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Introduction

Cachexia is often observed in patients with cancer and is associated with increased morbidity and decreased quality of life and survival. The etiology of weight loss and cachexia in cancer patients includes decreased intake, altered metabolism, and increased catabolism. This chapter addresses pediatric and adult nutritional issues and adjuvant therapy for patients with cancer, along with education for patients and caregivers.

I. Background

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References

(Cancer chapters from the 1st edition were contributed by Virginia Hermann, Patricia Fuhrman, Peggy Borum, Karyl Rickard, Barbara Godshall, Angelita Lopez, and Robert Weetman)

- I. **Background.** More than 1 million Americans are diagnosed with cancer each year. Cancer is the second leading cause of death after heart disease, claiming 23% of total deaths in the United States. Although overall cancer death rates and incidence rates have remained stable over the past few years, mortality rates of the four most common cancers (lung, colorectal, breast, and prostate) have continued to decline.¹ The leading cancers affecting men and women of all races are prostate cancer and breast cancer, respectively.
 - A. Adults — Cancer types more likely to result in nutritional alterations
 1. There is a relation between malnutrition/weight loss and tumor type.² Generally, malnutrition is more prevalent in patients with cancer of the proximal gastrointestinal (GI) tract.³
 2. Patients with pancreatic or gastric cancer had the highest prevalence of weight loss (83%–87%).⁴
 3. Patients with non-Hodgkin's lymphoma with less favorable outcomes, colon cancer, prostate cancer, and lung cancer had a 48% to 61% prevalence of weight loss.⁴
 4. Weight loss occurs in 43% to 61% of patients with lung cancer, depending on the stage of the disease.⁵
 5. Patients with subtypes of non-Hodgkin's lymphomas with more favorable outcomes, breast cancer, acute non-lymphocytic leukemia, and sarcomas had the lowest prevalence of weight loss (31%–41%) in this study.⁴
 - B. Pediatrics
 1. Cancer among children ages 0 to 19 years
 - a) The most common childhood cancers are leukemias, followed by cancer of the central nervous system, lymphomas, and reticuloendothelial neoplasms for all races.
 - b) Leukemias are more common among 1- to 4-year-olds, whereas lymphomas are more common among 15- to 19-year-olds.

2. Cancer trends⁶
 - a) The incidence of all childhood cancers has fluctuated but has generally increased over the period 1975–2000 for 0- to 19-year-olds.
 - b) The largest increase in incidence for all cancers occurred during 1975–1986.
 - c) Hepatic tumors had the largest percent increase in incidence for 1975–2000, followed by soft-tissue sarcomas and renal tumors.
 - d) Mortality from cancer has steadily decreased over the period 1975–2000.
 - e) The 5-year survival rates for all cancers steadily increased from 1975 to 1995.
 - f) The 5-year survival rates from 1985 to 1999 were highest for retinoblastoma, followed by renal tumors, germ-cell trophoblastic and other gonadal neoplasms, and carcinomas and other malignant epithelial neoplasms. Hepatic tumors had the lowest 5-year survival rate during the period.

3. Cancer types more likely to result in nutritional alterations
 - a) At diagnosis
 - (1) Children have lower energy reserves and higher metabolic demands than adults and are therefore more likely to experience nutritional depletion, particularly during growth spurts.^{7–10}
 - (2) At presentation, patients with sarcomas frequently have compromised nutritional status.¹¹ Patients with intra-abdominal solid tumors were significantly more malnourished than patients with leukemia or extra-abdominal solid tumors at diagnosis.¹²
 - (3) Nutritional status may be related to the length of time until diagnosis. Patients with prolonged time to diagnosis may experience more nutritional compromise.
 - (4) Patients with acute lymphoblastic leukemia (ALL), high-risk malignant disease, or various solid tumors had documented increases in catabolism prior to therapy, with protein breakdown significantly greater than protein synthesis.¹³
 - b) After therapy
 - (1) The frequency, intensity, and type of chemotherapy regimens may affect nutritional status. Patients with soft-tissue sarcomas and osteosarcomas had greater decreases in weight-for-height compared to patients with other types of cancer, which may be attributed to aggressive and frequent chemotherapy.¹¹ Steroid use in the treatment of other cancers (eg, ALL) may have prevented this decrease in weight-for-height. However, height-for-age Z scores decreased after therapy in patients with ALL, with a corresponding decrease in lean body mass and increase in body fat.¹⁴ Survivors of ALL were shown to have decreased height-for-age standard deviation scores during treatment and up to 20 years postdiagnosis, while their body mass index (BMI) standard deviation significantly increased during the period from diagnosis to final height.^{15,16} This tendency toward overweight in ALL survivors may be related in part to decreases in physical activity.^{16–18}

- (2) There are inconsistent results regarding metabolic rate before and after chemotherapy in patients with ALL.¹⁹⁻²² The difference in results may be related to the tumor burden prior to chemotherapy.²⁰ ALL patients with a greater tumor burden had higher resting energy expenditures than those with lower tumor burden initially. This difference disappeared after 1 to 2 weeks of chemotherapy, because the resting energy expenditure decreased in the group that had a high tumor burden.²⁰
- (3) Patients with cancers of the central nervous system tend to require enteral nutrition or parenteral nutrition (PN) for greater lengths of time than do lymphoma, leukemia, and bone marrow transplant patients (but not patients with solid tumors), likely owing to the effect of the disease on neurological processes involved with eating.²³

II. Nutritional Alterations in Patients With Cancer.

Cachexia comes from the Greek words *kakos hexos*, which literally means “bad condition of the body.” It is estimated to affect more than 80% of patients with advanced malignant disease. It is defined as a state of malnutrition characterized by anorexia, weight loss, muscle wasting, asthenia, depression, chronic nausea, and anemia and results in psychological distress, changes in body composition, and alterations in carbohydrate, lipid and protein metabolism.^{24,25} Alterations may occur in tissue water content, in acid-base balance, and in the concentrations of electrolytes, vitamin or mineral concentrations. These metabolic abnormalities may impair nutritional status and contribute to cachexia through the depletion of fat, protein, water, and mineral stores.²⁶ The degree of cachexia is inversely correlated with the survival time of the patient, and it implies a poor prognosis.²⁷

A. Weight loss and cachexia

1. Altered intake

- a) Anorexia or the loss of appetite and early satiety is present in up to one half of newly diagnosed cancer patients.^{4,28} Anorexia results in decreased food intake and weight loss and may lead to the development of malnutrition. Symptoms that interfere with food intake and are likely to be related to anorexia include early satiety, taste alterations, smell alterations, meat aversion, and nausea/vomiting.²⁹ The pathogenesis of cancer anorexia is multifactorial and is associated with disturbances of the central physiological mechanisms controlling food intake. Several factors that appear to play key roles in the development of cancer anorexia include hormones (leptin), neuropeptides (neuropeptide Y), cytokines (interleukin-1 and -6, tumor necrosis factor [TNF]), and neurotransmitters (serotonin and dopamine).²⁹
- b) Cancer treatment modalities, such as chemotherapy and radiotherapy, may cause nausea, vomiting, diarrhea, mucositis, and taste alterations. These side effects ultimately may decrease food intake and cause learned food aversions.
 - (1) Nausea and vomiting are the most feared side effects of cancer treatment. Acute nausea and vomiting occurs during the first 24 hours after treatment. Highly emetogenic chemotherapy, such as cisplatin and cyclophosphamide, may cause nausea and vomiting after 24 hours.³⁰
 - (2) Mucositis, a result of the effect of cancer therapy on rapidly dividing cells, can occur along the GI tract but occurs more

often in the mouth. Mucositis often occurs 5 to 7 days after chemotherapy and generally persists with bone marrow suppression from the treatment. Clinical manifestations include erythema, dryness, ulcers, bleeding, and pain. It is estimated to occur in 40% of cancer patients, and the incidence is the highest in bone marrow transplant patients.³⁰

- (3) Radiotherapy has direct short- and long-term effects on olfactory and secretory function, the digestive tract, and the mucous membranes. Long-term bone, dental, olfactory, secretory, and digestive sequelae can lead to reduced food intake and/or malabsorption of nutrients.³
 - c) Operative therapy may result in altered intake. Surgery of the head and neck may result in dysphagia. Pre- and postoperative nil per os and restrictive diets such as clear liquids further affect nutrient intake.
 - d) Biotherapy is associated with decreased appetite and fatigue.³⁰ Biotherapy, also known as biologic therapy or immunotherapy, is intended to strengthen the immune system's ability to recognize and attack cancer cells. Biotherapy is a diverse group of therapeutic strategies for cancer and includes immunotherapy, agents that inhibit angiogenesis or invasion, growth factor modulation, and small molecules (inhibitors of signal transduction).³¹ Although some of these treatments stimulate immune reactions against cancer cells, they sometimes interfere with immunity against infections. People who receive biological therapies may be at risk for immunosuppression and neutropenia.³²
 - e) Physical obstruction of the GI tract (stomach, small intestine, or colon) is generally associated with decreased intake or emesis after intake. Intestinal obstruction is well recognized in patients with progressive advanced gynecological and GI cancers, especially those with colon cancer or with metastasis from ovarian cancer.^{33,34}
 - f) Dysphagia, especially due to head and neck cancer, leads to significant weight loss even in the presence of reported normal appetite.³⁵
 - g) Depression, feelings of overwhelming sadness, and the fear and anxiety that accompany a diagnosis of cancer may lead to decreased intake. In the Psychosocial Collaborative Oncology Group Study, in which 215 adults with various types of cancers were studied, 47% of the subjects had a clinically apparent psychological disorder. Two thirds had either reactive anxiety or depressed mood, and 13% had major depression.³⁶ Depression has been associated more commonly with pancreatic cancer than with most other cancers.³⁷
2. Energy expenditure
- a) Tremendous variability in resting energy expenditure measurements has been reported in malnourished patients with cancer, ranging from hypometabolism to hypermetabolism.³⁸
 - b) Elevated resting energy expenditure was reported in pancreatic and lung cancer patients and unchanged in patients with gastric and colorectal cancer.^{28,39}
 - c) Hypermetabolism and weight loss are significant predictors of decreased survival.³⁸

- d) In a group of almost 300 patients with various types of cancer, about one half had elevated resting energy expenditures. The increase in energy expenditure was not associated with a different dietary intake compared to normometabolic patients.⁴⁰ Feedback regulation of dietary intake in relation to energy expenditure is frequently lost in patients with cancer, so that hypermetabolism is not compensated for by an increase in spontaneous food intake as it is in normometabolism.^{38,40}
3. Decreased absorption⁴¹
- a) Treatment modalities, such as surgery, chemotherapy, and radiotherapy, may result in malabsorption.
 - (1) Operative therapy may result in intestinal ileus and stasis of bowel contents, which adversely affects absorption. Pancreatic resection may be associated with malabsorption of fat and protein. Gastric resection may lead to dumping syndrome. Large segment resection of the small bowel or colon may affect absorption of nutrients, fluid, and electrolytes and sometimes results in long-term PN dependency.
 - (2) Chemotherapeutic agents often cause severe GI symptoms, such as mucositis and diarrhea, which may result in malabsorption.
 - (3) Radiotherapy causes both acute and delayed reactions that affect intestinal absorption. Acute reactions usually occur within days to weeks of therapy and include enteritis, diarrhea, and decreased production of saliva with consequently reduced enzymes. Late reactions to radiation therapy include persistent mucosal inflammation, intestinal fibrosis, and stricture.⁴²
 - b) Tumor involvement of the GI tract may result in mechanical obstruction, with decreased absorption and diarrhea. Serosal involvement of the bowel may cause functional malabsorption, pseudo-obstruction, or intestinal ileus, precluding optimal absorption.
 - c) Stasis of bowel contents from partial or complete intestinal obstruction may lead to bacterial overgrowth and interfere with absorption of nutrients.
4. Changes in the immune system
- a) It is now established that nutritional deficiency is commonly associated with impaired immune responses, particularly cell-mediated immunity, phagocyte function, cytokine production, secretory antibody response, antibody affinity, and the complement system.⁴³ Nutritional deprivation, such as protein energy malnutrition, often causes immunodeficiency, leading to increased frequency and severity of infection and an increased incidence of common infections affecting the upper and lower respiratory, urinary, and genital tracts.⁴⁴ In a study that examined the relationship between nutritional status as indicated by the presence or absence of the cutaneous delayed hypersensitivity response and treatment-related morbidity, disease recurrence, and survival at 2 years in 67 head and neck patients, survival was improved in

patients whose cell-mediated immunity was preserved compared with those who were anergic at completion of treatment. Morbidity due to surgical therapy and tumor recurrence rates were also higher in the anergic group.³⁵

- b) Immunodeficiency may result from treatment. Operative intervention, radiation therapy, and chemotherapeutic agents all affect cell-mediated immunity, even in well-nourished subjects.^{41,45}
 - c) T-cell function is also altered with certain hematologic malignancies, whereas humoral (B-cell) immunity is affected in chronic lymphocytic leukemia and multiple myeloma.⁴¹
 - d) Immunoglobulin A deficiency, noted in many malnourished patients, may play a role in facilitating bacterial translocation and absorption of endotoxin into the circulation.⁴¹
5. Hormones and cytokines
- a) Cytokines and other mediators play a major role in the complex cascade of biological responses leading to the wasting associated with cancer cachexia. Cytokines are a diverse group of soluble glycoproteins and low-molecular weight peptides that mediate interactions between cells and regulate cell and tissue functions.⁴⁶ In relation to cancer cachexia, they modulate gastric motility and emptying, either in the GI tract or via the brain, by altering efferent signals that regulate satiety.⁴⁷ Although elevated levels of numerous cytokines were found in the blood and urine of cancer patients, the absence of clinically detectable cytokine levels does not exclude the idea that cytokines play a role in systemic effects.^{46,48}
 - (1) TNF was one of the first cytokines thought to play a role in cancer cachexia. Early studies found that mice with tumors producing TNF also developed cachexia and that weight loss was reversed with TNF-neutralizing antibodies.^{46,49} TNF also suppresses lipoprotein lipase activity in adipocytes.⁵⁰
 - (2) Interleukin-1 (IL-1) is associated with the initiation of anorexia by blocking neuropeptide Y (NPY)-induced feeding.^{47,51}
 - (3) TNF and IL-1 may increase the levels of corticotropin-releasing hormone, which is a central nervous system neurotransmitter that suppresses food intake and the release of glucose-sensitive neurons and ultimately decreases food intake.^{47,52,53}
 - (4) Interleukin-6 (IL-6) and leukemia inhibitor factor (LIF) are produced by some cancers and may contribute to cachexia.^{46,50,54} Ciliary neurotropic factor, which is a member of the family of cytokines that includes IL-6 and LIF, is expressed in skeletal muscle and induces potent cachectic effects and acute-phase proteins in tumor-bearing mice.^{47,50,55}
 - (5) Interferon (IFN)- γ may be involved in cancer cachexia. In animals, the provision of antibodies against IFN- γ reversed the wasting syndrome, which clarified that there was an endogenous production of IFN- γ .^{47,56}
 - (6) Lipid-mobilizing factor induces lipolysis and correlates with weight loss.⁵⁷

- (7) Proteolysis-inducing factor induces protein degradation in skeletal muscle by upregulating the ubiquitin-proteasome proteolytic pathway and by decreasing protein synthesis.^{28,58} This factor also may increase cytokines and acute-phase proteins.^{28,59,60}
- b) Leptin, neuropeptides, and uncoupling proteins
 - (1) Leptin acts to control food intake and energy expenditure via neuropeptideric effector molecules within the hypothalamus.⁶¹ TNF, IL-1, and LIF increase plasma levels of leptin, despite a decrease in food intake that would normally suppress leptin expression.⁶²⁻⁶⁴ Increased leptin levels may contribute to anorexia by preventing the normal compensatory mechanisms in light of decreased food intake. Results on leptin levels are not consistent. Leptin levels were not elevated in tumor-bearing rats and in patients with cancer cachexia.⁶⁵⁻⁶⁷ On the other hand, very low levels of leptin with high levels of inflammatory cytokines were found in patients with advanced-stage cancer.⁶⁸
 - (2) NPY is the most potent feeding-stimulatory peptide activated by the fall of leptin. NPY is thought to restore normal energy balance and body fat stores under conditions of energy deficit, the signals of which are falling leptin and/or insulin.⁶²
 - (3) Uncoupling protein (UPC) 1, 2, and 3 may be involved in the control of energy metabolism. They are mitochondrial membrane proteins that mediate proton leakage and decrease the coupling of respiration to adenosine diphosphate phosphorylation, resulting in the generation of heat instead of adenosine triphosphate. UPC 1 is expressed only in brown adipose tissue, which in adult humans is very scarce and probably not functional.⁶⁹ UPC 2 is distributed and expressed in most tissues. UPC 3 is expressed in brown adipose tissue and skeletal muscle and may be of significant importance in energy expenditure. Changes in UPC expression may be induced by tumor products of cytokines.²⁸
- B. Metabolic alterations. Although altered nutrient intake and anorexia contribute to cancer cachexia, decreased food intake alone does not entirely account for the weight loss seen in cancer patients.⁷⁰ This is evident in studies in which the loss of muscle and adipose tissue precedes the fall in food intake and the provision of extra calories does not result in weight gain.^{70,71} It is clear that the cachectic cancer patient uses nutrients ineffectively and seems unable to adapt to the malnourished state as normal humans do by conserving lean body mass.⁷²
 1. Glucose homeostasis
 - a) There is an elevation in Cori cycle activity in malnourished cancer patients, and this increased activity accounts for approximately 300 kcal per day loss of energy.^{28,73} The demand for glucose carbons by the tumor tissue can increase demand for glucose production by the liver, especially if glucose cannot be fully oxidized by the tumor tissue itself. The inability to effectively oxidize glucose may explain

why some cancer patients exhibit an increase in Cori cycle activity and elevated glucose production.⁷³

- b) Increased lactate levels and production rates in cancer patients are due to increased glycolysis and lactate release by the tumor tissue and skeletal muscle tissue. Glucose is the main energy source of most solid tumors, and it is highly used by the tumor and host, with an associated release of substantial amounts of lactate. Lactate is then regenerated into glucose by the liver through the Cori cycle.⁷⁰
- c) Gluconeogenesis is increased to maintain glucose homeostasis in the cancer patient. Amino acids and glycerol from muscle and fat breakdown, respectively, are used as the main substrates in gluconeogenesis.⁷⁰ The reduced plasma levels of alanine, glycine, and glutamine seen in cachectic cancer patients may be caused by an increase in their use by the liver for glucose production.⁷⁴
- d) Glucose production, glucose intolerance, and insulin resistance often are increased in cancer patients. Glucose use by skeletal muscle is reduced due to insulin resistance. The counter regulatory hormones, such as glucocorticoids and glucagons, increase and may contribute to insulin resistance.⁵²

2. Protein metabolism

- a) Increased muscle catabolism. Muscle wasting is common in cancer patients and contributes to the asthenia, or lack of strength, seen in these patients. It is caused by an increase in protein breakdown and, to a lesser extent, a decrease in protein synthesis.⁷⁰
- b) Negative nitrogen balance may be present, whole body protein turnover is increased, and amino acid turnover is altered.^{58,75}
- c) Decreased muscle protein synthesis and increased liver and tumor protein synthesis occur. There is a shift from normal muscle protein and other tissue protein synthesis to increased hepatic protein synthesis, which is reprioritized with an increased production of acute-phase proteins.^{50,58,76}

3. Lipid metabolism

- a) Patients with cancer cachexia have a profound loss of adipose tissue due to an increase in lipolysis and a reduction in lipogenesis.^{28,50,52}
- b) Cancer patients with weight loss have a higher turnover of both glycerol and free fatty acids.²⁸
- c) Patients with cancer have been shown to have significantly reduced levels of lipoprotein lipase, the enzyme responsible for triglyceride clearance from plasma.^{50,52}
- d) The lipid profile in cancer patients is characterized by decreased high-density lipoproteins, decreased low-density lipoproteins, and relatively high serum triglycerides.^{77,78} Hypertriglyceridemia is a consequence of the decreased lipoprotein lipase activity, which results in a decrease in the plasma clearance of both endogenous and exogenous triglycerides.⁵²

C. Micronutrient deficiencies. Dietary compounds may affect cancer development through several mechanisms, including the alteration of carcinogen metabolism, antioxidation, enhancement of differentiation and growth inhibition, and immunologic modulation.⁷⁹

1. Vitamins

- a) Vitamin C and Vitamin E act as antioxidants, stimulate the immune system, and reduce nitrite, which prevents the formation of

nitrosamine and nitrosamine compounds known to induce tumor formation in experimental animals and humans.⁷⁹

- b) Studies on vitamins reveal reduced levels associated with different malignancies. Reduced levels of vitamins and minerals were found in the following cancer sites:

- (1) Vitamin A levels in colorectal cancer and esophageal cancer^{80,81} and in pretreatment pediatric leukemia and lymphoma⁸²
- (2) Beta-carotene in lung cancer, gastric cancer, pancreatic cancer, oral cancer, and thyroid cancer⁸³⁻⁸⁷ and in pediatric leukemia, lymphoma, and malignant bone tumors⁸²
- (3) Vitamin E in lung cancer, gastric cancer, pancreatic cancer, prostate cancer, and gallbladder cancer^{79,83-85,88} and in pediatric leukemia, lymphoma, malignant bone tumors, and central nervous system tumors⁸²
- (4) Vitamin C in lung cancer, gastric cancer, pancreatic cancer, esophageal cancer, colon cancer, and prostate cancer^{81,83-85,88,89}
- (5) Vitamin D (and calcium) in colon cancer⁸⁹

- c) A multivitamin and mineral supplement may be recommended for patients with an inadequate nutrient intake. Further evaluation of vitamin and mineral status may be indicated if deficiencies are suspected, such as in patients with prolonged poor nutrient intake and/or with malabsorption, and repletion may be warranted.

2. Trace elements

- a) Selenium, zinc, manganese, and copper are cofactors for various antioxidant enzymes such as glutathione peroxidase, RNA polymerase, superoxide dismutase, and diamine oxidase.⁷⁹
- b) Metabolism of metals, especially zinc, is affected in patients with cancer. There is an increase in urinary zinc with a variety of tumors, such as melanoma, gynecologic malignancies, and lung cancer. Low zinc levels were reported in the serum and tissues of cervical cancer patients⁹⁰ and in patients with prostate cancer and breast cancer,^{88,91,92} as well as in pediatric patients with leukemia, lymphoma, malignant bone tumors, and tumors of the central nervous system.⁸² Zinc is released during protein catabolism bound to amino acids and may pass the glomerular membrane.⁸⁰ Zinc deficiency may occur if nutrient intake is poor or GI losses are great.
- c) Copper functions as a cofactor in metabolic substrate pathways and nucleic acid synthesis. Levels may be low secondary to chronic decreased intake and absorption.
- d) Selenium deficiency has been reported in cancer patients, particularly those who are chronically malnourished or dependent on home nutrition support. Low serum and tissue selenium levels were reported in patients with cervical cancer.⁹⁰ Reduced levels of serum selenium were found in patients with hepatocellular carcinoma and breast cancer.⁹¹⁻⁹³
- e) Selenium deficiency is common among newly diagnosed pediatric cancer patients, even in the absence of malnutrition.⁹⁴

- f) Low serum, biliary, and tissue concentrations of selenium and zinc were reported in patients with carcinoma of the gallbladder as compared to patients with cholelithiasis.⁷⁹
- g) The copper-to-zinc ratio was demonstrated to be useful as a diagnostic tool in GI, lung, and gallbladder cancer and may contribute to an early diagnosis of these cancers.^{79,95,96}

D. Electrolyte disturbances

- 1. Hypercalcemia, hyperphosphatemia, hypocalcemia, and hyperkalemia are associated with tumor lysis syndrome (TLS).⁹⁷ TLS frequently occurs in patients with lymphoma and is defined as the metabolic derangements produced by rapid tumor breakdown, which can occur either spontaneously from rapid tumor growth followed by spontaneous tumor cell death or as a consequence of therapy. It is characterized by hyperuricemia due to DNA breakdown, hyperkalemia related to cytosol breakdown, hyperphosphatemia due to protein breakdown, and hypocalcemia secondary to the hyperphosphatemia. As phosphate levels rise, serum calcium decreases.⁹⁷
- 2. Hypocalcemia, hypomagnesemia, and hypophosphatemia are often observed in association with the use of platinum-containing therapy, and hyponatremia often accompanies treatment with cyclophosphamide and vincristine.⁹⁷

III. Nutritional Assessment of Patients With Cancer

A. Adults

1. Screening

- a) Early assessment of nutritional risk and serial reassessments throughout a cancer patient's course are necessary to ensure that interventions are timely and effective.⁹⁸ The focus of nutritional assessments varies depending on a patient's situation and needs.
- b) The Patient-Generated Subjective Global Assessment (PG-SGA), a modification of the Subjective Global Assessment, is an outcome-based assessment tool developed specifically for cancer patients (see Figure 11-1). It is applicable in varied health care settings and can be used to identify and prioritize nutritional risk and capture short-term changes in nutritional status.^{98,99} The PG-SGA is formatted so that components of the medical history can be completed first by the patient using a check-box format. This segment includes four sections: short-term weight status, food intake change, nutrition impact symptoms, and functional capacity. A three-part physical assessment section evaluating metabolic demand of underlying disease and degree of metabolic stress, and a subjective evaluation of fat stores, muscle status, and fluid status, are then completed by the clinician. In addition to a global rating of nourishment status, the scored PG-SGA incorporates a numerical score. The numerical score of the completed PG-SGA can guide the nutrition intervention pathway and assist in determining effective strategies, such as patient education, symptom management, aggressive oral nutrition, and enteral/parenteral support. An observational study of cancer patients demonstrated that the scored PG-SGA is a simple, valid, and reliable assessment tool.¹⁰⁰ The scored PG-SGA was adopted by the Oncology Nutrition Dietetic

Practice Group of the American Dietetic Association as the standard for nutrition assessment of cancer patients.

Worksheets for PG-SGA Scoring

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Boxes 1-4 of the PG-SGA are designed to be completed by the patient. The PG-SGA numerical score is determined using 1) the parenthetical points noted in boxes 1-4 and 2) the worksheets below for items not marked with parenthetical points. Scores for boxes 1 and 3 are additive within each box and scores for boxes 2 and 4 are based on the highest scored item checked off by the patient.

Worksheet 1 - Scoring Weight (Wt) Loss
 To determine score, use 1 month weight data if available. Use 6 month data only if there is no 1 month weight data. Use points below to score weight change and add one extra point if patient has lost weight during the past 2 weeks. Enter total point score in Box 1 of the PG-SGA.

Wt loss in 1 month	Points	Wt loss in 6 months
10% or greater	4	20% or greater
5-9.9%	3	10 - 19.9%
3-4.9%	2	6 - 9.9%
2-2.9%	1	2 - 5.9%
0-1.9%	0	0 - 1.9%

Score for Worksheet 1 =
 Record in Box 1

Worksheet 2 - Scoring Criteria for Condition
 Score is derived by adding 1 point for each of the conditions listed below that pertain to the patient.

Category	Points
Cancer	1
AIDS	1
Pulmonary or cardiac cachexia	1
Presence of decubitus, open wound, or fistula	1
Presence of trauma	1
Age greater than 65 years	1

Score for Worksheet 2 =
 Record in Box B

Worksheet 3 - Scoring Metabolic Stress
 Score for metabolic stress is determined by a number of variables known to increase protein & calorie needs. The score is additive so that a patient who has a fever of > 102 degrees (3 points) and is on 10 mg of prednisone chronically (2 points) would have an additive score for this section of 5 points.

Stress	none (0)	low (1)	moderate (2)	high (3)
Fever	no fever	>99 and <101	≥101 and <102	≥102
Fever duration	no fever	<72 hrs	72 hrs	> 72 hrs
Corticosteroids	no corticosteroids	low dose (<10mg prednisone equivalents/day)	moderate dose (≥10 and <30mg prednisone equivalents/day)	high dose steroids (≥30mg prednisone equivalents/day)

Score for Worksheet 3 =
 Record in Box C

Worksheet 4 - Physical Examination
 Physical exam includes a subjective evaluation of 3 aspects of body composition: fat, muscle, & fluid status. Since this is subjective, each aspect of the exam is rated for degree of deficit. Muscle deficit impacts point score more than fat deficit. Definition of categories: 0 = no deficit, 1+ = mild deficit, 2+ = moderate deficit, 3+ = severe deficit. Rating of deficit in these categories are *not* additive but are used to clinically assess the degree of deficit (or presence of excess fluid).

Fat Stores:	0	1+	2+	3+
orbital fat pads	0	1+	2+	3+
triceps skin fold	0	1+	2+	3+
fat overlying lower ribs	0	1+	2+	3+
Global fat deficit rating	0	1+	2+	3+

Fluid Status:	0	1+	2+	3+
ankle edema	0	1+	2+	3+
sacral edema	0	1+	2+	3+
ascites	0	1+	2+	3+
Global fluid status rating	0	1+	2+	3+

Muscle Status:	0	1+	2+	3+
temples (temporalis muscle)	0	1+	2+	3+
clavicles (pectoralis & deltoids)	0	1+	2+	3+
shoulders (deltoids)	0	1+	2+	3+
interosseous muscles	0	1+	2+	3+
scapula (latissimus dorsi, trapezius, deltoids)	0	1+	2+	3+
thigh (quadriceps)	0	1+	2+	3+
calf (gastrocnemius)	0	1+	2+	3+
Global muscle status rating	0	1+	2+	3+

Point score for the physical exam is determined by the overall subjective rating of total body deficit.

No deficit	score = 0 points
Mild deficit	score = 1 point
Moderate deficit	score = 2 points
Severe deficit	score = 3 points

Score for Worksheet 4 =
 Record in Box D

Worksheet 5 - PG-SGA Global Assessment Categories

Category	Stage A Well-nourished	Stage B Moderately malnourished or suspected malnutrition	Stage C Severely malnourished
Weight	No wt loss OR Recent non-fluid wt gain	~5% wt loss within 1 month (or 10% in 6 months) OR No wt stabilization or wt gain (i.e., continued wt loss)	> 5% wt loss in 1 month (or >10% in 6 months) OR No wt stabilization or wt gain (i.e., continued wt loss)
Nutrient Intake	No deficit OR Significant recent improvement	Definite decrease in intake	Severe deficit in intake
Nutrition Impact Symptoms	None OR Significant recent improvement allowing adequate intake	Presence of nutrition impact symptoms (Box 3 of PG-SGA)	Presence of nutrition impact symptoms (Box 3 of PG-SGA)
Functioning	No deficit OR Significant recent improvement	Moderate functional deficit OR Recent deterioration	Severe functional deficit OR recent significant deterioration
Physical Exam	No deficit OR Chronic deficit but with recent clinical improvement	Evidence of mild to moderate loss of SQ fat &/or muscle mass &/or muscle tone on palpation	Obvious signs of malnutrition (e.g., severe loss of SQ tissues, possible edema)

Global PG-SGA rating (A, B, or C) =

2. History and medication use

- a) A detailed nutritional focused history should supplement other parts of the nutritional evaluation. In cancer patients, a focused history

should evaluate for any impediments to food intake and tolerance, including previous medical conditions or surgeries, taste alterations and food aversions, complementary and alternative therapies (including supplements, herbs, and botanicals), rigid or restrictive dietary habits, food allergies, and oral or dental disease. Family members and significant others may provide useful information in the assessment.

- b) A history should be used to assess the impact that a medical condition, medication, and/or modified diet may have on nutritional care during treatment. If a patient has difficulty eating during cancer treatment, it may be appropriate to liberalize or discontinue a previously prescribed diet. A history of GI surgery might necessitate an adjustment in a patient's dietary pattern or consideration for nutrition support.
3. Physical examination and functional assessment. A physical examination and functional evaluation are incorporated in the PG-SGA.
 - a) Body weight is the most basic anthropometric measure. Body weight evaluation provides a simple, dependable, and proven measure of nutritional risk. More than 45% of hospitalized adult cancer patients have been identified as having significant (>10%) weight loss (from usual weight).¹⁰¹ Unlike people experiencing starvation who lose fat while lean body mass is preserved, cancer patients lose both fat and lean body mass.²⁸ Percent body weight loss from usual weight correlates with complications and mortality.¹⁰² Multiple factors (eg, location and stage of tumor, cancer treatment) affect weight status.¹⁰² Since weight loss may be masked by altered fluids (eg, edema, ascites), hydration status should be taken into consideration. Timely intervention for weight loss is essential, since weight loss may be stabilized or reversed in some cancer patients if quickly identified.⁹⁸ When body weight is being evaluated, a comparison should be made to usual or normal weight, not a reference standard. Accurate body weight may be needed to calculate a treatment dose.
 - b) The physical examination should evaluate for muscle wasting and edema or ascites. A decrease in protein and fat stores and an associated increase in extracellular fluid accounts for the changes in body composition observed in cancer patients.⁴¹ Peripheral edema suggests increased extracellular fluid or decreased visceral protein stores.⁴¹ Temporal wasting is a hallmark of cachexia that is seen in patients with depleted lean body mass. However, muscle mass in cachectic cancer patients may be underestimated, limiting the usefulness of this measurement.⁴¹ While muscle wasting is apparent in cachectic patients, it may be more subtle in obese patients.
 - c) A functional assessment should determine a patient's ability to perform activities of daily living. This evaluation should determine and then compare preexisting abilities and deficits to those after diagnosis and treatment. The Karnofsky Performance Status Scale can classify a patient's functional impairment. This scale may be used to compare the effects of varied treatments and to assess the prognosis in individual patients. Generally, the lower the Karnofsky score, the poorer the survival prognosis for cancer patients.¹⁰³

- d) Functional limitations may affect a patient's ability to purchase, prepare, and eat food without assistance.¹⁰⁴ A rehabilitation therapy referral may be appropriate if the patient has significant deficits.
 - e) Assessment of muscle function using tests such as grip strength, respiratory muscle function, and electrical stimulation of specific muscles has effectively detected malnutrition-related changes before biochemical levels fall.¹⁰⁵
 - f) Pain in cancer patients may be related to physical factors, such as the disease itself, cancer treatment, or psychological variables.¹⁰⁶ Since uncontrolled pain may affect a patient's appetite and ability to eat, an assessment of pain should be an integral part of a nutrition assessment of cancer patients.
4. Biochemical and laboratory tests
- a) A measure of visceral proteins is used to judge protein status and effectiveness of nutritional repletion. Although serum albumin is commonly used to evaluate nutritional status, its ability to reflect nutritional status is questionable, although it is considered predictive of morbidity and mortality. Prealbumin, with its shorter half-life, provides a better indication of nutritional status and nutritional recovery during nutritional support, and also serves as a prognostic indicator of outcome.¹⁰⁷
 - b) A low albumin, and to a lesser extent a lowered prealbumin, may reflect poor nutrition but may also indicate infection, over hydration, and decreased synthesis due to cytotoxic agents.¹⁰⁷
 - c) Laboratory tests to identify micronutrient deficiencies may be appropriate in limited circumstances when other areas of assessment suggest deficits.
 - d) Objective parameters, such as anthropometrics and biochemical and immunological measures, support other aspects of the nutritional assessment. However, their validity and predictive capability as sole measures have been questioned since nonnutritional factors may skew results.
5. Quality of life (QOL)
- a) Disease- and treatment-related symptoms affect a cancer patient's ability to eat and, therefore, are important aspects of a patient's QOL. A patient's willingness to eat also can be negatively affected by financial constraints, depressed psychological state, and poor attitude. Ultimately, disinterest in eating can lead to social isolation and conflict with caregivers and friends.
 - b) Weakness and fatigue, resulting from poor nutritional status and treatment side effects, may limit a patient's ability to work and carry out activities of daily living, thereby compromising QOL.¹⁰⁸
 - c) A patient's well-being is composed of a physical component and a spiritual, psychological, and emotional component; both components are crucial to a patient's QOL and should be addressed in assessment.^{106,109}
 - d) In a study of patients with head and neck cancer receiving radiation treatment, individualized nutrition counseling for symptom management not only improved nutrient intake but positively influenced QOL.¹¹⁰

B. Pediatrics

1. Screening

- a) A PG-SGA for pediatric oncology has yet to be validated. However, many of the areas covered by the adult PG-SGA may also be applied to pediatrics, with some additions.
- b) These additions include current height-for-age and weight-for-height or BMI-for-age as well as recent growth trends; food intake change; nutrition impact symptoms (nausea, vomiting, diarrhea, constipation); and functional capacity.

2. History and medication use

- a) A diet history similar to that described for adults should be performed with the child and family. It should also include assessment of feeding behavior and skills. In addition, the family's viewpoints about nutrition and the child's level of understanding of the importance of nutrition should be assessed. These factors may have an impact on the child's motivation to eat when not feeling well, to try oral nutritional supplements, and to tolerate specialized nutrition support.
- b) A medical history, including medication use, should be used when establishing the nutrition care plan and interpreting nutrition laboratory tests. Numerous medications often needed during disease and treatment, including antibiotics and diuretics, can alter vitamin, mineral, and electrolyte status. Certain medications may have greater nutritional impact in children. For example, glucocorticoids, which are often used chronically in leukemia and lymphoma treatment, interfere with bone metabolism, causing decreased bone mineral density.¹¹¹ Supplementation with calcium and vitamin D has been shown to significantly reduce the effects of corticosteroids on bone mineral density in adults,¹¹² and supplementation with calcium and vitamin D should be seriously considered in children receiving chronic steroids to ensure appropriate bone mineral accretion during childhood. However, recommended doses of calcium and vitamin D in children receiving steroids are not clear, so children who are taking calcium and vitamin D supplements should be closely monitored for the development of hypercalcemia and hypercalciuria.

3. Physical examination and functional assessment

a) Anthropometrics

- (1) Weight and height are essential tools in assessing acute and chronic nutritional status and changes in nutritional status in children. Height-for-age is a measure of chronic or long-term nutrition in children. Weight-for-height or BMI-for-age can be used to assess acute or recent nutritional status. The criteria for poor growth or malnutrition in children have included any of the following: weight-for-height or height-for-age that is 2 standard deviations below the mean for sex and age¹¹³; the downward crossing of more than 2 major percentile markings on the National Center for Health Statistics (NCHS) growth charts from a child's established growth curve¹¹⁴; or the stages of acute and chronic malnutrition described by the Waterlow criteria.¹¹⁵ The validity of specific cutoffs based on the 2000 NCHS

pediatric BMI-for-age data as a screen for underweight has yet to be assessed. However, the World Health Organization defines BMI below the 5th percentile as an indication of underweight.¹¹³ Meeting any of these criteria indicates the need for nutrition assessment. Keep in mind that serial measurements of growth over time provide much more information regarding the individual's nutritional status than a single point on the growth chart. A patient who has a decrease in height-for-age or weight-for-age or BMI-for-age from the patient's established curve can cause greater concern (even if the patient's current point is above the 10th percentile) than a child who is below the 5th percentile but following his or her established curve. Overweight and its comorbidities can also be problematic in children with cancer. BMI-for-age is used to classify adolescents as at risk for overweight if between the 85th and 95th percentile and as overweight if at the 95th percentile or greater.^{116,117} Recommendations for appropriate nutrition intervention as well as referral for additional medical workup have been described for healthy children over 2 years of age with elevated BMIs based on their age and their BMI-for-age percentile.^{116,117} These recommendations can be applied to cancer survivors. However, weight maintenance and weight loss recommendations for patients currently battling cancer are not appropriate except in extreme cases, as the patient is likely to experience unintentional weight loss.

- (2) When interpreting weight and height, one should bear in mind that other factors such as tumor size and hydration status can affect weight. Medication and length and type of treatment can affect growth. These factors should be considered when evaluating growth and determining the cause of growth delays in children.

b) Body composition

- (1) Caliper skinfold and circumference measurements should be used as part of a complete nutritional assessment and can be especially useful in situations where loss of lean body mass may not be apparent because of overall body weight maintenance due to edema. Triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle area, and subscapular skinfold thickness are common anthropometric measurements. Caliper skinfold measurements and circumference measurements can be compared to reference tables based on the age and sex of the child to determine relative fat and lean body mass composition.¹¹⁸ Typically, values less than the 5th percentile for sex and age are consistent with acute malnutrition.¹¹⁹ A triceps skinfold thickness greater than the 95th percentile in a child with a BMI-for-age above the 85th percentile can confirm that the child's BMI is elevated due to excessive fat rather than substantial lean body mass or frame size.¹¹⁶ Skinfold and circumference measurements can be used to track changes in

an individual patient over time when collected serially (every 3–6 months). The methodology for performing anthropometrics is described elsewhere.¹²⁰

- (2) Bioelectrical impedance analysis can be used in older children to determine total body composition. This is a quick, noninvasive tool and also can be used to track changes over time. However, factors such as fluid status may affect the validity of results. This tool has been validated in well-nourished and malnourished children.¹²¹
 - (3) A physical exam should involve assessment of muscle or fat depletion, fluid status, gastrointestinal symptoms, and pain. Edema may manifest as a clinical symptom of hypoalbuminemia, in which case aggressive protein repletion measures are often indicated. In some cases, severe hypoalbuminemia is due to protein losses via gut or capillary leakage, and increases in visceral protein levels may be limited by the rate of synthesis by the liver rather than by protein consumption. The liver may not be able to synthesize albumin at a rate that surpasses loss. Knowledge of the patient's hydration status is also important for accurate interpretation of body weight. Pain assessment is included in the physical evaluation as a factor that may reduce a child's appetite or capacity to eat.
 - (4) Functional assessment should determine the patient's ability to perform activities of daily living as compared to pretreatment capacity as well as to developmental stage. Having enough strength and energy to play is important psychosocially in children and should be considered as part of the functional assessment.
4. Biochemical and laboratory tests
- a) As in adults, serum albumin and prealbumin¹²² can be useful tools to assess the visceral protein status of children. A Prealbumin in Nutritional Care Consensus Group¹²³ developed the following levels of nutritional risk based on prealbumin levels: Less than 5 mg/dL indicates a poor prognosis; 5.0 to 10.9 mg/dL indicates significant risk and calls for aggressive nutrition support; and 11.0 to 15.0 mg/dL suggests increased risk with recommendation for close monitoring. When using this scale, bear in mind that each medical institution has its own normal standards for laboratory values based on analytical methods used, so that the values listed above may not exactly reflect the values in a given institution. In addition to indicating current nutritional status, prealbumin, with its rapid 2-day turnover rate, is useful in early assessment of the effectiveness of nutrition repletion regimens. A 1 mg/dL increase in prealbumin per day indicates adequate nutrition support in malnourished patients.^{123,124} Increasing trends in prealbumin suggest that at least 65% of energy and protein needs are being met.¹²³ However, numerous non nutrition factors may affect interpretations of both albumin and prealbumin levels. Infection, extremes in hydration, liver synthetic function, protein-losing enteropathies, corticosteroid

therapy, surgery, and impaired renal function may alter albumin and/or prealbumin levels.¹²⁵

- b) Absolute neutrophil count is important to monitor, as neutropenic patients must be especially careful to avoid food-borne pathogens.
- c) Electrolyte and mineral wasting can be due to medications used in cancer treatment and management or to side effects of cancer therapy, such as diarrhea and vomiting. Serum potassium, magnesium, calcium, and phosphorous levels should be monitored regularly and replaced, if low. Note that total serum calcium and magnesium levels underestimate true status when albumin is low. Serum ionized calcium and magnesium levels more accurately reflect true calcium and magnesium status when albumin is decreased.
- d) Glucose and lipids may be elevated with some commonly used medications, such as corticosteroids, and should be monitored regularly.

5. QOL

- a) A poor QOL can affect a patient's nutritional status. Children may be physically and socially isolated due to infection or risk of infection. Long-term isolation may cause them to become bored, anxious, and depressed, leading to poor intake. Recreation therapists, psychiatrists/psychologists, and spiritual advisors can be consulted to help in these situations.
- b) Conversely, poor nutrition may lead to a poor QOL. Undernourished patients are likely to feel fatigued and weak, which can affect their ability to play and enjoy life.
- c) Poor intake by the child may also affect the parent's QOL. Parents often equate good eating with good health, so poor intake can cause them much distress.
- d) QOL is an important issue to be assessed periodically as children undergo therapy or to evaluate when assessing the effectiveness of a palliative treatment in children who are at the end of life, but QOL is difficult to measure in children.¹²⁶ First, children pass through numerous developmental stages of physical, emotional, cognitive, and social functioning, meaning that no single measure can appropriately assess children of all ages.¹²⁷ Assessment tools must consider the developmental stage of the child being evaluated in terms of the child's ability to use the tool (Likert scale vs yes/no options) as well as the tool's ability to address the factors that may affect the child's QOL (fear of pain vs concern about appearance).¹²⁶ Longitudinal assessment of children may require use of different tools as they develop. Second, a proxy respondent is necessary for assessment of very young children who are unable to express their feelings in the structured manner of an assessment tool. However, proxy respondents may not accurately represent the child's perceptions or priorities. In a systematic review of studies examining proxy reports of QOL, children with chronic illness and their parents were found to have good agreement for domains reflecting physical activity, physical symptoms, and somatic distress but poor agreement for domains reflecting social and emotional issues.¹²⁸ Parents have been found to rate their children's

functioning in certain categories and overall QOL as lower than the children's ratings, possibly due to differences in perception of the situation.^{128,129} For example, parents may be considering long-term outcomes such as future fertility or compromised education, while a young child may be concerned with immediate consequences, such as missing friends.¹²⁹ This is not to say, however, that parental concerns are not important.

- e) Specific QOL assessment tools for use during cancer therapy in children include the Miami Pediatric Quality of Life Questionnaire,¹³⁰ the Pediatric Oncology Quality of Life Scale,¹³¹ and the Behavioral, Affective, and Somatic Experiences Scale.¹³² A common modular instrument (which combines generic as well as disease-specific scales) is the Pediatric Quality of Life Inventory.¹³³ Tools used to assess QOL of childhood cancer survivors include the Minneapolis-Manchester Quality of Life Instruments for both youth and adolescents.^{134,135} Other tools have also been used to measure the QOL of pediatric cancer patients after treatment.¹³⁶⁻¹⁴⁰

IV. Criteria for Intervention and Goals of Therapy

A. Nutritional considerations for specific cancer treatments

1. Nutritional considerations for chemotherapy
 - a) Nausea and vomiting
 - b) Mucositis
 - c) Constipation
 - d) Diarrhea
 - e) Neutropenia
 - f) Changes in taste
 - g) Loss of appetite
2. Nutritional considerations for radiation therapy
 - a) Mucositis
 - b) Diarrhea, nausea, vomiting if the GI tract is in the radiation field
 - c) Changes in taste
 - d) Dry mouth
 - e) Fatigue
 - f) Endocrinological effects (adverse endocrinological effects of cranial radiation have been reviewed)¹⁴¹⁻¹⁴³
3. Nutritional considerations for immunotherapy
 - a) Nausea, vomiting
 - b) Mucositis
 - c) Diarrhea
 - d) Changes in taste
 - e) Dry mouth
4. Nutritional considerations for surgery
 - a) One week before an operative procedure, patients should stop all herbal products or supplements (eg, borage or fish oil, vitamin E) that may affect blood thinning, unless otherwise advised by their physician.¹⁴⁴
 - b) Nutritional considerations vary depending on type and degree of surgical intervention. Potential issues depend on the patient's mechanical and physical impairment and ability to ingest, digest, and absorb adequate nutrients.

- c) The patient's perioperative and long-term nutritional needs should be taken into account and planned for from the onset.
- B. Adults
- 1. Criteria for intervention¹⁴⁵
 - a) Preoperative tube-feeding or PN support provided for at least 7 to 14 days preoperatively may benefit moderately and severely malnourished cancer patients, but the potential benefits of nutrition support should be appraised against the inherent risks of nutrition support and the delay in surgery.
 - b) Specialized nutrition support should not be used routinely in well-nourished or mildly malnourished patients receiving surgery, chemotherapy, or radiation therapy when reasonable oral intake is anticipated.
 - c) Specialized nutrition support is indicated in selected patients who are receiving cancer treatment and who are either severely malnourished or unable to consume and/or absorb an adequate oral diet for an extended period of time.
 - d) Palliative specialized nutrition support is seldom indicated in patients with terminal cancer that is unresponsive to conventional therapy.
 - 2. Goals
 - a) Maintenance of nutritional status or reversal of protein-calorie malnutrition
 - (1) The caloric needs of cancer patients depend on the tumor type and other medical factors such as fever or infection. Caloric needs are not static and can vary with medical changes throughout the treatment course.
 - (2) Nutrition support should provide calories sufficient to meet a cancer patient's needs by minimizing body catabolism without overfeeding. A variety of empiric formulas are available to estimate energy needs. See Chapter 2. However, ongoing monitoring is essential to ensure that the caloric estimate is appropriate. Providing most cancer patients with 25 to 35 kcal/kg per day is a reasonable estimate.¹⁰⁶ Although not routine and felt by some to be controversial, the use of indirect calorimetry to measure resting energy expenditure in the clinical setting may be of value.
 - (3) A cancer patient's degree of catabolism will dictate protein requirements. Generally, an intake of 1.2 to 1.5 g/kg/d protein is adequate,¹⁰⁶ although hypermetabolic or extremely wasted patients may have higher requirements.
 - (4) Although visceral proteins are influenced by non nutritional factors, monitoring them may provide an indication of a patient's protein status, and a nitrogen balance evaluation may be appropriate in selected cases.
 - b) Decreased morbidity, improved survival, and improved QOL
 - (1) There is no definitive evidence that specialized nutrition support in cancer patients increases treatment tolerance, decreases treatment complications, or extends survival; therefore, the effects of nutrition support in this regard remain controversial.^{146,147}

- (2) Provision of nutrition support to selected patients with cancer may improve QOL. As expectations of quality vary with individual patients, decision making requires multidisciplinary assessment and should be addressed on a case-by-case basis.
- (3) Use of home PN in a group of appropriately selected cancer patients resulted in improved performance status and reported improved QOL (judged as returning to work or previous activity level).⁹⁸
- (4) There is no conclusive evidence in humans that feeding cancer patients to replete the host will stimulate further tumor growth.^{148,149}
- (5) In head and neck cancer, preexisting poor intake commonly results from alcohol and nicotine abuse and difficulty swallowing due to obstruction from tumor. Multiple treatment modalities — such as surgery, radiation, and chemotherapy — may be employed and may affect diet tolerance and adequacy of intake. Multiple studies show that early enteral feeding with percutaneous endoscopic gastrostomy (PEG) or surgical jejunostomy before or during cancer treatment can minimize weight loss, dehydration, and interruptions in treatment and can limit hospital admissions.^{147,150–153} Prospective, randomized clinical trials (PRCTs) have failed to show improved survival in patients receiving parenteral or tube-feeding support with their cancer treatment.¹⁵⁴
- (6) Some nutrients, such as glutamine, arginine, essential fatty acids, and nucleic acids, were evaluated as having specific biologic effects on the tumor and the host. The potential benefits of these specific nutrients, individually or combined, in enhancing immune function, lessening the inflammatory response, and enabling recovery from surgery are inconclusive.^{145,151,155}

C. Pediatrics

1. Criteria for intervention

- a) Nutritional status is related to relapse rates and survival as well as to tolerance of treatment in pediatric oncology. This relationship varies based on the type and stage of cancer.

- (1) The cancer relapse rate has been shown to be increased in patients who are malnourished at diagnosis or referral in ALL^{156,157} and in solid tumors.¹⁵⁸ Five-year disease-free survival was significantly greater for patients with ALL who were well nourished compared to patients with ALL who were malnourished at diagnosis.¹⁵⁷ The time to relapse or death was significantly longer in patients with Stage IV neuroblastoma who were well nourished at diagnosis compared to those who were malnourished at diagnosis and received PN.¹⁵⁹ However, nutritional status was not related to survival in these patients, in a group of pediatric patients in El Salvador and Brazil that included various types of cancer,^{159,160} or in two large retrospective studies in pediatric

- ALL.^{161,162} Conversely, patients with pediatric lymphoma and solid tumor with localized disease and with good nutritional status at time of referral had significantly improved likelihood of survival compared to patients with poor nutritional status at referral. This significance did not hold true for patients with regional and metastatic disease.¹⁵⁸
- (2) Tolerance to treatment and treatment delays varies with type of cancer. Patients with ALL and Wilms' tumor who were malnourished at diagnosis required a reduction in drug therapy compared to patients who were well nourished at diagnosis, owing to poor tolerance of drug therapy.^{9,157} Treatments were delayed in significantly more patients with Stage IV neuroblastoma who were malnourished at diagnosis or who had early decrease in nutritional status than in patients who were well nourished at diagnosis or who had early improvement in their nutritional status.¹⁵⁹
 - (3) Nutritional status may serve as a marker, rather than a cause, of a particular outcome in cancer patients. There is insufficient evidence to support the assertion that improvements in nutritional status will result in improved patient outcomes.
- b) Indications for nutrition support
- (1) Specialized nutrition support and dietary interventions must be implemented to support normal growth and development and to provide the energy needed in patients who cannot meet requirements via oral intake.⁹⁹
 - (2) Palliative specialized nutrition support in terminally ill children with cancer is rarely indicated.⁹⁹
 - (3) Newly diagnosed pediatric cancer patients tend to consume 90% or less of the recommended dietary allowance for calories but have adequate protein intake.^{12,163} However, disease progression plus side effects from therapy may result in decreased oral consumption and the need for nutrition support.¹⁶⁴
 - (4) A task force formed by the American Academy of Pediatrics developed criteria for nutrition intervention in pediatric cancer patients.⁸ Andrassy and Chwals¹⁶⁵ and Ollenschlager et al¹⁶⁶ slightly modified and contributed to the criteria, which include
 - (a) Weight loss of more than 5% of preillness body weight
 - (b) Weight less than 90% of ideal body weight (IBW) or weight-for-height less than 10th percentile on NCHS growth curves.¹⁶⁷ The NCHS growth chart showing BMI-for-age can be used for older children.
 - (c) Serum albumin less than 3.2 mg/dL (barring acute metabolic stress within the last 14 days)
 - (d) Triceps skinfold less than the 5th percentile for age and sex

- (e) Decrease of weight- and/or height-for-age across 2 percentile increments on the NCHS growth curves
 - (f) Oral intake less than 70% of that needed for growth for more than 5 days in well-nourished patients
 - (g) Expected GI dysfunction for more than 5 days in well-nourished patients
 - (h) High risk for malnutrition based on type of tumor and cancer therapy
 - (i) Delayed cutaneous hypersensitivity anergy in children over 2 years old prior to treatment
- (5) Oral intake
- (a) Numerous studies show that pediatric cancer patients tend to experience significant weight loss and have decreases in arm muscle area and triceps skinfold measurements on an oral diet.^{10,168,169}
 - (b) Patients who experienced intervention by a registered dietitian while on an oral diet had significantly more weeks at a stable weight than did patients who did not receive intensive nutritional intervention.¹⁶⁶
 - (c) Counseling must be individualized to the type and stage of cancer, the degree of disease, symptoms, and the type and stage of treatment.
- (6) Enteral nutrition support
- (a) Indications for enteral support in children are similar to those in adults. In addition, children who fail to gain weight should be considered for nutrition support.
 - (b) Studies reveal that pediatric cancer patients significantly increase their body weight after 1, 3, and 4 months of tube feeding.^{168,170,171}
 - (c) In malnourished cancer patients, 60% of the patients reached 95% of their IBW in a mean of 4.9 months of tube feeding, and the remaining patients gained at least 7% of their IBW in that time.¹⁷²
 - (d) Lack of randomized studies has hampered the ability to determine the effectiveness of enteral nutrition support in pediatric cancer patients.
- (7) PN support
- (a) Indications for PN in children are similar to those in adults.
 - (b) Numerous PRCTs have examined the effectiveness of PN at nutritionally repleting pediatric cancer patients and improving their clinical outcome.
 - (c) PRCTs in primarily well-nourished cancer patients demonstrate that PN given for 17 to 104 days is able to significantly increase weight and nitrogen balance and results in increases in arm muscle area

and triceps skinfold measurements. In addition, PN promotes maintenance of total leukocyte and absolute granulocyte counts compared to those of control groups.^{169,173,174}

- (d) Other PRCTs in primarily well-nourished patients who were given PN through the first cycle of chemotherapy until recovery from myelosuppression showed no difference in survival rates, tumor response, or duration of myelosuppression and actually showed shorter remission in patients with parenteral nutrition (PN) than in controls.^{174,175}
- (e) Nonrandomized studies that administered PN for approximately 4 weeks showed a significant increase from baseline in arm muscle area, triceps skinfold measurements, subscapular skinfold measurements, and percentage of diagnosis weight. Serum transferrin, albumin, prealbumin, and retinol-binding protein levels were increased. In addition, there was a significant decrease in treatment delays compared to those in nourished patients receiving enteral nutrition.^{10,176-179}
- (f) Overall, PN seems to improve nutritional status but not clinical outcome.
- (g) The duration of PN provision necessary to achieve nutritional repletion is difficult to predict. Nine to 14 days of PN resulted in a slight weight gain and a significant increase in serum transferrin levels, but only 9 of 15 subjects repleted their weight, whereas all but 1 subject repleted their weight on 28 days of PN.¹⁰
- (h) The beneficial nutritional effects of PN fail to persist once PN is discontinued if the patient's clinical situation has not improved.¹⁷³
- (i) Comparing results from different studies is difficult because of variability in the type and stage of cancer, the type of therapy, the stage of treatment, and nutritional status. Furthermore, small sample sizes may prevent detection of differences between groups.

2. Goals

- a) Growth and/or maintenance of nutritional status or reversal of protein-calorie malnutrition
 - (1) Body weight should be greater than IBW.⁸
 - (2) Arm fat area should be greater than the 10th percentile for age and sex.⁸
 - (3) Serum albumin should be greater than 3.2 mg/dL.⁸
 - (4) Calorie and protein needs vary with age, disease state, type of treatment, presence of fever, infection, wound status, activity level, and individual needs. See Chapter 2 for help with determining calorie and protein needs.

(5) Fluid balance is important. See Chapter 2 for help with determining fluid requirements.

(6) Vitamin and mineral deficiency should be prevented. Monitor mineral and electrolyte levels regularly and other vitamins and minerals when deficiency or toxicity is suspected. For example, vitamin K levels may decrease with long-term antibiotic therapy, and copper and manganese levels may exceed normal levels when provided in TPN during cholestasis.^{180,181}

b) Decreased morbidity, improved survival, and improved QOL

(1) Improvement in nutritional status has not clearly been shown to increase the survival or treatment tolerance in pediatric oncology patients.

(2) Improvement in nutritional status can theoretically enhance QOL by increasing energy level and wound healing and reducing risk of infection. However, the inconvenience of some nutrition interventions (eg, time-consuming tube-feeding regimen that interferes with play time) may outweigh the potential benefits. The pros and cons should be presented to the child and family, allowing them to make the final decision.

V. Nutritional Management

A. Management for specific cancer treatments

1. Pharmacological

a) Commonly used antiemetics include¹⁸²

(1) Serotonin-receptor antagonists (eg, ondansetron, granisetron)

(2) Phenothiazines (eg, promethazine, chlorpromethazine)

(3) Antihistamines (eg, diphenhydramine, hydroxyzine)

(4) Benzodiazepines (eg, lorazepam)

(5) Steroids (eg, dexamethasone)

(6) Cannabinoids

b) Prevention/treatment of mucositis¹⁸²

(1) Salt, soda rinse

(2) Chlorhexidine

(3) Mouthwash consisting of diphenhydramine, antacid, and lidocaine

c) Bowel medications

(1) Stool softeners (docusate)

(2) Bulk laxatives (psyllium, calcium polycarbophil, methylcellulose)

(3) Lubricants (mineral oil)

(4) Osmotic agents (glycerin, lactulose)

(5) Saline laxatives (magnesium salts, sodium biphosphate/phosphate)

(6) Stimulants (bisacodyl, cascara sagrada, senna)

(7) Antidiarrheals (bismuth subsalicylate, difenoxin, kaolin/pectin, loperamide, opium tincture)

2. Nutritional

a) Nausea and vomiting

(1) Consume small, frequent meals or snacks.

(2) Eat slowly.

- (3) Choose cold, nonodorous foods.
 - (4) Select light, starchy, low-fat foods.
 - (5) Avoid very sweet or spicy foods.
 - (6) Save favorite foods for periods without nausea or vomiting.
 - (7) Rest and sit up after eating.
 - (8) Refrain from eating prior to therapies that cause nausea or vomiting.
- b) Mucositis
- (1) Choose bland, cold, soft foods.
 - (2) Moisten dry foods.
 - (3) Cut food into small pieces or puree.
 - (4) Use a straw with fluids.
 - (5) Coordinate eating with analgesic use.
- c) Constipation
- (1) Obtain adequate fluid intake.
 - (2) Increase insoluble fiber consumption.
 - (3) Drink hot beverages prior to the usual time of bowel movements.
 - (4) Incorporate physical activity as permitted by the medical team.
- d) Diarrhea
- (1) Consume extra fluid and potassium-rich food sources.
 - (2) Increase intake of soluble fiber and reduce insoluble fiber consumption.
 - (3) Avoid lactose and sugar alcohols.
 - (4) Select low-fat foods.
 - (5) Consume foods and beverages at room temperature.
- e) Neutropenia
- (1) Choose foods less likely to contain a high bacterial load.
 - (a) Wash raw fruits and vegetables well and reject any that have indications of damage or spoilage.
 - (b) Avoid unpasteurized products and ripened, soft cheeses.
 - (2) Follow safe handling, storage, thawing, and cooking procedures for meat, fish, poultry, and eggs.
 - (a) Keep raw meat, fish, and poultry separated from other foods to prevent cross-contamination.
 - (b) Store frozen foods at 0°F and refrigerated foods at 35 to 40°F.
 - (c) Thaw foods in the refrigerator, in the microwave, or in cold water that is changed every 30 minutes.
 - (d) Cook meat (including deli meats), fish, poultry, and eggs until well done (160°F).
 - (e) Do not leave perishable foods unrefrigerated for more than 2 hours. Dispose of leftovers after 2 to 3 days.
- f) Taste changes. Choose flavorful foods as tolerated, such as sour, seasoned, and spicy foods.
- g) Loss of appetite
- (1) Consume small, frequent meals.
 - (2) Save beverages for the end of meals.

- (3) Give priority to high-calorie and protein- and nutrient-dense foods.
 - (4) Do not force children to eat if they refuse.
 - h) Dry mouth
 - (1) Select sweet or sour foods.
 - (2) Moisten or puree dry foods.
 - (3) Sip water frequently.
 - i) Fatigue
 - (1) Consume small, frequent meals.
 - (2) Choose high-calorie and protein- and nutrient-dense foods.
- 3. Complementary and alternative approaches
 - a) Although gaps still exist, research is growing that indicates that complementary and alternative medicine (CAM) therapies can be effectively integrated into conventional medicine. Current evidence indicates that CAM usage is more effective in relieving cancer-related symptoms than in slowing disease progression.¹⁸³
 - b) CAM therapies commonly used by cancer patients that can be recommended for use¹⁸³ include acupuncture for chemotherapy-related nausea and vomiting or for pain, massage (except deep tissue or forceful) for anxiety or pain, moderate exercise to minimize fatigue, psychological and mind-body techniques (eg support groups, relaxation training, imagery), reduction of animal and saturated fat, and addition of soy in the diet of well-nourished men with prostate cancer.
 - c) Some CAM therapies should be discouraged in cancer patients.¹⁸³ These include very restrictive diets in patients with poor nutritional status; antioxidants in patients undergoing radiation or chemotherapy; supplements with anticoagulant effects in patients with thrombocytopenia, patients undergoing anticoagulation therapy, and postoperatively; acupuncture in patients with thrombocytopenia and anticoagulation therapy; and high-dose vitamin A and vitamin C in all cancer patients.
 - d) Any CAM therapy should be discouraged if any of the following apply:
 - (1) It delays conventional treatment.
 - (2) It has not been scientifically proven to be efficacious.
 - (3) It is provided by an unlicensed practitioner.
 - (4) It requires injection of substances not approved by the US Food and Drug Administration.¹⁸³

B. Adults

- 1. Special aspects of diet and nutritional supplements
 - a) Aggressive strategies to optimize oral intake and tolerance should be instituted early, especially for patients with preexisting nutritional problems. A patient's calorie and protein needs should be determined, diet strategies and oral supplements should be instituted, unnecessary diet restrictions should be eliminated, and eating times should be planned to be separated from treatment sessions.⁹⁸
 - b) Physiological and mechanical considerations of the disease and/or treatment may necessitate an alteration in the cancer patient's diet.¹⁸⁴ These considerations include the following:

- (1) Multiple feedings and postgastrectomy diet after gastric resection
 - (2) A soft diet for esophageal strictures
 - (3) A low-fat diet with or without enzyme supplementation for improved absorption in patients with pancreatic insufficiency
 - (4) Low fiber and lactose for radiation enteritis
- c) Oral supplements are a valuable addition to the diets of cancer patients. The use of oral supplements resulted in significantly increased protein and calorie intake without reducing foods consumed in a group of cancer patients counseled to use nutrition supplements between meals and at bedtime.¹⁸⁵ A limitation of oral supplementation use is taste fatigue; therefore, ongoing evaluation of acceptance is necessary, as are plans to provide varied alternatives for patients with anticipated long-term needs.
- d) There is evidence from animal studies that polyunsaturated fatty acids can promote cell growth by stimulating cell proliferation and by inhibiting apoptosis. Fish oil, on the other hand, can reduce the tumor growth rate and decrease host body weight loss in animals. In humans, a small, pilot trial of 20 patients with pancreatic cancer was conducted in which patients were given an eicosapentaenoic acid (EPA)-enriched supplemented oral diet.¹⁸⁶ Cachexia was reversed, and body weight was increased at 3 and 7 weeks. However, these results could not be replicated in a follow-up study of 200 patients with pancreatic cancer, possibly because several patients in the control group were taking EPA.¹⁸⁷
- e) Cancer patients can benefit from nutrition counseling not only before and during treatment but also later in their course. Cancer survivors are interested in making lifestyle changes to improve their diet and physical activity level. According to a survey, approximately 66% of survivors reported making lifestyle changes, 40% made one or more dietary changes, 21% started a new physical activity, and 48% started taking dietary supplements.¹⁸⁸
- f) Information on food safety issues should be incorporated into the nutrition education provided to neutropenic patients.

2. Special aspects of enteral nutrition

- a) Indications and goals
- (1) Aggressive nutritional support with enteral nutrition should be considered in selected instances in cancer patients who are unable to attain adequate oral intake. Patients with small-bowel resections and patients with mucosal injury from chemotherapy or radiation who are unable to ingest and/or digest nutrients may benefit from enteral feeding. Critically ill cancer patients may also benefit from enteral nutrition.¹⁵⁰
 - (2) The aim of enteral feeding is to meet macronutrient, micronutrient, and fluid needs with acceptable GI tolerance.
 - (3) Cycled and intermittent feedings may be well tolerated, allow patients more mobility, and encourage some oral intake. The ultimate goal is to transition to an oral diet as soon as the patient is able to attain adequate intake by mouth.

- b) Monitoring
 - (1) Cancer patients should be monitored for aspiration risk and GI tolerance. Preexisting treatment-related side effects, such as nausea or diarrhea, may be exacerbated during enteral feeds. In postoperative patients, ileus may preclude tolerance; and in critically ill patients who are receiving mechanical ventilation, poor perfusion may limit ability to maintain enteral feeds.
 - (2) Nasoenteric feeding tubes may be contraindicated in patients with severe thrombocytopenia, significant mucositis, or recent extensive neck resection.
 - (3) Immune-suppressed patients should be educated regarding careful tube-feeding technique to minimize the risk of feeding-related infection.
- 3. Special aspects of PN
 - a) Indications and goals
 - (1) PN is recommended in appropriately chosen cancer patients who need aggressive nutrition support when tube feeding has been unsuccessful or when use of the GI tract is not appropriate (eg, obstruction, high-output fistula).
 - (2) In cachectic cancer patients, given the metabolic alterations from advanced or untreated disease, the goal of nutrition support may be to minimize wasting rather than to nutritionally replete the patient.
 - b) Monitoring (see Chapter 8 for PN monitoring)
- 4. CAM aspects. Cancer patients may use a variety of CAM therapies in conjunction with or as a substitute for conventional treatment.¹⁸⁹ Many cancer patients are motivated to seek CAM therapies as a means of self-healing and of maintaining optimism when faced with the uncertainty of their disease.¹⁹⁰ Patients should be questioned about possible use of CAM therapies throughout treatment. Clinicians need to communicate openly and without judgment so patients feel comfortable disclosing CAM usage. Reputable and up-to-date Web sites and resources are available, so clinicians have access to reliable information describing the growing number of CAM therapies and detailing some dangerous interactions between these therapies and allopathic medicines.
- 5. Ethical issues
 - a) The goals of nutritional care in the framework of cancer treatment should be discussed with patients and their caregivers proactively in an open, straightforward, supportive manner. Patients should recognize the short- and long-term nutritional consequences of their treatments. For example, certain GI surgeries may necessitate long-term nutrition support or special diet modifications. Radiation treatment may cause lasting mucosal damage that affects diet tolerance. Patients requiring massive surgery and tube feeding, such as head and neck patients, have unique ethical issues related to disfigurement and dysfunction.^{33,98,191}
 - b) Transitioning a patient from active nutritional care to end-of-life care can present numerous challenges. The provision or withdrawal of nutrition support to patients with advanced disease is an issue that evokes medical, emotional, ethical, and legal considerations. Ethical

decision making should involve the multidisciplinary team, including the patient and caregivers, and should account for patient needs for autonomy, QOL, and a holistic structure. While there may be facility guidelines to help decision making, ultimately decisions need to be made on an individualized, case-by-case basis.¹⁹¹⁻¹⁹⁶

- c) Given that cancer patients are interested in CAM therapies, it is crucial for clinicians to recognize their ethical obligation when recommending, allowing, and guiding patients to these therapies and modalities. It is necessary to keep in mind the risk-to-benefit ratio when determining the appropriateness of any therapy, especially when there is limited or no scientific evidence to support it.¹⁹⁷

6. Patient and caregiver education

- a) Review all drug-nutrient interactions that apply to the patient.
- b) Educate the patient and family about the nutrition side effects commonly experienced with the cancer therapy being used and how to maximize calorie and protein intake when the patient faces these side effects.
- c) Teach the patient and caregivers the principles of the neutropenic diet and when it is to be followed.
- d) When implementing specialized nutrition support, help the patient and family to understand the reason it is being used, how the nutrients are being delivered, and the risks and benefits associated with the feeding method.
- e) Share the known effects of the CAMs being used with the patient and family, being sure to emphasize, when appropriate, the possible unknown effects due to lack of controlled studies.
- f) As long-term effects become known, patients with good outcomes to therapy should be educated on nutrition-related problems they may face later in life and the need for follow-up.

C. Pediatrics

1. Special aspects of diet and nutritional supplements

- a) When the appetite is at a preillness level, follow a well-balanced diet with a variety of foods according to the Food Guide Pyramid and Dietary Guidelines.
- b) If appetite or intake is compromised, make high-calorie, high-protein, and nutrient-dense foods a priority in the diet. A multivitamin/multimineral supplement may be indicated. However, extra iron should be avoided in patients who undergo numerous blood transfusions, and folate supplements should not be given with methotrexate therapy.
- c) Avoid favorite foods during periods of nausea and vomiting or therapies that lead to GI upset in order to minimize learned aversions to those foods.
- d) Oral supplements may be used to increase nutrient intake.
 - (1) Pediatric supplements are designed to meet the nutrient needs of children aged 1 to 10 years.
 - (2) Modular supplements (protein, carbohydrate, lipid) may be given to increase intake of a particular macronutrient.
 - (3) In cases of diarrhea or malabsorption, low osmolar nutritional supplements that contain hydrolyzed

carbohydrate and protein and a higher percentage of medium-chain triglycerides may be appropriate. These supplements should be flavored when taken orally.

- (4) The safety of fish oil supplementation in children has not been well studied.

2. Special aspects of enteral nutrition

a) Goals

- (1) Growth. Provide adequate calories, protein, and micronutrients to support growth along the NCHS growth curves.
- (2) Tolerance of feeds. The type of formula, concentration, and rate must be well tolerated by the patient to promote optimal absorption of the nutrients provided.
- (3) Minimization of the burden associated with tube feeding. Cycle the tube feeding, as tolerated, overnight, so that days are free for eating and playing, and so feedings are less often interrupted by medical procedures performed during the day. If the patient is unable to take anything by mouth, then provide boluses, as tolerated, to mimic meals during the day.
- (4) Prealbumin. Increase prealbumin by 1 mg/dL per day.^{123,124}

b) Monitoring

- (1) The most common complications associated with nasogastric tubes (NGTs) in pediatric cancer patients are tube dislodgment due to vomiting and feeding intolerances (diarrhea, nausea, vomiting).^{198,199} Diarrhea can often be controlled by adjusting the rate, strength, or osmolarity of feeds.^{172,198} Nausea and vomiting are well managed pharmacologically.¹⁹⁹ No episodes of epistaxis, sinusitis, or GI bleeding were reported,^{198,199} even in patients who had NGTs placed during thrombocytopenia and neutropenia.¹⁹⁸
- (2) Minor complications associated with PEGs and gastrostomy tubes (GTs) are common and primarily include insertion site inflammation.^{170,172,200-202} Other complications include feeding discharge from the GT site and GT occlusion.^{170,172,200-202}
- (3) Major complications included systemic infection and peritonitis. The rate of these ranged from 3% to 7%,^{170,200} 1.58 episodes/1000 days of GT use,¹⁷² or 4.5 episodes/1000 days of PEG use²⁰¹ in pediatric cancer patients.

3. Special aspects of PN

a) Goals

- (1) Growth. Adequate calories, protein, and micronutrients should be provided to support growth along the NCHS growth curves.
- (2) Catch-up growth. If the patient has protein calorie malnutrition, catch-up growth and repletion of lean body mass is the goal.
- (3) Prealbumin levels and trends. These can be monitored as one measure of the adequacy of energy and protein intake. Increases of 1 mg/dL per day indicate appropriate effectiveness of the nutrition regimen.^{123,124}

- (4) Replacement of any minerals and electrolytes that are being wasted, and provision of additional micronutrients at levels indicated by secondary conditions. For example, voluminous diarrhea may require the provision of additional zinc.
 - (5) Minimization of metabolic disturbances associated with PN. Glucose should be maintained at less than 180 mg/dL, and triglycerides should not exceed 300 mg/dL.
 - (6) Avoidance of refeeding syndrome by repleting mineral and electrolyte levels prior to starting PN and by initiating PN slowly in cases of severe malnutrition.
- b) Monitoring
- (1) Major complications with catheter insertion include hemothorax and infection at the insertion site, reported in one study to occur at a rate of 4.4%.²⁰³ A minor complication is hematoma, which reportedly occurred at a rate of 6.7%.²⁰³
 - (2) The most commonly reported complication with PN is sepsis. PN patients had significantly more days with fever; however, the catheter tip never cultured positively.²⁰⁴ Catheter-related sepsis has been reported to occur at a rate of 3%.²⁰⁵ This rate seems to vary depending on the nutritional status of the patient, with significantly more sepsis occurring in malnourished patients on PN than in well-nourished patients on PN.²⁰⁵
 - (3) Metabolic complications also can develop. They include hyperglycemia, hypophosphatemia, altered electrolytes, and increases in liver function tests and bilirubin levels.

4. CAM aspects. Reports from studies conducted in 1997–2000 in the United States suggest that anywhere from 47% to 84% of pediatric cancer patients have used at least one CAM since diagnosis.^{206–208} The most popular CAMs reported in these studies were faith healing, diet changes, and dietary or herbal supplements. Literature on the safety and efficacy of herbal supplements in children is lacking. In general, concerns include adverse interactions with standard medications and/or contamination of the herbal supplements with agents that can cause illness. Other CAMs include hypnosis and art therapy, the benefits of which have been reported in children.^{209–211} The International Society of Pediatric Oncology (SIOP) working committee on psychosocial issues in pediatric oncology developed guidelines for the use of nonconventional therapies in childhood cancer.²¹² The committee recommended that the health care team not automatically discourage the use of CAM therapies if they are deemed nonharmful, even if the patient or family benefits only psychologically.²¹² On the other hand, the health care team should attempt to maintain open communication with the patient and family about use of nonconventional therapies and should be vigilant about discouraging therapies that may be harmful, either physically or psychologically.²¹² The committee also warned that parents should be wary of therapies that have the following characteristics: the therapy is a secret that is known only by the promoter of the therapy; the therapy is touted as a cure for a wide range of cancers; the promoter attacks the medical community or claims to be persecuted by it; or treatment with the therapy requires a large sum of money to be paid up front.²¹²
5. Ethical issues
 - a) The same ethical considerations that exist for adult cancer patients exist for pediatric cancer patients.
 - b) The use of specialized nutrition support in terminally ill patients is controversial but should be considered if it may improve QOL.
 - c) Discontinuance of nutritional support can be the factor that transitions the parents/caregivers to acceptance of the end-of-life status of their child. Sensitivity to the significance of nutrition to the family and caregivers in this regard is very important.
6. Patient and caregiver education
 - a) The same topics should be covered with pediatric patients that are covered with adults (see Section V.B.6).
 - b) With increasing survival of pediatric cancer patients, the long-term effects of cancer treatments must be considered. Long-term gastrointestinal toxicity may be one adverse effect of cancer therapy in patients who survive into adolescence and adulthood.²¹³ Survivors of ALL tend to become overweight by the time they reach their final height,^{15,16} and decreased physical activity has been purported to be a likely cause.^{17,18} Survivors of brain tumors may also experience intractable weight gain if the hypothalamus is damaged during therapy.²¹⁴ Numerous long-term health-related issues secondary to radiotherapy and chemotherapy have been reviewed.^{140–142} As long-term effects continue to become known, patients with good outcomes to therapy should be educated on possible nutrition-related problems they may face later in life and the need for follow-up.

- VI. Patient and Caregiver Education Internet Resources
- A. Internet resources for the patient and caregiver
1. American Cancer Society, www.cancer.org
 - a) Contains information for patients, family and friends, survivors, health information seekers, American Cancer Society supporters, and professionals.
 - b) The health information section contains information about food and fitness, such as guidelines for eating well and being active, cooking smart, and taking control of one's weight; the power of fruits and vegetables; recipes; and nutrition during treatment.
 2. American Institute for Cancer Research, www.aicr.org
 - a) AICR is the cancer charity that fosters research on diet and cancer prevention and educates the public about the results.
 - b) The site contains information for survivors and health professionals.
 - c) The nutrition information includes eating healthier with the new American plate, a recipe corner, strategies for cooking for lower cancer risk, and special featured topics
 3. Cancer Centers, www.cancerlinksusa.com
 - a) This is the Web site of the Cancer Information Network. A newsletter is also available.
 - b) The site provides information about various types of cancers and discusses a wide array of topics.
 4. Cancer Research and Prevention Foundation, www.preventcancer.org
 - a) The mission of the Cancer Research and Prevention Foundation is the prevention and early detection of cancer through scientific research and education. It focuses on cancers that can be prevented through lifestyle changes or early detection followed by prompt treatment. These include breast, cervical, colorectal, lung, oral, prostate, skin, and testicular cancers.
 - b) The Web site spotlights topics and discusses cancer prevention in the news. There is information for patients and researchers.
 5. Diet Guidelines for Immunosuppressed Patients, www.fhrc.org/clinical/ltfu/
 - a) The Web site of the Fred Hutchinson Cancer Research Center in Seattle, Washington.
 - b) The site provides guidelines for adult and pediatric patients, including a patient and caregiver resource manual with guidelines on food and water safety, diet, adult nutrition, pediatric nutrition, and GI diets.
 6. National Cancer Institute, www.cancer.gov
 - a) A comprehensive site that includes information on cancer topics, clinical trials, cancer statistics, research and funding, and news.
 - b) Eating Hints for Cancer Patients, <http://www.cancer.gov/cancertopics/eatinghints>, provides nutritional advice for before treatment begins, advice on managing eating problems during treatment, special notes for caregivers, discussion of the posttreatment period, recipes, and more.
 7. OncoLink, <http://www.oncolink.upenn.edu/>
 - a) The Web site of the Abramson Cancer Center of the University of Pennsylvania.

- b) This site highlights daily and weekly cancer-related news and offers a newsletter. There are sections on types of cancer, treatment options, coping with cancer, clinical trials, cancer resources, and expert advice.
8. Oncology Nutrition Dietetic Practice Group, www.oncologynutrition.org
- a) The Oncology Nutrition Dietetic Practice Group is a dietetic practice group of the American Dietetic Association. Its mission is to provide direction and leadership for quality oncology nutrition practice through education and research. It is a national organization with over 1200 members.
 - b) The practice of oncology nutrition covers research, prevention, treatment, recovery, palliative care, and hospice. Oncology nutritionists provide dietetic professionals with resources and networking opportunities to deal with the complexities of oncology practice. Members work in clinical, public health, education, and research settings.

References

1. Weir HK, Thun MJ, Hankey BF, et al. Annual report to the nation on the status of cancer, 1975–2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst.* 2003;95(17):1276–1299.
2. Bozzetti F. Rationale and indications for preoperative feeding of malnourished surgical cancer patients. *Nutrition.* 2002;18(11–12):953–959.
3. Duguet A, Bachmann P, Lallemand Y, Blanc-Vincent MP. Summary report of the Standards, Options and Recommendations for malnutrition and nutritional assessment in patients with cancer (1999). *Br J Cancer.* 2003;89(suppl 1):S92–97.
4. Dewys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med.* 1980;69(4):491–497.
5. Gail MH, Eagan RT, Feld R, et al. Prognostic factors in patients with resected stage I non-small cell lung cancer. A report from the Lung Cancer Study Group. *Cancer.* 1984;54(9):1802–1813.
6. Surveillance, epidemiology, and end results cancer statistics review. Available at: http://seer.cancer.gov/csr/1975_2000/. Accessed August 21, 2004
7. Han-Markey T. Nutritional considerations in pediatric oncology. *Semin Oncol Nurs.* 2000;16(2):146–151.
8. Mauer AM, Burgess JB, Donaldson SS, et al. Special nutritional needs of children with malignancies: a review. *J Parenter Enteral Nutr.* 1990;14(3):315–324.
9. Lahorra JM, Ginn-Pease ME, King DR. The prognostic significance of basic anthropometric data in children with advanced solid tumors. *Nutr Cancer.* 1989;12(4):361–369.
10. Rickard KA, Grosfeld JL, Kirksey A, Ballantine TV, Baehner RL. Reversal of protein-energy malnutrition in children during treatment of advanced neoplastic disease. *Ann Surg.* 1979;190(6):771–781.
11. Carter P, Carr D, van Eys J, Coody D. Nutritional parameters in children with cancer. *J Am Diet Assoc.* 1983;82(6):616–622.
12. Smith DE, Stevens MC, Booth IW. Malnutrition at diagnosis of malignancy in childhood: common but mostly missed. *Eur J Pediatr.* 1991;150(5):318–322.
13. Attard-Montalto SP, Hadley J, Kingston JE, Eden OB, Saha V. Ongoing assessment of nutritional status in children with malignant disease. *Pediatr Hematol Oncol.* 1998;15(5):393–403.

14. Halton JM, Atkinson SA, Barr RD. Growth and body composition in response to chemotherapy in children with acute lymphoblastic leukemia. *Int J Cancer Suppl.* 1998;11:81–84.
15. Birkebaek NH, Clausen N. Height and weight pattern up to 20 years after treatment for acute lymphoblastic leukaemia. *Arch Dis Child.* 1998;79(2):161–164.
16. Didi M, Didcock E, Davies HA, Ogilvy-Stuart AL, Wales JK, Shalet SM. High incidence of obesity in young adults after treatment of acute lymphoblastic leukemia in childhood. *J Pediatr.* 1995;127(1):63–67.
17. Warner JT, Bell W, Webb DK, Gregory JW. Daily energy expenditure and physical activity in survivors of childhood malignancy. *Pediatr Res.* 1998;43(5):607–613.
18. Reilly JJ, Ventham JC, Ralston JM, Donaldson M, Gibson B. Reduced energy expenditure in preobese children treated for acute lymphoblastic leukemia. *Pediatr Res.* 1998;44(4):557–562.
19. Vaisman N, Stallings VA, Chan H, Weitzman SS, Clarke R, Pencharz PB. Effect of chemotherapy on the energy and protein metabolism of children near the end of treatment for acute lymphoblastic leukemia. *Am J Clin Nutr.* 1993;57(5):679–684.
20. Stallings VA, Vaisman N, Chan HS, Weitzman SS, Hahn E, Pencharz PB. Energy metabolism in children with newly diagnosed acute lymphoblastic leukemia. *Pediatr Res.* 1989;26(2):154–157.
21. Bond SA, Han AM, Wootton SA, Kohler JA. Energy intake and basal metabolic rate during maintenance chemotherapy. *Arch Dis Child.* 1992;67(2):229–232.
22. Delbecque-Boussard L, Gottrand F, Ategbo S, et al. Nutritional status of children with acute lymphoblastic leukemia: a longitudinal study. *Am J Clin Nutr.* 1997;65(1):95–100.
23. Tyc VL, Vallelunga L, Mahoney S, Smith BF, Mulhern RK. Nutritional and treatment-related characteristics of pediatric oncology patients referred or not referred for nutritional support. *Med Pediatr Oncol.* 1995;25(5):379–388.
24. Emery PW. Cachexia in experimental models. *Nutrition.* 1999;15(7–8):600–603.
25. Bruera E, Sweeney C. Cachexia and asthenia in cancer patients. *Lancet Oncol.* 2000;1:138–147.
26. Bloch A. Cancer. In: Matarese L, Gottschlich M, eds. *Contemporary Nutrition Support Practice.* 1st ed. Philadelphia: W.B. Saunders Company; 1998:475–495.
27. Argiles JM, Moore-Carrasco R, Fuster G, Busquets S, Lopez-Soriano FJ. Cancer cachexia: the molecular mechanisms. *Int J Biochem Cell Biol.* 2003;35(4):405–409.
28. Tisdale MJ. Cachexia in cancer patients. *Nat Rev Cancer.* 2002;2(11):862–871.
29. Laviano A, Meguid MM, Rossi-Fanelli F. Cancer anorexia: clinical implications, pathogenesis, and therapeutic strategies. *Lancet Oncol.* 2003;4(11):686–694.
30. Finley JP. Management of cancer cachexia. *AACN Clin Issues.* 2000;11(4):590–603.
31. Khanna C, the Perseus Foundation. Biotherapy of cancer. Available at: <http://www.perseusfoundation.org/page33.html>. Accessed August 24, 2004.
32. American Cancer Society. Infections in individuals with cancer. Available at: www.cancer.org/docroot/ETO/content/ETO_1_2X_Infections_in_Individuals_with_Cancer.asp. 2004. Accessed August 24, 2004.
33. Echenique M, Correia MI. Nutrition in advanced digestive cancer. *Curr Opin Clin Nutr Metab Care.* 2003;6(5):577–580.
34. Ripamonti C, Bruera E. Palliative management of malignant bowel obstruction. *Int J Gynecol Cancer.* 2002;12(2):135–143.
35. Lopez MJ, Robinson P, Madden T, Highbarger T. Nutritional support and prognosis in patients with head and neck cancer. *J Surg Oncol.* 1994;55(1):33–36.
36. Derogatis LR, Morrow GR, Fetting J, et al. The prevalence of psychiatric disorders among cancer patients. *JAMA.* 1983;249(6):751–757.

37. Ellison NM, Chevlen E, Still CD, Dubagunta S. Supportive care for patients with pancreatic adenocarcinoma: symptom control and nutrition. *Hematol Oncol Clin North Am.* 2002;16(1):105–121.
38. Bosaeus I, Daneryd P, Lundholm K. Dietary intake, resting energy expenditure, weight loss and survival in cancer patients. *J Nutr.* 2002;132(11 suppl):3465S–3466S.
39. Guirao X. Impact of the inflammatory reaction on intermediary metabolism and nutrition status. *Nutrition.* 2002;18(11–12):949–952.
40. Bosaeus I, Daneryd P, Svanberg E, Lundholm K. Dietary intake and resting energy expenditure in relation to weight loss in unselected cancer patients. *Int J Cancer.* 2001;93(3):380–383.
41. Herrmann V, Fuhrman MP, Borum P. Wasting diseases. In: Merritt R, ed. *The A.S.P.E.N. Nutrition Support Practice Manual.* Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 1998:11/11–11/15.
42. Hunter AM. Nutrition management of patients with neoplastic disease of the head and neck treated with radiation therapy. *Nutr Clin Pract.* 1996;11(4):157–169.
43. Chandra RK. Nutrition and the immune system from birth to old age. *Eur J Clin Nutr.* 2002;56(suppl 3):S73–76.
44. Marcos A, Nova E, Montero A. Changes in the immune system are conditioned by nutrition. *Eur J Clin Nutr.* 2003;57(suppl 1):S66–69.
45. Miller JS. Biology of natural killer cells in cancer and infection. *Cancer Invest.* 2002;20(3):405–419.
46. Dunlop RJ, Campbell CW. Cytokines and advanced cancer. *J Pain Symptom Manage.* 2000;20(3):214–232.
47. Argiles JM, Moore-Carrasco R, Busquets S, Lopez-Soriano FJ. Catabolic mediators as targets for cancer cachexia. *Drug Discov Today.* 2003;8(18):838–844.
48. Todorov P, Cariuk P, McDevitt T, Coles B, Fearon K, Tisdale M. Characterization of a cancer cachectic factor. *Nature.* 1996;379:739–742.
49. Yoneda T, Alsina M, Chavez J, Bonewald L, Nishimura R, Mundy G. Evidence that tumor necrosis factor plays a pathogenetic role in the paraneoplastic syndrome of cachexia, hypercalcaemia, and leucocytosis in a human tumor in nude mice. *J Clin Invest.* 1991;87:977–985.
50. Barber MD, Ross JA, Fearon KC. Cancer cachexia. *Surg Oncol.* 1999;8(3):133–141.
51. Plata-Salaman C. Central nervous system mechanisms contributing to the cachexia-anorexia syndrome. *Nutrition.* 2000;16(10):1009–1012.
52. Argiles JM, Lopez-Soriano FJ. New mediators in cancer cachexia. *Nestle Nutr Workshop Ser Clin Perform Programme.* 2000;4:147–162; discussion 163–165.
53. Argiles JM, Busquets S, Lopez-Soriano FJ. Cytokines in the pathogenesis of cancer cachexia. *Curr Opin Clin Nutr Metab Care.* 2003;6(4):401–406.
54. Yasumoto K, Mukaida N, Harada A, et al. Molecular analysis of the cytokine network involved in cachexia in colon 26 adenocarcinoma-bearing mice. *Cancer Res.* 1995;55(4):921–927.
55. Wang M, Forsberg N. Effects of ciliary neurotrophic factor (CNTF) on protein turnover in cultured muscle cells. *Cytokine.* 2000;12(1):41–48.
56. Matthys P, Heremans H, Opdenakker G, Billiau A. Anti-interferon-gamma antibody treatment, growth of Lewis lung tumours in mice and tumour-associated cachexia. *Eur J Cancer.* 1991;27(2):182–187.
57. Islam-Ali B, Khan S, Price SA, Tisdale MJ. Modulation of adipocyte G-protein expression in cancer cachexia by a lipid-mobilizing factor (LMF). *Br J Cancer.* 2001;85(5):758–763.
58. Strasser F, Bruera ED. Update on anorexia and cachexia. *Hematol Oncol Clin North Am.* 2002;16(3):589–617.

59. Watchorn TM, Waddell I, Dowidar N, Ross JA. Proteolysis-inducing factor regulates hepatic gene expression via the transcription factors NF-(kappa)B and STAT3. *FASEB J*. 2001;15(3):562–564.
60. Lorite MJ, Smith HJ, Arnold JA, Morris A, Thompson MG, Tisdale MJ. Activation of ATP-ubiquitin-dependent proteolysis in skeletal muscle in vivo and murine myoblasts in vitro by a proteolysis-inducing factor (PIF). *Br J Cancer*. 2001;85(2):297–302.
61. Mantovani G, Maccio A, Massa E, Madeddu C. Managing cancer-related anorexia/cachexia. *Drugs*. 2001;61(4):499–514.
62. Inui A. Cancer anorexia-cachexia syndrome: are neuropeptides the key? *Cancer Res*. 1999;59(18):4493–4501.
63. Sarraf P, Frederich RC, Turner EM, et al. Multiple cytokines and acute inflammation raise mouse leptin levels: potential role in inflammatory anorexia. *J Exp Med*. 1997;185(1):171–175.
64. Finck BN, Kelley KW, Dantzer R, Johnson RW. In vivo and in vitro evidence for the involvement of tumor necrosis factor-alpha in the induction of leptin by lipopolysaccharide. *Endocrinology*. 1998;139(5):2278–2283.
65. Chance WT, Sheriff S, Moore J, Peng F, Balasubramaniam A. Reciprocal changes in hypothalamic receptor binding and circulating leptin in anorectic tumor-bearing rats. *Brain Res*. 1998;803(1–2):27–33.
66. Jensen PB, Blume N, Mikkelsen JD, et al. Transplantable rat glucagonomas cause acute onset of severe anorexia and adipisia despite highly elevated NPY mRNA levels in the hypothalamic arcuate nucleus. *J Clin Invest*. 1998;101(2):503–510.
67. Wallace AM, Sattar N, McMillan DC. Effect of weight loss and the inflammatory response on leptin concentrations in gastrointestinal cancer patients. *Clin Cancer Res*. 1998;4(12):2977–2979.
68. Mantovani G, Maccio A, Mura L, et al. Serum levels of leptin and proinflammatory cytokines in patients with advanced-stage cancer at different sites. *J Mol Med*. 2000;78(10):554–561.
69. Klaus S. Adipose tissue as a regulator of energy balance. *Curr Drug Targets*. 2004;5(3):241–250.
70. Cravo ML, Gloria LM, Claro I. Metabolic responses to tumour disease and progression: tumour-host interaction. *Clin Nutr*. 2000;19(6):459–465.
71. Ovesen L, Allingstrup L, Hannibal J, Mortensen EL, Hansen OP. Effect of dietary counseling on food intake, body weight, response rate, survival, and quality of life in cancer patients undergoing chemotherapy: a prospective, randomized study. *J Clin Oncol*. 1993;11(10):2043–2049.
72. Heslin MJ, Brennan MF. Advances in perioperative nutrition: cancer. *World J Surg*. 2000;24(12):1477–1485.
73. Eden D, Edstrom S, Bennegard K, Schersten T, Lundholm K. Glucose flux in relation to energy expenditure in malnourished patients with and without cancer during periods of fasting and feeding. *Cancer Res*. 1984;44(4):1718–1724.
74. Burt ME, Aoki TT, Gorschboth CM, Brennan MF. Peripheral tissue metabolism in cancer-bearing man. *Ann Surg*. 1983;198(6):685–691.
75. Argiles JM, Busquets S, Lopez-Soriano FJ. Metabolic interrelationships between liver and skeletal muscle in pathological states. *Life Sci*. 2001;69(12):1345–1361.
76. Wigmore SJ, McMahon AJ, Sturgeon CM, Fearon KC. Acute-phase protein response, survival and tumour recurrence in patients with colorectal cancer. *Br J Surg*. 2001;88(2):255–260.
77. Fiorenza AM, Branchi A, Sommariva D. Serum lipoprotein profile in patients with cancer. A comparison with non-cancer subjects. *Int J Clin Lab Res*. 2000;30(3):141–145.
78. Halton JM, Nazir DJ, McQueen MJ, Barr RD. Blood lipid profiles in children with acute lymphoblastic leukemia. *Cancer*. 1998;83(2):379–384.

79. Shukla VK, Adukia TK, Singh SP, Mishra CP, Mishra RN. Micronutrients, antioxidants, and carcinoma of the gallbladder. *J Surg Oncol*. 2003;84(1):31–35.
80. Hronek M, Zadak Z, Solichova D, Jandik P, Melichar B. The association between specific nutritional antioxidants and manifestation of colorectal cancer. *Nutrition*. 2000;16(3):189–191.
81. Brown LM, Blot WJ, Schuman SH, et al. Environmental factors and high risk of esophageal cancer among men in coastal South Carolina. *J Natl Cancer Inst*. 1988;80(20):1620–1625.
82. Malvy DJ, Arnaud J, Burtschy B, et al. Antioxidant micronutrients and childhood malignancy during oncological treatment. *Med Pediatr Oncol*. 1997;29(3):213–217.
83. Yong LC, Brown CC, Schatzkin A, et al. Intake of vitamins E, C, and A and risk of lung cancer. The NHANES I epidemiologic followup study. First National Health and Nutrition Examination Survey. *Am J Epidemiol*. 1997;146(3):231–243.
84. Choi MA, Kim BS, Yu R. Serum antioxidative vitamin levels and lipid peroxidation in gastric carcinoma patients. *Cancer Lett*. 1999;136(1):89–93.
85. Woutersen RA, Appel MJ, Van Garderen-Hoetmer A. Modulation of pancreatic carcinogenesis by antioxidants. *Food Chem Toxicol*. 1999;37(9–10):981–984.
86. Gupta PC, Hebert JR, Bhonsle RB, Murti PR, Mehta H, Mehta FS. Influence of dietary factors on oral precancerous lesions in a population-based case-control study in Kerala, India. *Cancer*. 1999;85(9):1885–1893.
87. D'Avanzo B, Ron E, La Vecchia C, Francaschi S, Negri E, Zleglar R. Selected micronutrient intake and thyroid carcinoma risk. *Cancer*. 1997;79(11):2186–2192.
88. Kristal AR, Stanford JL, Cohen JH, Wicklund K, Patterson RE. Vitamin and mineral supplement use is associated with reduced risk of prostate cancer. *Cancer Epidemiol Biomarkers Prev*. 1999;8(10):887–892.
89. La Vecchia C, Braga C, Negri E, et al. Intake of selected micronutrients and risk of colorectal cancer. *Int J Cancer*. 1997;73(4):525–530.
90. Cunzhi H, Jiexian J, Xianwen Z, Jingang G, Shumin Z, Lili D. Serum and tissue levels of six trace elements and copper/zinc ratio in patients with cervical cancer and uterine myoma. *Biol Trace Elem Res*. 2003;94(2):113–122.
91. Huang YL, Sheu JY, Lin TH. Association between oxidative stress and changes of trace elements in patients with breast cancer. *Clin Biochem*. 1999;32(2):131–136.
92. Borella P, Bargellini A, Caselgrandi E, Piccinini L. Observations on the use of plasma, hair and tissue to evaluate trace element status in cancer. *J Trace Elem Med Biol*. 1997;11(3):162–165.
93. Yu MW, Horng IS, Hsu KH, Chiang YC, Liaw YF, Chen CJ. Plasma selenium levels and risk of hepatocellular carcinoma among men with chronic hepatitis virus infection. *Am J Epidemiol*. 1999;150(4):367–374.
94. Postovsky S, Arush MW, Diamond E, Elhasid R, Shoshani G, Shamir R. The prevalence of low selenium levels in newly diagnosed pediatric cancer patients. *Pediatr Hematol Oncol*. 2003;20(4):273–280.
95. Poo JL, Romero RR, Robles JA, et al. Diagnostic value of the copper/zinc ratio in digestive cancer: a case control study. *Arch Med Res*. 1997;28(2):259–263.
96. Ferrigno D, Buccheri G, Camilla T. Serum copper and zinc content in non-small cell lung cancer: abnormalities and clinical correlates. *Monaldi Arch Chest Dis*. 1999;54(3):204–208.
97. Cabanillas F. Metabolic abnormalities in lymphoma. *Clin Lymphoma*. 2002;3(suppl 1):S32–36.
98. Ottery F. Nutritional oncology: a proactive, integrated approach to the cancer patient. In: Shikora S, Blackburn G, eds. *Nutrition Support: Theory and Therapeutics*. New York, NY: Chapman and Hall; 1997:394–409.
99. Ferguson M. Patient-generated subjective global assessment. *Oncology (Huntingt)*. 2003;17(2 suppl 2):13–14; discussion 14–16.

100. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr.* 2002;56(8):779–785.
101. Shils ME. Principles of nutritional therapy. *Cancer.* 1979;43(5 suppl):2093–2102.
102. Whitman MM. The starving patient: supportive care for people with cancer. *Clin J Oncol Nurs.* 2000;4(3):121–125.
103. Karnofsky DA, Abelman WH, Craver LF, et al. The use of nitrogen mustards in the palliative treatment of carcinoma. *Cancer.* 1948;1:634–656.
104. Bloch A, Charuhas P. Cancer and cancer therapy. In: Gottschlich MM ed. *The Science and Practice of Nutrition Support: A Core-Based Curriculum 2001.* Dubuque, IA: American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), Kendall/Hunt Publishing; 2001:643–662.
105. Jeejeebhoy KN. Nutritional assessment. *Gastroenterol Clin North Am.* 1998;27(2):347–369.
106. Turk DC, Monarch ES, Williams AD. Cancer patients in pain: considerations for assessing the whole person. *Hematol Oncol Clin North Am.* 2002;16(3):511–525.
107. Robinson MK, Trujillo EB, Mogensen KM, Rounds J, McManus K, Jacobs DO. Improving nutritional screening of hospitalized patients: the role of prealbumin. *J Parenter Enteral Nutr.* 2003;27(6):389–395; quiz 439.
108. Capra S, Ferguson M, Ried K. Cancer: impact of nutrition intervention outcome — nutrition issues for patients. *Nutrition.* 2001;17(9):769–772.
109. Berger A, Baker K, Bolle J, Pereira D. Establishing a palliative care program in a research center: evolution of a model. *Cancer Invest.* 2003;21(2):313–320.
110. Ravasco P, Monteiro Grillo I, Marques Vidal P, Camilo M. Nutritional counselling vs supplements: A prospective randomised controlled trial in head-neck cancer patients undergoing radiotherapy. *Clin Nutr.* 2003;22(S1):S63–64.
111. Schimmer BP, Parker KL. Adrenocorticotrophic hormone; adrenocortical steroids and their synthetic analogs; inhibitors of the synthesis and actions of adrenocortical hormones. In: Hardman JG, Limbird LE, Molinoff PB, Ruddon TW, Goodman Gilman A, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics.* 9th ed. New York, NY: McGraw-Hill; 1996
112. Amin S, LaValley MP, Simms RW, Felson DT. The role of vitamin D in corticosteroid-induced osteoporosis: a meta-analytic approach. *Arthritis Rheum.* 1999;42(8):1740–1751.
113. *Physical Status: The Use and Interpretation of Anthropometry.* WHO Technical Support Series 854. Geneva, Switzerland: World Health Organization; 1995.
114. Corrales KM, Utter SL. Failure to thrive. In: Samour PQ, Helm KK, Lang CE, eds. *Handbook of Pediatric Nutrition.* 2nd ed. Boston, MA: Jones and Bartlett Publishers; 2004:395–412.
115. Waterlow JC. Classification and definition of protein-calorie malnutrition. *Br Med J.* 1972;3(826):566–569.
116. Barlow SE, Dietz WH. Obesity evaluation and treatment: Expert Committee recommendations. The Maternal and Child Health Bureau, Health Resources and Services Administration and the Department of Health and Human Services. *Pediatrics.* 1998;102(3):E29.
117. Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services: recommendations from an expert committee. The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services. *Am J Clin Nutr.* 1994;59(2):307–316.
118. Frisancho AR. *Anthropometric Standards for the Assessment of Growth and Nutritional Status.* Ann Arbor, MI: University of Michigan Press; 1990.
119. Motil KJ. Sensitive measures of nutritional status in children in hospital and in the field. *Int J Cancer Suppl.* 1998;11:2–9.

120. Lohman TG, Roche AF, Martorell R. *Anthropometric Standardization Reference Manual*. Champaign, IL: Human Kinetics Books; 1988.
121. Fjeld CR, Freundt-Thurne J, Schoeller DA. Total body water measured by 18-O dilution and bioelectrical impedance in well and malnourished children. *Pediatr Res*. 1990;27(1):98–102.
122. Elhasid R, Laor A, Lischinsky S, Postovsky S, Weyl Ben Arush M. Nutritional status of children with solid tumors. *Cancer*. 1999;86(1):119–125.
123. Measurement of visceral protein status in assessing protein and energy malnutrition: standard of care. Prealbumin in Nutritional Care Consensus Group. *Nutrition*. 1995;11(2):169–171.
124. Spiekerman AM. Nutritional assessment (protein nutriture). *Anal Chem*. 1995;67(12):429R–436R.
125. Beck FK, Rosenthal TC. Prealbumin: a marker for nutritional evaluation. *Am Fam Physician*. 2002;65(8):1575–1578.
126. Nathan PC, Furlong W, Barr RD. Challenges to the measurement of health-related quality of life in children receiving cancer therapy. *Pediatr Blood Cancer*. 2004;43(3):215–223.
127. Rosenbaum P, Cadman D, Kirpalani H. Pediatrics: assessing quality of life. In: Spilker B, ed. *Quality of Life Assessments in Clinical Trials*. New York, NY: Raven Press; 1990:205–215.
128. Eiser C, Morse R. Can parents rate their child's health-related quality of life? Results of a systematic review. *Qual Life Res*. 2001;10(4):347–357.
129. Vance YH, Morse RC, Jenney ME, Eiser C. Issues in measuring quality of life in childhood cancer: measures, proxies, and parental mental health. *J Child Psychol Psychiatry*. 2001;42(5):661–667.
130. Armstrong FD, Toledano SR, Miloslavich K, et al. The Miami Pediatric Quality of Life Questionnaire: Parent Scale. *Int J Cancer Suppl*. 1999;12:11–17.
131. Boggs SR, Durning P. The Pediatric Oncology Quality of Life Scale: development and validation of a disease-specific quality of life measure. In: Drotar D, ed. *Measuring Health-Related Quality of Life in Children and Adolescents: Implications for Research and Practice*. Mahwah, NJ: Lawrence Erlbaum Associates; 1998:187–202.
132. Phipps S, Hinds PS, Channell S, Bell GL. Measurement of behavioral, affective, and somatic responses to pediatric bone marrow transplantation: development of the BASES scale. *J Pediatr Oncol Nurs*. 1994;11(3):109–117; discussion 118–119.
133. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. *Cancer*. 2002;94(7):2090–2106.
134. Bhatia S, Jenney ME, Bogue MK, et al. The Minneapolis-Manchester Quality of Life Instrument: reliability and validity of the Adolescent Form. *J Clin Oncol*. 2002;20(24):4692–4698.
135. Bhatia S, Jenney ME, Wu E, et al. The Minneapolis-Manchester Quality of Life Instrument: reliability and validity of the Youth Form. *J Pediatr*. 2004;145(1):39–46.
136. Eiser C, Havermans T, Craft A, Kernahan J. Development of a measure to assess the perceived illness experience after treatment for cancer. *Arch Dis Child*. 1995;72(4):302–307.
137. Feeny D, Furlong W, Barr RD, Torrance GW, Rosenbaum P, Weitzman S. A comprehensive multiattribute system for classifying the health status of survivors of childhood cancer. *J Clin Oncol*. 1992;10(6):923–928.
138. Barr RD, Furlong W, Dawson S, et al. An assessment of global health status in survivors of acute lymphoblastic leukemia in childhood. *Am J Pediatr Hematol Oncol*. 1993;15(3):284–290.

139. Barr RD, Simpson T, Whitton A, Rush B, Furlong W, Feeny DH. Health-related quality of life in survivors of tumours of the central nervous system in childhood — a preference-based approach to measurement in a cross-sectional study. *Eur J Cancer*. 1999;35(2):248–255.
140. Barr RD, Chalmers D, De Pauw S, Furlong W, Weitzman S, Feeny D. Health-related quality of life in survivors of Wilms' tumor and advanced neuroblastoma: a cross-sectional study. *J Clin Oncol*. 2000;18(18):3280–3287.
141. Moshang T Jr, Grimberg A. The effects of irradiation and chemotherapy on growth. *Endocrinol Metab Clin North Am*. 1996;25(3):731–741.
142. DeLaat CA, Lampkin BC. Long-term survivors of childhood cancer: evaluation and identification of sequelae of treatment. *CA Cancer J Clin*. 1992;42(5):263–282.
143. Gleeson HK, Shalet SM. Endocrine complications of neoplastic diseases in children and adolescents. *Curr Opin Pediatr*. 2001;13(4):346–351.
144. Norred C. Hot topics in healthcare. Thomson American Health Consultants. Available at: http://www.ahcpub.com/ahc_root_html/hot/archive/atwh042001.html. Accessed August 24, 2004.
145. A.S.P.E.N. Board of Directors and The Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr*. 2002;26(1 suppl):83SA.
146. A.S.P.E.N. Board of Directors and The Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr*. 2002;26(1 suppl):82SA.
147. Barrera R. Nutritional support in cancer patients. *J Parenter Enteral Nutr*. 2002;26(5 suppl):S63–71.
148. Laviano A, Meguid MM. Nutritional issues in cancer management. *Nutrition*. 1996;12(5):358–371.
149. Archer SB, Burnett RJ, Fischer JE. Current uses and abuses of total parenteral nutrition. *Adv Surg*. 1996;29:165–189.
150. Flynn MB, Leighty FF. Preoperative outpatient nutritional support of patients with squamous cancer of the upper aerodigestive tract. *Am J Surg*. 1987;154(4):359–362.
151. Wong PW, Enriquez A, Barrera R. Nutritional support in critically ill patients with cancer. *Crit Care Clin*. 2001;17(3):743–767.
152. Fietkau R, Iro H, Sailer D, Sauer R. Percutaneous endoscopically guided gastrostomy in patients with head and neck cancer. *Recent Results Cancer Res*. 1991;121:269–282.
153. Nayel H, el-Ghoneimy E, el-Haddad S. Impact of nutritional supplementation on treatment delay and morbidity in patients with head and neck tumors treated with irradiation. *Nutrition*. 1992;8(1):13–18.
154. Klein S, Koretz RL. Nutrition support in patients with cancer: what do the data really show? *Nutr Clin Pract*. 1994;9(3):91–100.
155. Klein S, Kinney J, Jeejeebhoy K, et al. Nutrition support in clinical practice: review of published data and recommendations for future research directions. Summary of a conference sponsored by the National Institutes of Health, American Society for Parenteral and Enteral Nutrition, and American Society for Clinical Nutrition. *Am J Clin Nutr*. 1997;66(3):683–706.
156. Reilly JJ, Odame I, McColl JH, McAllister PJ, Gibson BE, Wharton BA. Does weight for height have prognostic significance in children with acute lymphoblastic leukemia? *Am J Pediatr Hematol Oncol*. 1994;16(3):225–230.
157. Lobato-Mendizabal E, Ruiz-Arguelles GJ, Marin-Lopez A. Leukaemia and nutrition, I: malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukaemia. *Leuk Res*. 1989;13(10):899–906.
158. Donaldson SS, Wesley MN, DeWys WD, Suskind RM, Jaffe N, vanEys J. A study of the nutritional status of pediatric cancer patients. *Am J Dis Child*. 1981;135(12):1107–1112.

159. Rickard KA, Detamore CM, Coates TD, et al. Effect of nutrition staging on treatment delays and outcome in Stage IV neuroblastoma. *Cancer*. 1983;52(4):587–598.
160. Pedrosa F, Bonilla M, Liu A, et al. Effect of malnutrition at the time of diagnosis on the survival of children treated for cancer in El Salvador and Northern Brazil. *J Pediatr Hematol Oncol*. 2000;22(6):502–505.
161. Weir J, Reilly JJ, McColl JH, Gibson BE. No evidence for an effect of nutritional status at diagnosis on prognosis in children with acute lymphoblastic leukemia. *J Pediatr Hematol Oncol*. 1998;20(6):534–538.
162. Ringwald-Smith K, Todd J, Liu A, Hancock M, Pui C-H. Nutritional status: potential impact on survival in children with acute lymphoblastic leukemia [abstract]. *J Am Diet Assoc*. 1998;98(suppl):A-107.
163. Carter P, Carr D, van Eys J, Ramirez I, Coody D, Taylor G. Energy and nutrient intake of children with cancer. *J Am Diet Assoc*. 1983;82(6):610–615.
164. Skolin I, Axelsson K, Ghannad P, Hernell O, Wahlin YB. Nutrient intake and weight development in children during chemotherapy for malignant disease. *Oral Oncol*. 1997;33(5):364–368.
165. Andrassy RJ, Chwals WJ. Nutritional support of the pediatric oncology patient. *Nutrition*. 1998;14(1):124–129.
166. Ollenschlager G, Thomas W, Konkol K, Diehl V, Roth E. Nutritional behaviour and quality of life during oncological polychemotherapy: results of a prospective study on the efficacy of oral nutrition therapy in patients with acute leukaemia. *Eur J Clin Invest*. 1992;22(8):546–553.
167. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data*. 2000(314):1–27.
168. Bakish J, Hargrave D, Tariq N, Laperriere N, Rutka JT, Bouffet E. Evaluation of dietetic intervention in children with medulloblastoma or supratentorial primitive neuroectodermal tumors. *Cancer*. 2003;98(5):1014–1020.
169. Hays DM, Merritt RJ, White L, Ashley J, Siegel SE. Effect of total parenteral nutrition on marrow recovery during induction therapy for acute nonlymphocytic leukemia in childhood. *Med Pediatr Oncol*. 1983;11(2):134–140.
170. Barron MA, Duncan DS, Green GJ, et al. Efficacy and safety of radiologically placed gastrostomy tubes in paediatric haematology/oncology patients. *Med Pediatr Oncol*. 2000;34(3):177–182.
171. den Broeder E, Lippens RJ, van't Hof MA, et al. Effects of naso-gastric tube feeding on the nutritional status of children with cancer. *Eur J Clin Nutr*. 1998;52(7):494–500.
172. Aquino VM, Smyrl CB, Hagg R, McHard KM, Prestridge L, Sandler ES. Enteral nutritional support by gastrostomy tube in children with cancer. *J Pediatr*. 1995;127(1):58–62.
173. Donaldson SS, Wesley MN, Ghavimi F, Shils ME, Suskind RM, DeWys WD. A prospective randomized clinical trial of total parenteral nutrition in children with cancer. *Med Pediatr Oncol*. 1982;10(2):129–139.
174. Shamberger RC, Brennan MF, Goodgame JT Jr, et al. A prospective, randomized study of adjuvant parenteral nutrition in the treatment of sarcomas: results of metabolic and survival studies. *Surgery*. 1984;96(1):1–13.
175. Shamberger RC, Pizzo PA, Goodgame JT Jr, et al. The effect of total parenteral nutrition on chemotherapy-induced myelosuppression. A randomized study. *Am J Med*. 1983;74(1):40–48.
176. Rickard KA, Foland BB, Detamore CM, et al. Effectiveness of central parenteral nutrition versus peripheral parenteral nutrition plus enteral nutrition in reversing protein-energy malnutrition in children with advanced neuroblastoma and Wilms' tumor: a prospective randomized study. *Am J Clin Nutr*. 1983;38(3):445–456.

177. Rickard KA, Godshall BJ, Loghmani ES, et al. Integration of nutrition support into oncologic treatment protocols for high and low nutritional risk children with Wilms' tumor. A prospective randomized study. *Cancer*. 1989;64(2):491–509.
178. Rickard KA, Becker MC, Loghmani E, et al. Effectiveness of two methods of parenteral nutrition support in improving muscle mass of children with neuroblastoma or Wilms' tumor. A randomized study. *Cancer*. 1989;64(1):116–125.
179. Rickard KA, Loghmani ES, Grosfeld JL, et al. Short- and long-term effectiveness of enteral and parenteral nutrition in reversing or preventing protein-energy malnutrition in advanced neuroblastoma. A prospective randomized study. *Cancer*. 1985;56(12):2881–2897.
180. Leung FY. Trace elements in parenteral micronutrition. *Clin Biochem*. 1995;28(6):561–566.
181. Helpingstine CJ, Bistran BR. New Food and Drug Administration requirements for inclusion of vitamin K in adult parenteral multivitamins. *J Parenter Enteral Nutr*. 2003;27(3):220–224.
182. Bryant R. Managing side effects of childhood cancer treatment. *J Pediatr Nurs*. 2003;18(2):113–125.
183. Weiger WA, Smith M, Boon H, Richardson MA, Kaptchuk TJ, Eisenberg DM. Advising patients who seek complementary and alternative medical therapies for cancer. *Ann Intern Med*. 2002;137(11):889–903.
184. Rivadeneira DE, Evoy D, Fahey TJ 3rd, Lieberman MD, Daly JM. Nutritional support of the cancer patient. *CA Cancer J Clin*. 1998;48(2):69–80.
185. McCarthy D, Weihofen D. The effect of nutritional supplements on food intake in patients undergoing radiotherapy. *Oncol Nurs Forum*. 1999;26(5):897–900.
186. Barber MD, Ross JA, Voss AC, Tisdale MJ, Fearon KC. The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer. *Br J Cancer*. 1999;81(1):80–86.
187. Fearon KC, Von Meyenfeldt MF, Moses AG, et al. Effect of a protein and energy dense N-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial. *Gut*. 2003;52(10):1479–1486.
188. Patterson RE, Neuhouser ML, Hedderson MM, Schwartz SM, Standish LJ, Bowen DJ. Changes in diet, physical activity, and supplement use among adults diagnosed with cancer. *J Am Diet Assoc*. 2003;103(3):323–328.
189. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. *JAMA*. 1998;280(18):1569–1575.
190. Ritvo P, Irvine J, Katz J, Matthew A, Sacamano J, Shaw BF. The patient's motivation in seeking complementary therapies. *Patient Educ Couns*. 1999;38(2):161–165.
191. Schenck DP. Ethical considerations in the treatment of head and neck cancer. *Cancer Control*. 2002;9(5):410–419.
192. Breier-Mackie S, Newell CJ. Home parenteral nutrition: an ethical decision making dilemma. *Aust J Adv Nurs*. 2002;19(4):27–32.
193. Chiu TY, Hu WY, Chuang RB, Chen CY. Nutrition and hydration for terminal cancer patients in Taiwan. *Support Care Cancer*. 2002;10(8):630–636.
194. Eberhardie C. Nutrition support in palliative care. *Nurs Stand*. 2002;17(2):47–52; quiz 54–55.
195. Angus F, Burakoff R. The percutaneous endoscopic gastrostomy tube: medical and ethical issues in placement. *Am J Gastroenterol*. 2003;98(2):272–277.
196. Daugherty CK. Examining ethical dilemmas as obstacles to hospice and palliative care for advanced cancer patients. *Cancer Invest*. 2004;22(1):123–131.

197. Adams KE, Cohen MH, Eisenberg D, Jonsen AR. Ethical considerations of complementary and alternative medical therapies in conventional medical settings. *Ann Intern Med.* 2002;137(8):660–664.
198. Pietsch JB, Ford C, Whitlock JA. Nasogastric tube feedings in children with high-risk cancer: a pilot study. *J Pediatr Hematol Oncol.* 1999;21(2):111–114.
199. Deswarte-Wallace J, Firouzbakhsh S, Finklestein JZ. Using research to change practice: enteral feedings for pediatric oncology patients. *J Pediatr Oncol Nurs.* 2001;18(5):217–223.
200. Mathew P, Bowman L, Williams R, et al. Complications and effectiveness of gastrostomy feedings in pediatric cancer patients. *J Pediatr Hematol Oncol.* 1996;18(1):81–85.
201. Skolin I, Hernell O, Larsson MV, Wahlgren C, Wahlin YB. Percutaneous endoscopic gastrostomy in children with malignant disease. *J Pediatr Oncol Nurs.* 2002;19(5):154–163.
202. Pedersen AM, Kok K, Petersen G, Nielsen OH, Michaelsen KF, Schmiegelow K. Percutaneous endoscopic gastrostomy in children with cancer. *Acta Paediatr.* 1999;88(8):849–852.
203. van Eys J, Wesley MN, Cangir A, et al. Safety of intravenous hyperalimentation in children with malignancies: a cooperative group trial. *J Parenter Enteral Nutr.* 1982;6(4):291–294.
204. Ghavimi F, Shils ME, Scott BF, Brown M, Tamaroff M. Comparison of morbidity in children requiring abdominal radiation and chemotherapy, with and without total parenteral nutrition. *J Pediatr.* 1982;101(4):530–537.
205. van Eys J, Copeland EM, Cangir A, et al. A clinical trial of hyperalimentation in children with metastatic malignancies. *Med Pediatr Oncol.* 1980;8(1):63–73.
206. Kelly KM, Jacobson JS, Kennedy DD, Braudt SM, Mallick M, Weiner MA. Use of unconventional therapies by children with cancer at an urban medical center. *J Pediatr Hematol Oncol.* 2000;22(5):412–416.
207. Neuhaus ML, Patterson RE, Schwartz SM, Hedderson MM, Bowen DJ, Standish LJ. Use of alternative medicine by children with cancer in Washington state. *Prev Med.* 2001;33(5):347–354.
208. McCurdy EA, Spangler JG, Wofford MM, Chauvenet AR, McLean TW. Religiosity is associated with the use of complementary medical therapies by pediatric oncology patients. *J Pediatr Hematol Oncol.* 2003;25(2):125–129.
209. Lioffi C, Hatira P. Clinical hypnosis versus cognitive behavioral training for pain management with pediatric cancer patients undergoing bone marrow aspirations. *Int J Clin Exp Hypn.* 1999;47(2):104–116.
210. Lioffi C, Hatira P. Clinical hypnosis in the alleviation of procedure-related pain in pediatric oncology patients. *Int J Clin Exp Hypn.* 2003;51(1):4–28.
211. Aasgaard T. An ecology of love: aspects of music therapy in the pediatric oncology environment. *J Palliat Care.* 2001;17(3):177–181.
212. Jankovic M, Spinetta JJ, Martins AG, et al. Non-conventional therapies in childhood cancer: guidelines for distinguishing non-harmful from harmful therapies: a report of the SIOP Working Committee on Psychosocial Issues in Pediatric Oncology. *Pediatr Blood Cancer.* 2004;42(1):106–108.
213. Bottomley SJ, Kassner E. Late effects of childhood cancer therapy. *J Pediatr Nurs.* 2003;18(2):126–133.
214. Lustig RH, Post SR, Srivannaboon K, et al. Risk factors for the development of obesity in children surviving brain tumors. *J Clin Endocrinol Metab.* 2003;88(2):611–616.