs are from Brazil and were provided by Dr. T. Kuske, reproduced from Feldman, E.B., *Essentials of Clinical Nutrition*, Philadelphia, F.A. Davis, 1988, pp. 321-325. With permission.

TABLE 63.1

Classification of Protein-Energy Malnutrition (PEM)

	Mild	Moderate	Severe
Children			
Weight for height[a] (deficit = wasting)	80-89	70-79	<70 or with edema
Height for age[a] (deficit = stunting)	90-94	85-89	<85
Adults			
Weight:height[b], % of std	90-95	80-90	<80
Triceps skinfold[c], % of std	60-90	40-60	<40
Body Mass Index[d] (wt/ht^2, kg/m^2)	17.0-18.4	16.0-16.9	<16.0

[a] % relative to modern NCHS standards.[47]
[b] Midrange of medium-frame values of the 1959 Metropolitan Life Insurance Tables.
[c] Men 12.5 mm, Women 16.5 mm.
[d] James WP, Ferro-Luzzi A, Waterlow JC. *Eur J Clin Nutr* 42: 969-981; 1988.

severe PEM is principally based on dietary history and clinical features, described later and in the section on Nutritional Assessment.

Etiology and Epidemiology

Causes of PEM may be primary, i.e., as a result of inadequate food intake, or secondary when it is the result of other diseases which lead to limited food intake, poor nutrient absorption or utilization, and/or increased nutrient requirements or losses. Factors that may modify the expression of PEM include age of the patient, cause of the deficiency, and association with other nutritional defects or infectious disease. PEM is the most important nutritional disease in developing countries, especially because of its impact on childhood mortality, growth, and development. In more developed countries, PEM is often seen in chronically ill patients, the elderly, and hospitalized individuals. PEM often develops gradually and is characterized by a series of metabolic and behavioral responses in an attempt to adapt to the reduced food intake. Some of the causes of PEM are listed in Table 63.2.

The global magnitude of PEM is difficult to estimate because mild cases are often not recorded, and many of those afflicted do not receive medical attention. It is estimated that there are about 800 million undernourished people in the world. Most malnourished persons live in developing countries (Africa, Southern and Eastern Asia, Latin America, and the Caribbean). PEM primarily affects infants and preschool children, making it the main cause of growth retardation. About 31% of children under five years of age in developing countries are moderately to severely underweight, 39% are stunted, and 11% are wasted based on a deficit of more than two standard deviations below the WHO/National Center for Health Statistics (NCHS) reference values.[9] There has been a gradual decrease in the prevalence of childhood malnutrition, provided the countries have not been ravaged by natural or manmade disasters such as war, drought, economic crisis, etc. However, the total number of malnourished children worldwide has not decreased because of the rise in populations in countries where malnutrition is prevalent.

TABLE 63.2

Causes of PEM

Primary
Insufficient food intake
Ingestion of proteins of poor nutritional quality
Associated with poverty, ignorance, infectious disease, low food supply
Biologic Factors
Maternal malnutrition prior to and/or during pregnancy
Infectious diseases
Environmental
Overcrowded and/or unsanitary life conditions
Agricultural, climatic, man-made catastrophe (war or forced migration)
Poor food storage

TABLE 63.3

Characteristics of Patients at High Risk for Developing PEM

Gross underweight (<80% weight for height)
Gross overweight (because requirements often overlooked)
Recent weight loss of >10% body weight
Alcoholism
NPO orders >10 days on 5% dextrose in water solution intravenously
Protracted nutrient losses (gut, fistulas, dialysis, extensive exudative or exfoliative cutaneous lesions, or deep decubitus ulcerations)
Increased metabolic needs
Catabolic, anorexogenic, or antinutrient therapies (steroids, chemotherapy, immunosuppression)
Elderly, with polypharmacy and concurrent illness
Infections, especially in those with marginal nutritional status

In industrialized countries, primary PEM is seen among young children of the lower socioeconomic groups, the elderly living alone, adults addicted to alcohol and drugs, or individuals with chronic diseases who have limited food intake. Of interest, in the U.S., 1% of children under five are considered moderately to severely underweight, 1% are wasted, and 2% are stunted.[9] Kwashiorkor has been reported in the U.S. due to peculiar dietary habits imposed upon children by their parents (e.g., unbalanced vegetarian diets), almost total removal of protein in diets of children considered (often incorrectly) to have cow's milk sensitivity, and replacement of milk by low-protein non-dairy creamers. The prevalence of PEM in adults in developed countries is high when considering those who are hospitalized, suffer from chronic diseases, or are disabled. In a recently published study on 369 patients at least 70 years old admitted to a general medical service, 24% were moderately malnourished and 16% severely malnourished.[10] Malnutrition in these patients was associated with greater mortality, delayed functional recovery, and higher rates of nursing home use. These findings emphasize the importance of recognizing and treating PEM if we are to have any impact on the health and well-being of the world population. Some of the characteristics that place patients in the hospital at high risk for PEM are listed in Table 63.3.

Diagnosis

The classical feature of mild to moderate PEM is weight loss (≥5% in 1 month or ≥10% in 6 months in adults; weight for height <80% standard in children). A reduction in subcutaneous adipose tissue is apparent as well as in lean tissue, particularly skeletal muscle, resulting in a marked reduction in upper arm circumference, temporal muscle, and generalized muscle wasting. In infancy and early childhood, poor weight gain is the earliest and most consistent finding with PEM, followed by slowing of linear growth. Some of the physical findings suggestive of PEM are listed in Table 63.4 and illustrated in Color Figure 63.2.

Biochemical information is often not consistent in mild and moderate PEM. Laboratory data related to low protein intake may include low urinary excretion of urea nitrogen and creatinine, altered plasma amino acid patterns (decreased branched-chain amino acids), decreased serum concentrations of albumin and transferrin, and reduced total lymphocyte counts. Severe PEM may be characterized by biochemical changes such as a decline in transport proteins (e.g., transferrin, ceruloplasmin, retinol-, cortisol-, and thyroxine-bind-

TABLE 63.4

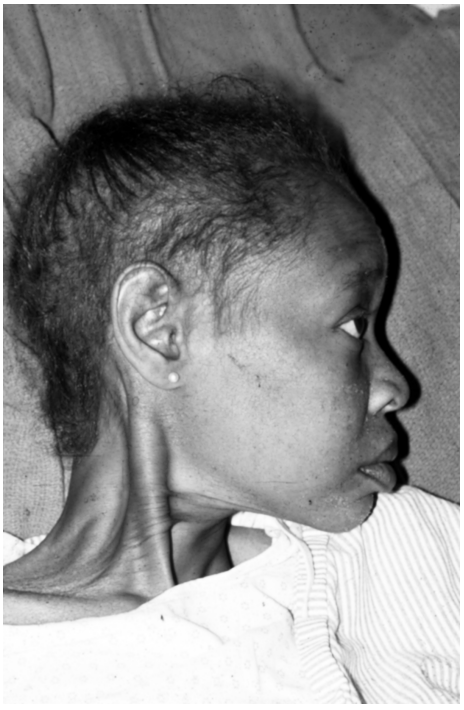
Physical Findings Associated with PEM

Area	Findings
General	Poor growth
	Decreased subcutaneous tissue
	Muscle wasting
	Edema
Skin	Dry, scaling, flaking dermatitis
	Altered skin pigmentation
Hair	Dull, altered texture, depigmented, or reddish
	Alopecia
Nails	Transverse ridging, fissuring
Lips	Cheilosis
Tongue	Atrophic lingual papillae
Abdomen	Distention, hepatomegaly

ing proteins, α-, and β- lipoprotein), and decreased enzyme concentrations (e.g., amylase, pseudocholinesterase, alkaline phosphatase). In addition, serum or plasma transaminase concentrations may be increased while the urea cycle or other enzymes associated with degradation (e.g., xanthine oxidase, glycolic acid oxidase, cholinesterase) may be lower. Enzymes utilized in amino acid synthesis may be increased in both forms of PEM.

PEM develops over weeks or months, allowing for a series of metabolic and behavioral adjustments which decrease nutrient demands, and results in a nutritional equilibrium compatible with a lower level of nutrient availability for the cells. Some of the adaptive responses are shown in Table 63.5.[11,12] Many are directed at preserving body protein and essential protein-dependent functions. Energy deficits are initially responded to by a decrease in energy expenditure.[13,14] When compensation fails, fat is mobilized to produce fuel for energy production.[15] This may be followed by protein catabolism, with visceral protein preserved longer.[16] The adaptive response is also characterized by endocrine changes aimed at regulating fuel availability and utilization.[17] As in acute fasting, weight loss early in semistarvation is rapid, but gradually slows even if there is no change in the starvation diet. The reduction in total energy expenditure helps to bring the starving individual back to energy equilibrium, which is further maintained by a reduction in lean tissue mass.

Successful adaptation involves the process of controlled protein loss, which should stop when just enough has been sacrificed to permit energy balance. Since the rate of lean tissue loss is roughly proportional to the amount of lean mass, it automatically slows as the mass of lean tissue decreases.[18] Simultaneously, there is increased efficiency of dietary protein retention until a new state of protein equilibrium is reached.[11] An inverse relationship exists between the amount of lean tissue and the efficiency of retention of protein in the diet. This relationship is affected by the concentration of protein in the diet. As starvation progresses and the lean tissue store diminishes, the rate of protein depletion slows as the amount of protein retained from each meal increases. A new equilibrium is established, and lean tissue loss ceases when a line depicting the relationship between the amount of lean tissue and the rate at which it is depleted crosses over the line which describes the relationship between the amount of lean tissue and the efficiency of retention of protein in the diet. The "price" paid to achieve this physiologic adaptation is the reduction in lean tissue stores. This analytical approach illustrates that a high protein diet may permit protein equilibrium only after moderate lean tissue wasting and that a low-protein diet may also be compatible with protein equilibrium, but the cost, in terms of protein wasting, will be greater.[11]



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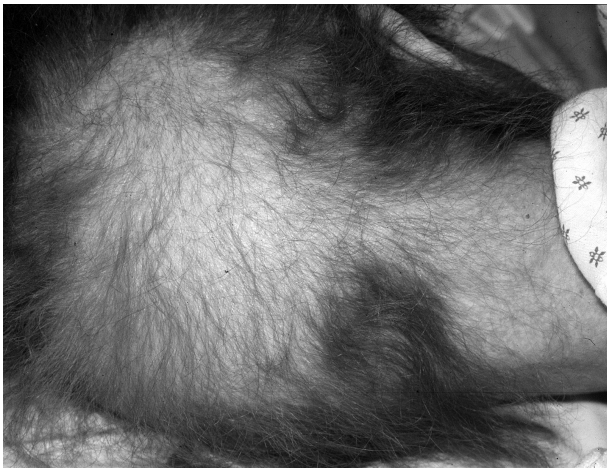

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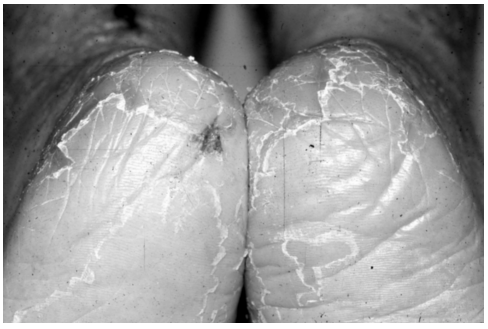

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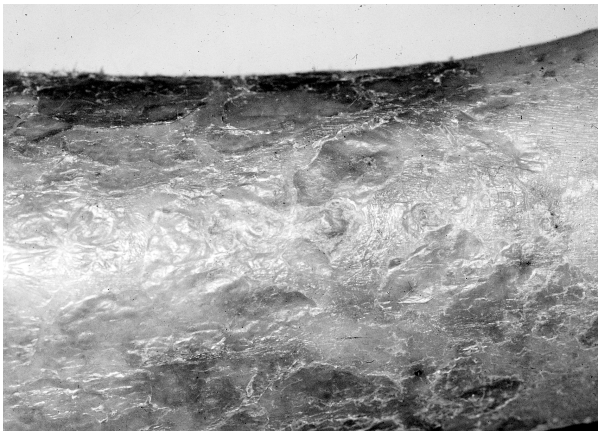

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FIGURE 63.2
(See Color Figure 63.2) Examples of some of the physical findings associated with PEM. (1) Reddish hair, (2) hair loss, (3) flaking skin of the heels, and (4) legs. (Photos of patients at the Medical College of Georgia, Augusta courtesy of Elaine B. Feldman, M.D.)

TABLE 63.5

Adaptive Responses to Protein-Energy Starvation

Hypometabolism (↓ energy expenditure, ↓ physical activity, ↓ protein turnover)
Endocrine changes (↓ serum T_3, ↓ insulin, ↑↓ catecholamines, ↓ IGF-1)
Cardiovascular and renal function (↓ cardiac output, ↓ heart rate, ↓ blood pressure, ↓ renal plasma flow, ↓ glomerular filtration)
Immune system (lymphocyte depletion, ↓ complement components, alterations in monokines or cytokines)

The intimate relationship between dietary energy and the maintenance of body protein should be underscored. Many studies have shown that energy intake influences nitrogen (N) balance at a constant protein intake.[19] The effect of energy is most potent in the modestly submaintenance range of protein and energy intake.[11,20] The amount of dietary energy in surplus or in deficit after energy expenditure is accounted for will influence N balance, making the assessment of energy balance important in managing therapy.[11,20]

Management

Mild to Moderate PEM

If semistarvation is the principal cause for the development of PEM, the patient's response to complete nutrition support is excellent. The response is characterized by marked efficiency of protein utilization when protein intakes increase from the Recommended Daily Allowances (RDA) (0.8 g/kg) to high (1.5 g/kg) and when energy intakes are increased from maintenance to surfeit. In the case of mild to moderate PEM, treating the precipitating event and increasing protein and energy on the basis of the actual height in children and ideal weight in adults may be sufficient. Specific supplementation of individual nutrients is indicated by the presence of signs of specific nutrient deficiency. Table 63.6 outlines the general approach to the treatment of mild to moderate PEM. In children, treatment of mild and moderate PEM corrects the acute signs of the disease, but catch-up growth in height takes a long time or might never be achieved. Weight for height can be restored early but the child may remain stunted. Many severely malnourished children appear to have residual behavioral and mental problems, but the causal role of PEM and poor living conditions are difficult to dissociate.

Severe PEM

Mortality rates in severe PEM can be as high as 40%, with the immediate cause of death being infection. Treatment strategies of severe PEM can be divided into three stages: 1) resolving the life-threatening conditions, 2) restoring nutritional status without disrupting homeostasis, and 3) ensuring nutritional rehabilitation. The most frequent life-threatening conditions associated with severe PEM are described in Table 63.7.

Assessing dehydration in severe PEM is not easy, because the classic signs (sunken eyeballs, decreased skin turgor) may also be found in well-hydrated malnourished

TABLE 63.6

Approach to Treatment of Mild and Moderate PEM

Setting	Ambulatory setting preferred
Foods	Home diet supplemented with easily digested foods containing proteins of high biologic value, high energy density, and adequate micronutrients
Intake Goals	At least twice the protein and 1.5 times the energy requirement (e.g., pre-school child — 2-2.5 g protein and 500-625 KJ (120-150 kcal)/kg body weight)
Food Facts	Appetizing, ready-made or easy to prepare, little commercial value outside the home to avoid sale of items for cash
Special Attention	Avoid a decrease in breastfeeding for infants, ensure adequate vitamins and minerals, perhaps with the use of fortified foods

TABLE 63.7

Life-Threatening Conditions Associated with Severe PEM

Fluid and electrolyte disturbances
Hypoosmolarity with moderate hyponatremia (but intracellular Na excess)
Intracellular K^+ depletion without hypokalemia
Mild to moderate metabolic acidosis
Hypocalcemia
Decreased body magnesium with or without hypomagnesemia
Severe vitamin A deficiency
Infections
Hemodynamic alterations
Cardiac failure secondary to intravenous fluids or after introduction of high-protein and high energy feeding or a diet with high Na^+ content
Pulmonary edema
Severe anemia
Treat only if hemoglobin <4g/dL
Hypothermia
Hypoglycemia

TABLE 63.8

General Approaches to Therapy

Fluid repletion	Allow diuresis of at least 200 ml/24 hrs in children; 500 ml in adults
	Oral or nasogastric rehydration preferred
Electrolytes (if urinating)	~6 mEq K
	2-3 mEq Na
	2-3 mEq Ca^{+2}
Antibiotics	Not used prophylactically
	Choice depends on suspected etiology
Anemia	Treat only in severe cases (hemoglobin <4 g/dL)
Vitamin A deficiency	50,000-100,000 IU for infants and children on day 1
	100,000-200,000 IU for older children and adults on day 1
	Followed by 5000 IU orally each day for the duration of treatment

patients. Furthermore, hypovolemia may coexist with subcutaneous edema. Because of the peculiarities of water and electrolyte disturbances in severe PEM (Table 63.7), the therapeutic approach differs from that used in well-nourished individuals (Table 63.8). Fluid repletion should allow a diuresis of at least 200 ml per 24 hours in children, and 500 ml in adults.[21] Whenever possible, oral or nasogastric rehydration should be used. Although many use the oral rehydration solution (ORS) promoted by the WHO, it is preferable to use solutions that provide more potassium and magnesium, and less sodium (especially for edematous PEM).[22]

Table 63.9 shows the composition of a mineral mix which can complement the diet or be combined with WHO's regular ORS and sucrose to prepare a modified ORS. This modified ORS would be prepared by diluting one standard WHO ORS packet and two 3.12 g packets or 40 mL of concentrated mineral mix and 50 g sucrose in two liters of water. This modified ORS would contain the following: glucose (125 mmol/L), sodium (45 mmol/L), potassium (40 mmol/L), chloride (70 mmol/L), citrate (7 mmol/L), magnesium (3 mmol/L), zinc (0.3 mmol/L), copper (0.04 mmol/L). The osmolarity of this solution would be 300 mOsm/L. The modified ORS solution will have magnesium to begin replenishing the body stores and help potassium retention as well as replace other mineral deficiencies in severe PEM. An approach for rehydration in cases of severe PEM is outlined in Table 63.10.

TABLE 63.9

Mineral Mix for Oral Dehydration Salt Solution and to Complement Liquid Foods

Salt	Amount (g)	mmol in 1 g	mmol in 3.71 g
Potassium chloride	89.5	6.47 K	24 K
Tripotassium chloride	32.4	1.62 K	6 K
Magnesium chloride · $6H_2O$	30.5	0.81 Mg^{2+}	3 Mg
Zinc acetate · $2H_2O$	3.3	0.081 Zn^{2+}	0.300 Zn
Copper sulfate · $7H_2O$	0.56	0.011 Cu^{2+}	0.040 Cu
Total	156.26[a]		

Note: 1 mmol K = 39.1 mg; 1 mmol Mg = 24.3 mg; 1 mmol Zn = 65.4 mg; 1 mmol Cu = 63.5 mg.

[a] Add water to make 1000 mL concentrated mineral mix that can be stored at room temperature or prepare packets with 3.12 g of dry mineral mix. Add 20 mL of concentrated solution or 1 packet to each liter of oral rehydration solution (ORS) or liquid food.

Based on WHO recommendations.

Taken from Torun B, Chew F. Protein-energy malnutrition, *Modern Nutrition in Health and Disease* 9th ed, Shils ME, Olson JA, Shike M, Ross AC. Williams and Wilkins, Baltimore, 1999, pg 963-988. With permission.

TABLE 63.10

Approach to Oral Rehydration for Severe PEM

Initiation	Small sips to provide 70-100 mL/kg body weight over 12 hours (10 ml/kg/hr during first 2 hours for mild to moderate dehydration; up to 30 ml/kg/hr for severe dehydration)
Compensation for ongoing losses	50-100 ml after each loose stool or vomiting for those under 2 years of age; 100-200 ml for older children Continue breast feeding
Evaluation	Monitor every hour; as soon as improvement is seen (usually 4-6 hrs after initiation), small amounts of liquid dietary formula with potassium, calcium, magnesium and other electrolytes may be offered every 2-3 hours
Persistent dehydration	Continue ORS for another 12 hours If signs of overhydration (puffy eyelids, ↑ **edema, distended jugular veins,** ↑ **respiratory rate), use breast milk or liquid diet instead of ORS**

Nasogastric tubes may be used in children who vomit constantly or cannot be fed orally. Small portions are key, but if hydration is not improved after four hours, intravenous rehydration may be used. Hypoosmolar solutions (200 to 280 mOsm/L) must be used, and sodium should not be >3 mmol/kg per day. Potassium (not >6 mmol/kg per day) may be added when urination is established. Glucose should provide approximately 63-126 kJ (15 to 30 kcal)/kg/day. The approach to intravenous rehydration is described in Table 63.11.[12]

Hypocalcemia may occur secondary to magnesium deficiency. If magnesium levels cannot be determined, it is necessary to give both calcium and magnesium. Intramuscular or oral magnesium should follow initial parenteral magnesium until repletion with magnesium is complete. A general guideline is intravenous magnesium as a 50% solution of magnesium sulfate in doses of 0.5, 1, and 1.5 mL for patients who weigh less than 7, between 7 and 10, and more than 10 kg, respectively. This may be repeated every 12 hours until there is no recurrence of hypocalcemic symptoms. Calcium replacement may be

TABLE 63.11

Suggested Intravenous Rehydration Regimen

Solutions
1:1 mixture of 10% dextrose with isotonic saline or Ringer's lactated solution (=5% glucose in 0.5 N saline)
Rate
10-30 mL/kg for the first hour followed by 5% dextrose in 0.2 N saline at 5-10 ml/kg/hr
Add K^+ when patient is urinating
Patients with severe hypoproteinemia (<30 g/L), anemia and signs of impending circulatory collapse should be given 10 mL plasma per kg in 1-2 hours followed by 20 mL/kg/hr of a mixture of 2 parts 5% dextrose and one part isotomic saline for 1-2 hours. If diuresis does not improve, the dose of plasma may be repeated 2 hours later.

discontinued when the symptoms disappear or serum Ca^{+2} levels rise to normal. Oral magnesium supplementation of 0.25 to 0.5 mmol magnesium (0.5 to 1 mEq)/kg/day can be given later as described for maintenance therapy.

Infections are frequently the immediate cause of death in severe PEM, and when suspected, appropriate antibiotic therapy should be started immediately. The choice depends on the suspected etiology, patterns of drug resistance, and severity of the disease. Prophylactic antibiotics are not recommended but may be used if close monitoring for signs of infection by experienced personnel is not available. Clinicians should be aware that PEM may alter drug metabolism and that detoxification mechanisms may be compromised.[21] Delayed absorption, abnormal intestinal permeability, reduced protein binding, changes in volume of distribution, decreased hepatic conjugation or oxidation, and decreased renal clearance may all occur. Treatment for intestinal parasites should be deferred until nutritional rehabilitation is under way, because this is rarely urgent. Vaccination against measles for every child over six months should be carried out with a second dose after discharge, because seroconversion may be impaired.

Hemodynamic alterations may occur in severe PEM, especially in the presence of severe anemia, during or after administration of intravenous fluids or shortly after the introduction of high protein and high energy feeding, or a diet with high sodium content. Diuretics such as furosemide (10 mg intravenously or intramuscularly, repeated as necessary) may be given, and other supportive measures taken. The use of diuretics merely to accelerate the disappearance of edema in kwashiorkor, however, is contraindicated. Routine use of blood transfusions for anemia endangers the patients; therefore, it should be given only to those with severe anemia with hemoglobin of <4g/dL, <12% packed cell volume (hematocrit), clinical signs of hypoxia, or impending cardiac failure. In countries with a high prevalence of infection with human immunodeficiency virus (HIV) and few or no resources for screening the blood supply, the risk of transmission of HIV is significant. Therefore, use of blood transfusions should be restricted except in life-threatening situations. 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 edematous PEM. Transfusions must be given slowly, over 2 to 3 hours, and may be repeated as necessary after 12 to 24 hours. At signs of heart failure, 2.5 mL blood/kg should be withdrawn before the transfusion is started and at hourly intervals until the total volume of blood transfusion equals volume of anemic blood removed.

Hypothermia, defined as body temperature below 35.5°C and hypoglycemia, defined as plasma glucose concentrations below 3.3 mmol/L (or 60 mg/dL), may be due to impaired thermoregulation, reduced fuel substrate availability, or severe infection. Asymptomatic hypoglycemia is usually treated by feeding the small volumes of glucose- or sucrose-containing diets described above, whereas severe symptomatic hypoglycemia must be treated with intravenous 50% glucose solution followed by oral or nasogastric administration of 10% glucose solutions at two-hour intervals. Low body temperature will

usually rise with frequent feedings of glucose-containing diets or solutions, but patients must be closely monitored when external heat sources are used to reduce the loss of body heat, because they may become rapidly hypothermic when the heat source is removed.

Vitamin A deficiency is usually associated with severe PEM, and therefore a large dose of vitamin A should be given on admission. Water miscible vitamin A as retinol should be given orally or intramuscularly on the first day at a dose of 52 to 105 µmol (15,000 to 30,000 µg or 50,000 to 100,000 IU) for infants and preschool children, or 105 to 210 µmol (30,000 to 60,000 µg or 100,000 to 200,000 IU) for older children and adults, followed by 5.2 µmol (1500 µg or 5000 IU) orally each day for the duration of treatment. Corneal ulceration should be treated with ophthalmic drops of 1% atropine solution and antibiotic ointments or drops until the ulcerations heal.[12]

The refeeding syndrome may develop in severely wasted patients during the first week of nutritional repletion.[23-25] The hyperinsulinemia stimulated by increased carbohydrate consumption results in an antinatriuretic effect.[26] Increased body sodium also results from increased sodium intake. In addition, hypophosphatemia and hypocalemia as well as hypomagnesemia can occur as a result of a stimulation of glycogen synthesis with the refeeding of carbohydrate. Close monitoring is therefore necessary to avoid acute deficiencies, especially of phosphorous and potassium.

Following the attention to life-threatening conditions as described above, the next objective of therapy is to restore nutritional status as rapidly and safely as possible. This may be done with liquid formula diets fed orally or by nasogastric tube, and for older children and adults with good appetites, the liquid formula can be substituted with solid foods that have a high density of high quality and easily digested nutrients. The marasmic patient may require larger amounts of dietary energy after one or two weeks of dietary treatment, which can be provided by adding vegetable oil to increase the energy density of the diet. Intravenous alimentation is not justified in primary PEM, and can actually increase mortality.[27] The protein source in all foods must be of high biologic value and easily digested. Cow's milk protein is frequently available, and although there is concern about lactose malabsorption, cow's milk is usually well tolerated. Eggs, meat, fish, soy isolates, and some vegetable protein mixtures are also good sources of high quality protein. Vitamin and mineral supplements should be included at doses slightly higher than the RDA, and can be accomplished by adding the appropriate amounts of the mineral mix outlined in Table 63.9. Older children and adults should have their diets tailored to their age and general food availability. Initial maintenance treatment should provide average energy and protein requirements followed by a gradual increase to about 1.5 times the energy and 3 to 4 times the protein requirements by the end of the first week. Marasmic patients may need to have further increase in dietary energy intake. Initially, responses to the diet may be no change in weight or a decrease because of the loss of edema and a large diuresis. After 5 to 15 days, there is usually a period of rapid weight gain or "catch-up," but this is usually slower in marasmic patients than kwashiorkor patients.

The final step is ensuring nutritional rehabilitation in patients treated for PEM and usually begins two to three weeks after admission. Traditional foods should be introduced into the dietary regimen, and for the malnourished child, emotional and physical stimulation are important. Adult patients should exercise regularly, with gradual increases in their cardiorespiratory workload. Although the major emphasis of this section appears to be for infants and children, the same physiologic changes and principles apply to adolescents and adults with severe PEM. A brief summary of the approach is provided in Table 63.12. Because adults and adolescents often do not want to eat anything other than habitual foods and resist the intake of formula diets, added sugar and oil may be used to increase the energy density of the traditional diet. Liquid diets with vitamins and minerals can be given between meals and at night.

TABLE 63.12

Dietary Treatment of Adolescents and Adults with Severe PEM

Initial
Energy and protein appropriate for age (45 kcal and 0.75 g protein/kg/day for adolescents; 40 kcal and 0.6 g protein/kg/day for adults)
Rehabilitation
Gradual increase to 1.5 times the energy and 3 to 4 times the protein requirements
RDA for minerals and vitamins
Vitamin A — single dose of 210 µmol (60 mg or 200,000 IU) retinol should be given for all except pregnant women
Monitoring
Supplementary feeding should continue until BMI exceeds 15, 16.5, and 18.5 kg/m^2 for adolescents 11 to 13 years old, 14 to 17 years old, and adults respectively

Monitoring

Monitoring the individual's response to initial therapy encompasses the same principles used to monitor the treatment of life-threatening conditions. Table 63.13 lists the characteristics associated with poor prognosis in patients with PEM. Treatment until full recovery from PEM should not be in the hospital. Ideally, the patient should be followed in a nutrition clinic or rehabilitation center to continue treatment until after all life-threatening conditions have been controlled and the appetite is good, edema and skin lesions have resolved, and the patient appears content and interacts with the staff and other patients. The caretaker of the individual must understand the importance of continuing a high-energy, high-protein diet until full recovery has taken place. An increase in plasma protein or albumin concentration indicates a good response but not full recovery. The most practical criterion for recovery is weight gain, and almost all fully recovered patients should reach the weight expected for their height. Weight for height measures do not necessarily indicate protein repletion, and therefore it is good to use these measures in conjunction with other body composition indices such as creatinine-height index (CHI).[28-31] Table 63.14 summarizes guidelines for CHI and N balance.[31] Premature termination of treatment increases possibility of the recurrence of malnutrition. If body composition cannot be assessed, dietary therapy must continue for a month after the patient admitted with edematous PEM reaches an adequate weight for height without edema and clinical and overall performances are adequate, or for 15 days after the marasmic patient reaches that

TABLE 63.13

Characteristics Associated with Poor Prognosis in Patients with PEM

Age ≤6 months or ≥ 65 years
Significant deficits in weight for age >40% or weight for height >30%
Infections, especially bronchopneumonia or measles, septicemia
Total serum proteins ≤ 3 g/dL
Severe anemia with signs of hypoxia
Hypoglycemia
Hypothermia
Circulatory collapse or signs of heart failure, respiratory distress
Coma, stupor, or other changes in awareness
Severe dehydration or electrolyte disturbance

TABLE 63.14

Guidelines for Creatinine-Height Index and Nitrogen Balance

Creatinine-Height Index (CHI)[31]
CHI = observed creatinine excretion/expected creatinine excretion x patient ideal weight for height, where expected = 18 mg/kg (women) or 23 mg/kg (men)
60-80% = moderate muscle mass depletion
<60% = severe muscle mass depletion
Nitrogen Balance
Dietary nitrogen (g protein/6.25) – (urinary urea N + 4 g)
Catabolic Index (CI)
Urinary urea N – (0.5 dietary N intake + 3 g)
CI = 0, no significant stress
CI = 1 to 5, mild stress
CI = >5, moderate to severe stress

weight.[12] The minimum normal limits should be 92% for weight expected for height, or one standard deviation below the reference mean. For children, assuring continual growth at a normal rate with no functional impairments is important.

Nitrogen balance (Table 63.14) is useful for estimating the degree of catabolism and monitoring the response to treatment. N balance is the difference between the quantity of dietary N ingested and the amount of N lost. Because dietary protein is assumed to have an average N content of 16%, protein intake is multiplied by 0.16 or divided by 6.25 to convert protein to N. Since most N is lost in urine as urea, total N excretion may be estimated by adding a correction factor of 4 g to measured urea N: 2 g N for fecal and cutaneous losses, and 2 g for nonurea nitrogenous compounds. One g of N represents approximately 30 g of lean tissue. The catabolic index (CI) (Table 63.14) may be used as an estimate of the degree of stress in an individual. In this case, the amount by which the measured value exceeds the estimated amount is an indicator of the level of stress.[32]

The goal is complete nutritional recovery within three to four months. In children, clearly measurable laboratory changes may be seen within two to three weeks, and anthropomorphic changes from three weeks onwards. Changes in adults are slower unless the PEM was acute and of short duration. Comprehensive programs of nutrition education, psychosocial stimulation, and progressive increments in physical activity must be undertaken.

Impact on Prognosis, Morbidity, and Mortality for Other Illnesses, Especially in the Elderly

PEM is also common in hospitalized patients and individuals with chronic diseases. This has been known since the early 1970s.[33] PEM is an inevitable consequence of chronic liver disease, and reversal of malnutrition is one of the key aims of liver transplantation.[34] Some of the factors contributing to PEM in end-stage liver disease are listed in Table 63.15. Patients with renal disease requiring dialysis are also at significant risk for PEM.[35,36] One of the challenges is to provide adequate nutrition to dialysis patients. Approaches often include dietary supplements, enteral tube feeding, intradialytic parenteral nutrition, and total parenteral nutrition. Appetite stimulants (e.g., megestrol acetate) and growth factors (e.g., anabolic steroids, recombinant growth hormone, or insulin-like growth factor-1) have been used.[37] Another prevalent disease with high incidence of PEM is HIV/acute immunodeficiency disease syndrome (AIDS). PEM is one of the more common findings in AIDS.

TABLE 63.15

Factors Contributing to PEM in End-Stage Liver Disease

Reduced energy intake
Vomiting
Fat malabsorption
Abnormal carbohydrate and protein metabolism
Increased energy requirements
Vitamin and mineral deficiencies

TABLE 63.16

SCALES: Rapid Screen for Risk of PEM

S:	Sadness
C:	Cholesterol < 4.14 mmol/l (160 mg/dl)
A:	Albumin < 40 g/l (4 g/dl)
L:	Loss of weight
E:	Eating problems (cognitive or physical)
S:	Shopping problems or inability to prepare a meal

From Morley JE. *Proc Nutr Soc* 57: 587; 1998. With permission.

Chronic inflammatory bowel disease (e.g., Crohn's disease), anorexia nervosa, or other eating disorders are also commonly associated with PEM.

An important complication of PEM is its impact on wound healing and the development of pressure sores or decubitus ulcers. The majority of studies have looked at the relationship between nutritional factors and the development of pressure ulcers in hospitalized and nursing home patients, most of whom were elderly. Nutritional factors associated with the development of decubitus ulcers include inadequate energy and protein intake, making it one of the many risk factors that is potentially reversible.[38] Providing a diet that is complete in nutrient requirements results in the optimum environment for recovery and healing. A reasonable provision of protein is 1.0 to 1.5 g/kg per day and caloric intake ranging from 30 to 35 kcal/kg per day. Two other nutrients important for wound healing are vitamin C and zinc. Studies have shown that supplements of specific nutrients in patients who are not clinically deficient has little effect on the healing of pressure ulcers.[38] However, since the diagnosis of a subclinical deficiency status is difficult to make, physiologic replacement of dietary deficiencies is prudent when the diet is obviously lacking in sources of vitamins and minerals.

The group at greatest risk for PEM is the elderly, either with or without underlying diseases. Severe PEM occurs in 10 to 38% of older outpatients,[39-41] 5 to 12% of homebound patients,[42] and 5 to 85% of institutionalized older individuals.[43-45] As discussed earlier, a significant number of older hospitalized patients are also at risk for PEM.[10] Unfortunately, the presence of PEM is rarely recognized by physicians, and even when recognized is rarely treated.[41] A number of screening tests for malnutrition risk have been developed, but the SCALES (Table 63.16) was developed to use as a screening tool in the clinic. It has been cross-validated with the Mini Nutritional Assessment (MNA), developed for older subjects.[46] SCALES appears to have superior ability to the MNA to identify subsequent nutritionally associated problems, but has the disadvantage of requiring blood tests. Weight loss remains one of the most sensitive indicators of malnutrition. A useful mnemonic for causes of weight loss, especially in the elderly is shown in Table 63.17. These tables and statistics, however, cannot replace the astute physician or health care provider who remains sensitive to the needs of the elderly and cognizant of this commonly overlooked problem — PEM. Table 63.18 provides a simple checklist which may be useful in the prevention and treatment of PEM in any hospitalized patient.

TABLE 63.17

"Meals on Wheels" Mnemonic for the Causes of Weight Loss

M:	Medications
E:	Emotional (depression)
A:	Alcoholism, anorexia tardive[a], or abuse of elders
L:	Late-life paranoia
S:	Swallowing problems (dysphagia)
O:	Oral problems
N:	No money (poverty)
W:	Wandering and other dementia-related problems
H:	Hyperthyroidism, pheochromocytoma
E:	Enteric problems (malabsorption)
E:	Eating problems
L:	Low-salt low-cholesterol diet
S:	Stones

[a] New onset of food refusal related to a desire to maintain a thin body habitus.[48]

From Morley JE. *Proc Nutr Soc* 57: 587; 1998. With permission.

TABLE 63.18

Checklist of Procedures to Prevent and Treat PEM

1. Accurate record of admission height and weight and weekly follow-up weights.
2. Write specific diet orders; monitor ability to eat and maintain weight.
3. Consult dietician to assess follow-up. Collaborate on oral- and tube-feeding regimens.
4. Regularly check to be sure nutrition composition is sufficient to cover basal and stress-related needs.
5. Know your standard nutrition diets and supplements available.
6. Do not wait >3-5 days before adding protein, kcalories, and other nutrients. Avoid prolonged use of 5% dextrose in water and saline solutions.
7. Use anthropometric measures and available laboratory data to assess and monitor nutritional status.
8. Be cognizant that "hospital food," withholding meals for tests, and anorexia from medications and illness can contribute to malnutrition.
9. Consult Nutrition Support Service when in doubt.
10. Be especially cognizant of patients at high risk (see Tables 63.3 and 63.15).

Adapted from Marliss EB. Protein Calorie Malnutrition, *Cecil Textbook of Medicine* 17th ed, Wyngaarden JB, Smith LH, Jr, Eds, WB Saunders, 1985.

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