characteristics of patients at risk for chronic disease–related malnutrition are less predictable and likely represent a mixture of the two extremes depicted in Table 97-2.

Metabolic Rate In starvation and semistarvation, the resting metabolic rate falls between 10% and 30% as an adaptive response to energy restriction, slowing the rate of weight loss. By contrast, the resting metabolic rate rises in the presence of physiologic stress in proportion to the degree of the insult. The rate may increase by ~10% after elective surgery, 20–30% after bone fractures, 30–60% with severe infections such as peritonitis or gram-negative septicemia, and as much as 110% after major burns.

If the metabolic rate (energy requirement) is not matched by energy intake, weight loss results—slowly in hypometabolism and quickly in hypermetabolism. Losses of up to 10% of body mass are unlikely to be detrimental; however, greater losses in acutely ill hypermetabolic patients may be associated with rapid deterioration in body functions.

Protein Catabolism The rate of endogenous protein breakdown (*catabolism*) to supply energy needs normally falls during uncomplicated energy deprivation. After ~10 days of total starvation, an unstressed individual loses about 12–18 g of protein per day (equivalent to ~60 g of muscle tissue or ~2–3 g of nitrogen). In contrast, in injury and sepsis, protein breakdown accelerates in proportion to the degree of stress, reaching 30–60 g/d after elective surgery, 60–90 g/d with infection, 100–130 g/d with severe sepsis or skeletal trauma, and >175 g/d with major burns or head injuries. These losses are reflected by proportional increases in the excretion of urea nitrogen, the major by-product of protein breakdown.

Gluconeogenesis The major aim of protein catabolism during a state of starvation is to provide the glucogenic amino acids (especially alanine and glutamine) that serve as substrates for endogenous glucose production (*gluconeogenesis*) in the liver. In the hypometabolic/starved state, protein breakdown for gluconeogenesis is minimized, especially as ketones derived from fatty acids become the substrate preferred by certain tissues. In the hypermetabolic/stress state, gluconeogenesis increases dramatically and in proportion to the degree of the insult to increase the supply of glucose (the major fuel of reparation). Glucose is the only fuel that can be utilized by hypoxemic tissues (*anaerobic glycolysis*), white blood cells, and newly generated fibroblasts. Infusions of glucose partially offset a negative energy balance but do not significantly suppress the high rates of gluconeogenesis in catabolic patients. Hence, adequate supplies of protein are needed to replace the amino acids used for this metabolic response.

In summary, a hypometabolic patient is adapted to starvation and conserves body mass through reduction of the metabolic rate and use of fat as the primary fuel (rather than glucose and its precursor amino acids). A hypermetabolic patient also uses fat as a fuel but rapidly breaks down body protein to produce glucose, with consequent loss of muscle and organ tissue and danger to vital body functions.

MICRONUTRIENT MALNUTRITION

The same illnesses and reductions in nutrient intake that lead to PEM often produce deficiencies of vitamins and minerals as well (Chap. 96e). Deficiencies of nutrients that are stored in small amounts (such as the water-soluble vitamins) occur because of loss through external secretions, such as zinc in diarrhea fluid or burn exudate, and are probably more common than is generally recognized.

Deficiencies of vitamin C, folic acid, and zinc are relatively common in sick patients. Signs of scurvy, such as corkscrew hairs on the lower extremities, are found frequently in chronically ill and/or alcoholic patients. The diagnosis can be confirmed by determination of plasma vitamin C levels. Folic acid intakes and blood levels are often less than optimal, even among healthy persons; with illness, alcoholism, poverty, or poor dentition, these deficiencies are common. Low blood zinc levels are prevalent in patients with malabsorption syndromes such as inflammatory bowel disease. Patients with zinc deficiency often exhibit poor wound healing, pressure ulcer formation, and impaired immunity. Thiamine deficiency is a common complication of alcoholism but may be prevented by therapeutic doses of thiamine in patients treated for alcohol abuse.

Patients with low plasma vitamin C levels usually respond to the doses in multivitamin preparations, but patients with deficiencies should be supplemented with 250–500 mg/d. Folic acid is absent from some oral multivitamin preparations; patients with deficiencies should be supplemented with ~1 mg/d. Patients with zinc deficiencies resulting from large external losses sometimes require oral supplementation with 220 mg of zinc sulfate one to three times daily. For these reasons, laboratory assessments of the micronutrient status of patients at high risk are desirable.

Hypophosphatemia develops in hospitalized patients with remarkable frequency and generally results from rapid intracellular shifts of phosphate in underweight or alcoholic patients receiving intravenous glucose (Chap. 63). The adverse clinical sequelae are numerous; some, such as acute cardiopulmonary failure, are collectively called *refeeding syndrome* and can be life-threatening.

GLOBAL CONSIDERATIONS

Many developing countries are still faced with high prevalences of the classic forms of PEM: marasmus and kwashiorkor. *Food insecurity*, which characterizes many poor countries, prevents consistent dietary sufficiency and/or quality and leads to endemic or cyclic malnutrition. Factors threatening food security include marked seasonal variations in agricultural productivity (rainy season–dry season cycles), periodic droughts, political unrest or injustice, and disease epidemics (especially of HIV/AIDS). The coexistence of malnutrition and disease epidemics exacerbates the latter and increases complications and mortality rates, creating vicious cycles of malnutrition and disease.

As economic prosperity improves, developing countries have been observed to undergo an epidemiologic transition, a component of which has been termed the *nutrition transition*. As improved economic resources make greater dietary diversity possible, middle-income populations (e.g., in southern Asia, China, and Latin America) typically begin to adopt lifestyle habits of industrialized nations, with increased consumption of energy and fat and decreased levels of physical activity. These changes lead to rising levels of obesity, metabolic syndrome, diabetes, cardiovascular disease, and cancer, sometimes coexisting in populations with persistent undernutrition.

Micronutrient deficiencies also remain prevalent in many countries of the world, impairing functional status and productivity and increasing mortality rates. Vitamin A deficiency impairs vision and increases morbidity and mortality rates from infections such as measles. Mild to moderate iron deficiency may be prevalent in up to 50% of the world, resulting from poor dietary diversity coupled with periodic blood loss and pregnancies. Iodine deficiency remains prevalent, causing goiter, hypothyroidism, and cretinism. Zinc deficiency is endemic in many populations, producing growth retardation, hypogonadism, and dermatoses and impairing wound healing. Fortunately, public health supplementation programs have substantially improved vitamin A and zinc status in developing countries during the past two decades, reducing mortality rates from measles, diarrheal diseases, and other manifestations. However, with the advancing nutrition transition and a shift toward nutritionally related chronic noncommunicable conditions, it is estimated that nutrition remains one of the three greatest contributors of risk for morbidity and mortality worldwide.

NUTRITIONAL ASSESSMENT

Because interactions between illness and nutrition are complex, many physical and laboratory findings reflect both underlying disease and nutritional status. Therefore, the nutritional evaluation of a patient requires an integration of history, physical examination, anthropometrics, and laboratory studies. This approach helps both to detect nutritional problems and to prevent the conclusion that isolated findings indicate nutritional problems when they do not. For example, hypoalbuminemia caused by an inflammatory illness does not necessarily indicate malnutrition.