

Cachexia. PEM is a common complication in patients with AIDS or advanced cancers, and in these settings it is known as *cachexia*. Cachexia occurs in about 50% of cancer patients, most commonly in individuals with gastrointestinal, pancreatic, and lung cancers, and is responsible for about 30% of cancer deaths. It is a highly debilitating condition characterized by extreme weight loss, fatigue, muscle atrophy, anemia, anorexia, and edema. Mortality is generally the consequence of atrophy of the diaphragm and other respiratory muscles.

The precise causes of cachexia are not known, but it is clear that mediators secreted by tumors and during chronic inflammatory reactions contribute to its development:

- *Proteolysis-inducing factor*, which is a glycosylated polypeptide excreted in the urine of weight-losing patients with pancreatic, breast, colon, and other cancers
- *Lipid-mobilizing factor*, which increases fatty acid oxidation, and proinflammatory cytokines, such as TNF (originally known as *cachectin*), and IL-6.

Proteolysis-inducing factor and proinflammatory cytokines cause skeletal muscle breakdown through the NF- κ B-induced activation of the ubiquitin proteasome pathway, which promotes the degradation of skeletal muscle structural proteins such as myosin heavy chain by upregulating the expression of several muscle-specific ubiquitin ligases. Other data implicate acquired abnormalities of the myofibril dystrophin-glycoprotein complex (Fig. 9-23), the same

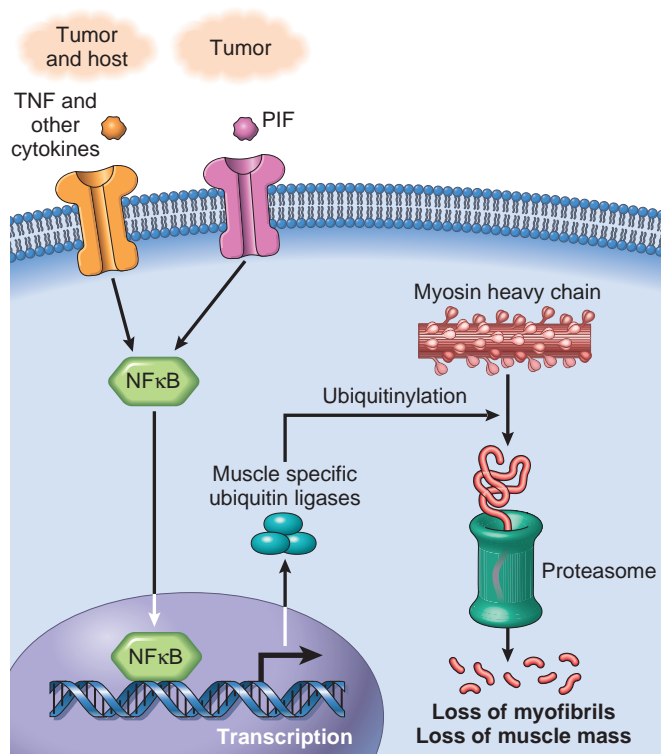


Figure 9-23 Mechanisms of cancer cachexia. Proteolysis-inducing factor (PIF) produced by tumors and TNF and other cytokines produced by host immune cells activate NF- κ B and initiate the transcription of the muscle-specific ubiquitin ligases. These ligases in turn ubiquitinate structural components of myofibrils such as myosin heavy chain, leading to their degradation by the proteasome.

membrane complex that is defective in several forms of muscular dystrophy (Chapter 27).

Anorexia Nervosa and Bulimia

Anorexia nervosa is self-induced starvation, resulting in marked weight loss; *bulimia* is a condition in which the patient binges on food and then induces vomiting. Anorexia nervosa has the highest death rate of any psychiatric disorder. Bulimia is more common than anorexia nervosa, and generally has a better prognosis; it is estimated to occur in 1% to 2% of women and 0.1% of men, with an average onset at 20 years of age. These eating disorders occur primarily in previously healthy young women who have developed an obsession with body image and thinness. The neurobiologic underpinnings of these diseases are unknown, but it has been suggested that altered serotonin metabolism may be an important component.

The clinical findings in anorexia nervosa are generally similar to those in severe PEM. In addition, effects on the endocrine system are prominent. *Amenorrhea*, resulting from decreased secretion of gonadotropin-releasing hormone, and subsequent decreased secretion of luteinizing hormone and follicle-stimulating hormone, is so common that its presence is considered a diagnostic feature. Other common findings related to *decreased thyroid hormone release* include cold intolerance, bradycardia, constipation, and changes in the skin and hair. In addition, dehydration and electrolyte abnormalities are frequently present. The skin becomes dry and scaly. *Bone density is decreased*, most likely because of low estrogen levels, mimicking the postmenopausal acceleration of osteoporosis. Anemia, lymphopenia, and hypoalbuminemia may be present. A major complication of anorexia nervosa (and also bulimia) is an increased susceptibility to *cardiac arrhythmia* and *sudden death*, resulting from hypokalemia.

In bulimia, *binge eating* is the norm. Large amounts of food, principally carbohydrates, are ingested, only to be followed by induced vomiting. Although menstrual irregularities are common, amenorrhea occurs in less than 50% of bulimic patients because weight and gonadotropin levels remain near normal. The major medical complications relate to frequent vomiting and the chronic use of laxatives and diuretics. They include (1) *electrolyte imbalances* (hypokalemia), which predispose the patient to cardiac arrhythmias; (2) *pulmonary aspiration* of gastric contents; and (3) *esophageal and gastric rupture*. Nevertheless, there are no specific signs or symptoms; thus, the diagnosis of bulimia relies on a comprehensive psychological assessment of the person.

Vitamin Deficiencies

Thirteen vitamins are necessary for health; vitamins A, D, E, and K are *fat-soluble*, and all others are *water-soluble*. The distinction between fat- and water-soluble vitamins is important. Fat-soluble vitamins are more readily stored in the body, but they may be poorly absorbed in fat malabsorption disorders, caused by disturbances of digestive functions (Chapter 17). Certain vitamins can be synthesized endogenously – vitamin D from precursor steroids, vitamin K and biotin by the intestinal microflora, and niacin from tryptophan, an essential amino acid.