

43. Palmer JL, Fisch MJ. Association between symptom distress and survival in outpatients seen in a palliative care cancer center. *J Pain Symptom Manage* 2005;29:565-571.

SUGGESTED READING

- Homsy J, Walsh D, Nelson KA, et al. The impact of a palliative medicine consultation service in medical oncology. *Support Care Cancer* 2002;10:337-342.
- Homsy J, Walsh D, Rivera N, et al. Symptom evaluation in palliative medicine: Patient report versus systematic assessment. *Support Care Cancer* 2006;14:444-453.
- Miaskowski C, Dodd M, Lee K. Symptom clusters: The new frontier in symptom management research. *J Natl Cancer Inst Monogr* 2004;32:17-21.
- Patrick DL, Ferketich SL, Frame PS, et al. National Institutes of Health State-of-the-Science Conference Statement: Symptom management in cancer: Pain, depression, and fatigue, July 15-17, 2002. *J Natl Cancer Inst Monogr* 2004;32:9-16.
- Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: Relationship to age, gender, and performance status in 1,000 patients. *Support Care Cancer* 2000;8:175-179.



CHAPTER 150

Anorexia and Weight Loss

Aurelius G. Omlin and Florian Strasser

KEY POINTS

- The anorexia-cachexia syndrome is a wasting state involving loss of muscle and fat caused by the underlying illness and mediated indirectly by secondary factors. Reduced oral intake and complex metabolic changes result in chronic negative energy and protein balance in combination with accelerated metabolism.
- Assessment requires a multidisciplinary approach at the onset.
- Secondary causes must be ruled out to identify potentially treatable conditions.
- Pharmacotherapy is only one pillar of treatment, which includes nutritional interventions, counseling, and improved physical activity.
- Effective communication with patients and their families is essential for treatment.

Anorexia-cachexia syndrome (ACS) occurs in numerous chronic end-stage disease processes, such as cancer, acquired immunodeficiency syndrome (AIDS), chronic pulmonary disease, chronic renal insufficiency, and heart failure¹ (see Chapter 106). ACS is a result of complex interactions among a chronic incurable disease, the central nervous system, and metabolic abnormalities.²⁻⁴

The definition is based on involuntary weight loss and loss of appetite or reduced oral intake. Various criteria are

used, including symptom scales (threshold $\geq 3/10$) or perceived burden (no threshold) for appetite, caloric intake (≤ 20 kcal/kg), and weight loss ($>5\%$ in 6 months or $>2\%$ in 2 months). Subjective perceptions are symptoms, whereas a syndrome includes objective variables (i.e., weight loss, caloric intake, and symptoms).⁵⁻¹¹

Novel definitions are being developed, including variables of caloric intake, loss of fat and muscle mass, and chronic inflammation. It is likely that subtypes (phenotypes) will be characterized, including typical consequences such as reduced physical activity, impaired quality of life, and changes in body composition.

Working with patients suffering from ACS and their families requires careful assessment of ACS and concurrent physical and psychosocial distress, including the prognosis of a chronic incurable disease. Treatment includes counseling patients and relatives, treatment of potentially reversible secondary factors, and pharmacological and nutritional interventions (see Chapter 107). Promising pharmacological treatments have entered randomized, controlled trials. Nonpharmacological measures merit intensified future research.

BASIC SCIENCE AND PATHOPHYSIOLOGY

Differentiation between primary and secondary ACS is important. *Primary* ACS represents a metabolic status directly caused by the tumor or the chronic illness, in which complex metabolic and neuroendocrine modifications occur in an ongoing, altered inflammatory state. Catabolism is accelerated despite declining food and energy intake, and there is mobilization of peripheral proteins and lipids that maintain augmented liver synthesis of acute phase proteins. Losses of fat and body cell mass, particularly skeletal muscle, are approximately equal.^{3,9,11,12} Based on animal models of primary ACS, different phenotypes exist that could be offered targeted therapy (see Chapter 106). *Secondary* ACS refers to cachexia occurring from impaired oral intake, including severe symptoms (e.g., pain, depression), concurrent catabolic states, loss of proteins, or loss of muscle tissue due to reduced physical activity (deconditioning) (Table 150-1).^{8,10}

EPIDEMIOLOGY AND PREVALENCE

ACS is a silent syndrome that is easily overlooked. Early assessment and clinical suspicion seems crucial for efficient therapy^{8,10} (see Chapter 63). Anorexia affects up to three fourths of cancer patients. It can occur independently of cachexia and is a poor prognostic factor.^{5,10} The frequency of cachexia in patients with advanced solid tumors (except breast cancer) ranges from about 25% to more than 80% before death.^{2,10} Weight loss has a significant impact on quality of life and is a poor prognostic factor.¹⁰⁻¹³

CLINICAL MANIFESTATIONS

ACS manifests with appetite loss, weight loss, and fatigue, often combined with chronic nausea, early satiety, and taste problems (see Chapter 169). The patient may or may not have weight loss, and edema or ascites may occur (Fig. 150-1). The family members may be distressed about the

TABLE 150-1 Checklist for Secondary Anorexia and Cachexia

MEDICAL CONDITION OR STATE	MECHANISM LEADING TO ANOREXIA OR CACHEXIA	POSSIBLE TREATMENT OPTIONS
REDUCED ORAL INTAKE FROM IMPAIRED GASTROINTESTINAL FUNCTION OR INTEGRITY		
Mouth		
Stomatitis or mucositis*	Pain, reduced taste	Topical mouth care
Xerostomia†	Reduced taste	Pilocarpin, change medication
Dysgeusia or hypogeusia†	Reduced taste	Zinc supplementation
Tooth problems†	Pain, inability to chew	Dentist
Osteonecrosis of jaw†	Pain, infection, inability to chew	Surgeon or dentist
Dysphagia or odynophagia	Pain	Depends on underlying cause
Thrush†	Pain	Antifungal medication
Upper gastrointestinal tract		
Bone metastasis of jaw	Pain, discomfort	Bisphosphonates, radiation therapy
Gastroesophageal reflux†	Pain or inflammation	Proton pump inhibitors, antacids
Gastric ulcer or gastritis†	Postprandial pain	Proton pump inhibitors, antacids
Chronic nausea	Reduced oral intake	Depends on underlying cause, pharmacotherapy
Acute nausea or emesis†	Reduced oral intake	Antiemetics, counseling
Lower gastrointestinal tract		
Constipation*	Loss of appetite, nausea, early satiety	Laxatives
Bowel obstruction	Pain, nausea, emesis	Depends on underlying cause
Anal fissures or hemorrhoids†	Pain	Local therapy, depends on underlying cause
Radiation-induced esophagitis†	Pain, dysphagia	Consider total parenteral nutrition
Chronic diarrhea	Malabsorption, fear of fecal incontinence	Depends on underlying cause
REDUCED ORAL INTAKE WITH NORMAL GASTROINTESTINAL FUNCTION OR INTEGRITY		
Shortness of breath*	Reduced oral intake	Depends on underlying cause, morphine
Pain*	Anorexia, opioid-associated nausea, constipation	Analgesic therapy, depends on underlying cause
Delirium*	Reduced oral intake	Depends on underlying cause
Anxiety	Fear of fecal incontinence, fear of postprandial abdominal pain, fear of nausea	Counseling, depends on underlying cause
Fatigue	Inability to cook, shop, eat	Counseling, depends on underlying cause
Depression	Reduced appetite, anhedonia	Counseling, antidepressants
Wrong diet (e.g., too healthy, mono-item diets, Breuss hunger cure)	Inappropriate distribution of carbohydrates, proteins, and fats	Counseling
Fasting state (e.g., diagnostic tests, planned operation)	Insufficient oral intake	Consider total parenteral nutrition
Presentation of food (e.g., portions too large, unpleasant atmosphere, bad taste, social isolation, hectic ambience, bed-ridden state)	Loss of appetite, reduced oral intake	Counseling, improvement of environment
Language barrier (e.g., cannot order preferred food)	Insufficient oral intake	Counseling, translation service
Social distress (e.g., loneliness, lack of support, financial problems)	Insufficient oral intake or mono diet	Counseling, social support
Spiritual or existential distress (e.g., fear of death, unemployment)	Loss of appetite, insufficient oral intake	Counseling, support
LOSS OF PROTEINS		
Nephrotic syndrome	Protein loss	Depends on underlying cause
Frequent paracentesis or thoracentesis	Loss of proteins	Depends on underlying cause
Malabsorption or maldigestion	Loss of fat and proteins	Depends on underlying cause, pancreas enzyme substitution, slow down gut motility
Long-term cortisol therapy	Protein degradation	Depends on underlying cause
Extensive wounds	Loss of proteins	Depends on underlying cause
Bed-ridden state	Loss of physical activity, protein loss	Depends on underlying cause
Hypogonadism	Loss of muscle tissue	Hormone substitution
CATABOLIC STATES		
Hyperthyroidism	Increased catabolism, diarrhea	Depends on underlying cause
Infection or inflammation	Increased metabolism, acute phase production	Depends on underlying cause
Chronic heart, renal, or hepatic insufficiency; chronic obstructive pulmonary disease	Increased metabolism, impaired anabolism	Depends on underlying cause
Uncontrolled diabetes	Increased metabolism, impaired anabolism	Counseling, pharmacotherapy

*Very common causes of secondary anorexia or cachexia.

†Possible side effects of radiation therapy, chemotherapy, or pharmacotherapy.

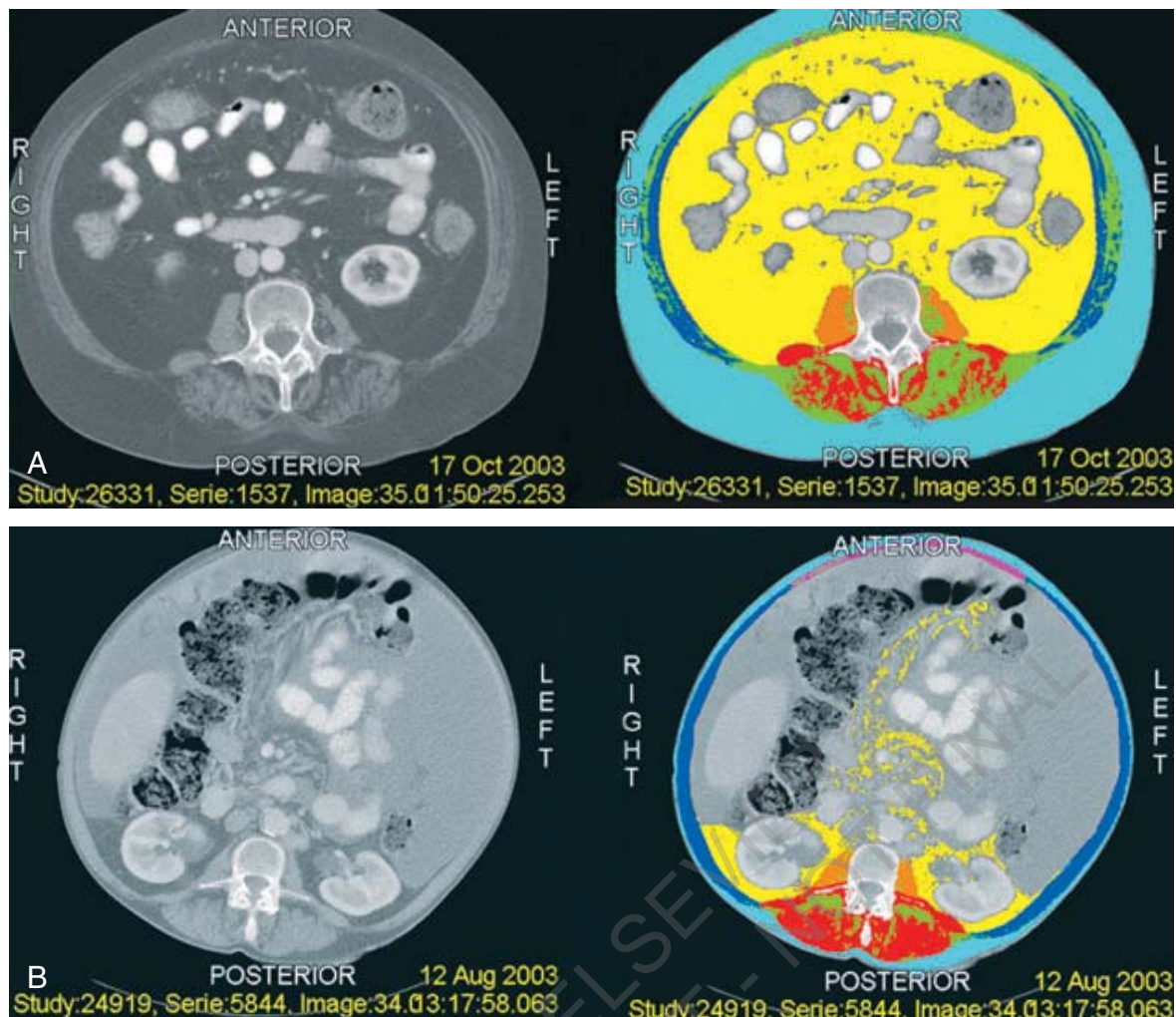


FIGURE 150-1 The clinical picture of anorexia-cachexia syndrome is complex. The two patients have a diagnosis of advanced cancer. The existence of fat hides the significant loss of muscle mass in one patient (**A**), whereas the other patient (**B**) can be directly identified as cachectic. Locations of adipose tissue are indicated by color: visceral (*yellow*), subcutaneous (*light blue*), and intramuscular (*green*). Muscle tissue also is indicated by color: paraspinal (*red*), psoas (*orange*), lateral abdominal (*dark blue*), and rectus abdominis (*purple*). (Courtesy of Professor Vickie Baracos, Department of Oncology, University of Alberta, Cross Cancer Institute, Edmonton, Alberta.)

weight loss, or they may complain about lack of concern by staff members.

EVALUATION

In clinical practice, a structured, multilevel assessment strategy seems attractive (Fig. 150-2). We propose a two-step approach with a basic assessment (level I) that includes screening for ACS and for consequences that often guide primary actions (Boxes 150-1 and 150-2). If ACS is a priority in palliative management, in-depth assessment (level II) is necessary. Level III assessments are performed in specialized settings.

Basic Assessment

Basic assessment (level I) of ACS has two parts: screening and estimation of consequences (see Box 150-1). Screening reliably and quickly determines whether the patient has ACS (see “Case Study: Managing Anorexia-Cachexia Syndrome”). ACS is likely if one of the following is identified: loss of appetite (scored as 3/10 or higher on a numeric rating or visual analogue scale), weight loss (i.e., 2% or more in 2 months or 5% or more in 6 months), reduced oral intake ($\geq 25\%$ less than normal by patient report), or

Box 150-1 Basic Assessment (Level I) for Anorexia-Cachexia Syndrome

- A. Screening for anorexia-cachexia-syndrome
 1. Anorexia (≥ 3 of 10 on numeric rating or visual analogue scale) or
 2. Weight loss (2% in 2 months, 5% in 6 months) or
 3. Patients perceived reduction of oral intake ($\geq 25\%$ of normal)
- B. Estimation of consequences of anorexia-cachexia syndrome
 1. Does the patient look malnourished (i.e., body composition or nutritional status)?
 2. Does the patient suffer from reduced strength or energy (i.e., physical activity or energy expenditure)?
 3. Does the patient report fatigue, early satiety, chronic nausea, bloating, tension due to edema, dry mouth, or other common symptoms (i.e., associated symptoms)?
 4. Is the patient or his or her relatives bothered by the loss of appetite or loss of weight (i.e., psychosocial-existential distress)?

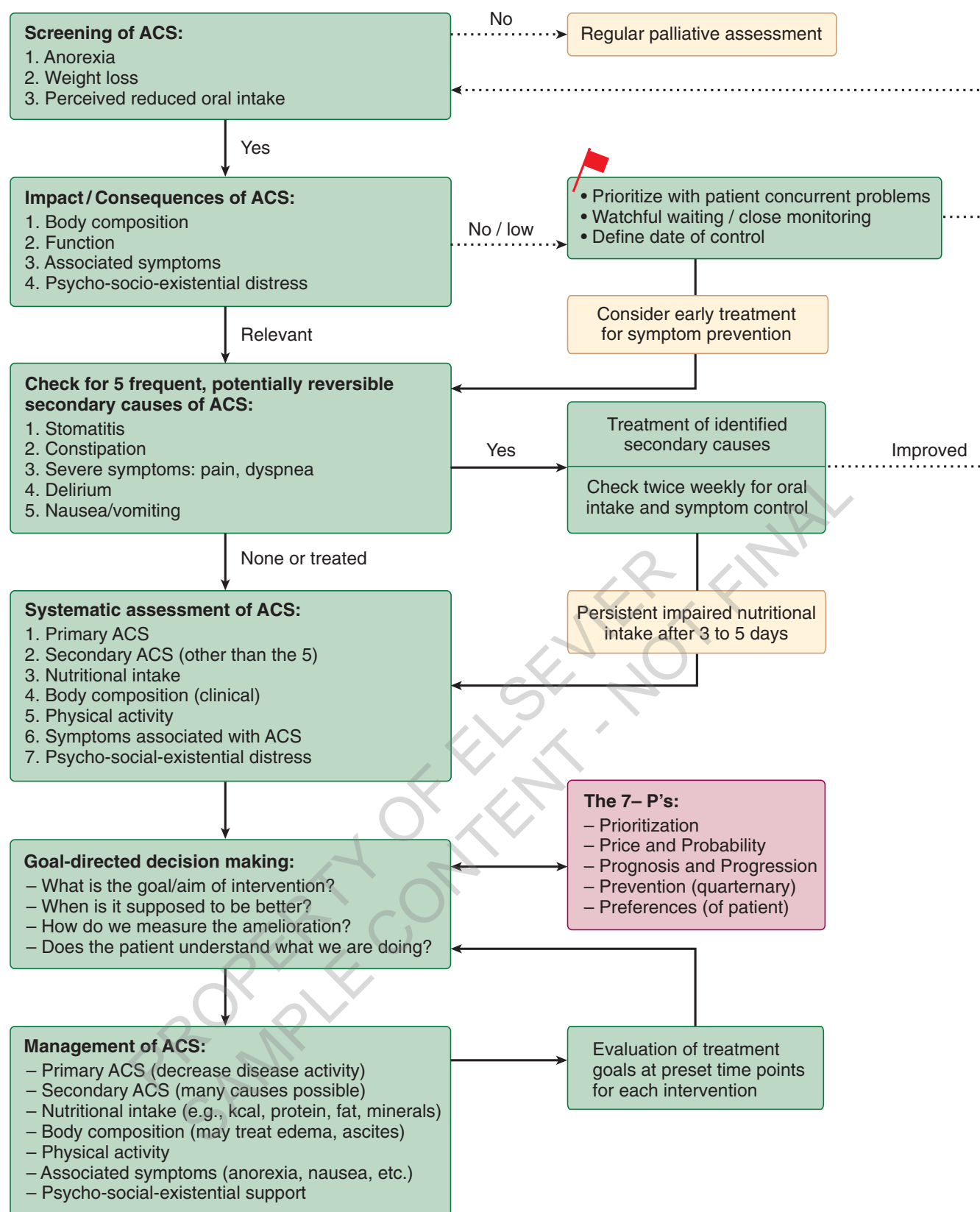


FIGURE 150-2 Flow chart for screening assessment, decision making, and management of anorexia-cachexia syndrome (ACS).

reduced intake (<20 kcal/kg). If the screening result is positive, simultaneous estimation of the impact guides further strategies.

ACS has many consequences, including nutritional status, physical function, the effects of associated symptoms, and psychosocial effects on patients and their families. ACS alters the patient's body composition and nutritional status. Bedside assessment of body composition is based on the physician's visual impression (e.g., well nourished, malnourished), an estimation of muscle

and body fat, and the clinical evaluation of edema, ascites, or pulmonary effusion.

A proxy for physical function is the Karnofsky Performance Status scale, which allows the clinician to grade patients' functioning from normal physical activity to severely disabled. A brief history allows further evaluation of activities of daily living (ADLs) or instrumental activities of daily living (IADLs).

The Edmonton Symptom Assessment Scale provides information on eight additional symptoms: pain, fatigue,

Box 150-2 In-Depth Assessment (Level II) of Anorexia-Cachexia Syndrome

1. Assessment of primary anorexia-cachexia syndrome (ACS), tumor dynamics, prognosis, response to disease-oriented treatment
2. Assessment of secondary factors contributing to ACS, including ongoing disease-oriented therapy
3. Assessment of caloric intake
4. Assessment of nutritional status, body composition, conditional essential nutrients (i.e., laboratory parameters)
5. Assessment of physical function, physical activity, energy expenditure
6. Assessment of psycho-social-existential consequences of ACS on patients and families
7. Assessment of symptom burden associated with ACS

nausea, depression, shortness of breath, tiredness, anxiety, and well-being. It may identify a reason for the ACS or its consequences. For example, a patient may feel depressed because of anorexia and reduced oral intake, or preexisting depression may lead to loss of appetite and reduced oral intake.

Patients may be asked questions to assess the impact of ACS on them or their relatives: “Does the weight loss bother you?” or “Are your relatives bothered by your poor appetite?” It is important to recognize patients’ concerns about symptoms. Many are disturbed because anorexia and weight loss may represent tumor progression and death.

Systematic Assessment

Systematic assessment (level II) of ACS is important because findings guide individualized treatments. An algorithm combines early treatment of potentially correctable causes of secondary ACS before comprehensive assessment (see Fig. 150-2).

The first step is assessment of primary ACS, tumor dynamics, prognosis, and response to disease-oriented treatment. None of the common laboratory parameters is a reliable indicator of primary ACS. Serum albumin concentration is downregulated in chronic inflammation (serum half-life of 19 days), and it can be used to monitor long-term treatment. Prealbumin (i.e., transthyretin), with a serum half-life of 48 hours, may serve for short-term assessment.^{5,8} C-reactive protein (CRP) is a nonspecific acute phase protein, and the level often is high in patients with advanced cancer or disease progression.⁵ The diagnostic value, sensitivity, and specificity of proteolysis-inducing factor (PIF) and lipid-mobilizing factor (LMF) are being investigated. Further studies should clarify the role of leptin, neuropeptide Y, ghrelin, melanocortin, and other hormones and peptides. To evaluate disease dynamics (including tumor markers), the actual tumor load, tumor activity, and the expected response to antitumor therapy should be considered.

The second step is assessment of secondary, potentially reversible factors. Little information is available on the frequency and relative importance of the five common secondary factors: stomatitis, constipation, pain and dyspnea, delirium, and nausea or vomiting (see Chapters

CASE STUDY

Managing Anorexia-Cachexia Syndrome

Mr. A is a 62-year-old farmer who was diagnosed with non-small cell lung cancer with bone metastasis. After four cycles of chemotherapy, stable disease was demonstrated by computed tomography. At a routine visit 3 months later, his wife complains that he has lost weight despite all her extra cooking. Mr. A is worried because he had seen a close friend with an incurable pancreatic cancer “starve to death.” Mrs. A is concerned that she is not looking after her husband’s nutrition very well. Her sister told her that he should be given nutritional supplements or total parenteral nutrition.

Mr. A (initial weight of 140 pounds and height of 172 cm) has lost 28 pounds since his first visit 6 months earlier; this corresponds to a 20% loss of his premorbid weight and a change in the body mass index from 23.6 to 18.9 kg/m². The patient is distressed because of his weight loss, perceived reduced oral intake, and loss of appetite (score of 9/10).

Because the patient has lost muscle mass, he has a lack of energy and pain during movement. He has stayed at home most of the time and even stopped going for walks with his beloved dog. He expresses a fear of dying, and his wife is distressed and desperate.

The patient has no sign of stomatitis, but he reports constipation, which is confirmed on an abdominal radiograph. The patient has been using a fentanyl patch without breakthrough doses, but he was not taking laxatives. Pain for the last 24 hours was rated as 7/10, dyspnea as 3/10, and nausea as 2/10. When he achieves a (rare) bowel movement, appetite improves slightly. The patient showed no signs of cognitive impairment.

To manage the discomfort, the pain medication was adapted with adequate breakthrough dosing, adjuvant analgesics were given, and radiation therapy for the painful bone metastasis was initiated. The patient got bi-daily oral combination laxative therapy and daily enemas. Patient and spouse were educated. Pain and constipation were re-evaluated after 3 and 5 days of the new regimen. Because of persistent anorexia-cachexia syndrome (i.e., perceived oral intake only slightly better and anorexia score of 6/10), in-depth assessment was initiated by estimating primary and secondary factors, nutritional intake over 3 days, clinical body composition, symptom burden, physical function, and eating-related distress of the patient and family.

Management was agreed on with the patient, family, and interdisciplinary team. It consisted of nutritional counseling (i.e., many meals, protein-rich meals, and supplements), psychosocial counseling to enable the family to express and cope with illness-associated distress by other means than eating, home physical exercise (i.e., two sets of 10 minutes of stair climbing), intramuscular administration of testosterone, use of megestrol acetate to stimulate appetite (with re-evaluation after 2 weeks), and second-line chemotherapy (i.e., docetaxel).

169 and 232). A secondary anorexia-cachexia checklist can help identify many different causes (see Table 150-1).

Radiation therapy may cause nausea and vomiting if it is administered to the abdomen. Chemotherapy side effects (i.e., mucositis, diarrhea, or infections) can affect nutritional intake. Side effects of opioids and other pharmacological treatments are common but often unrecognized in patients with ACS.

The third step is assessment of caloric intake. Most methods depend on the patient's ability to retrospectively report what was eaten or keep a prospective dietary record over 3 days. An observer calculating or weighing food consumed at each meal improves accuracy. An approach that includes photographs of plates before and after the meal followed by calculation of caloric intake by a nutritionist has been used in research.^{5,8}

The fourth step is assessment of nutritional status, body composition, conditional essential nutrients, and laboratory parameters. Measuring weight includes the history of involuntary weight loss, assessing body weight and body mass index, calculating the ideal body weight (height in centimeters – 100), and recognizing confounding conditions such as significant ascites, pleural effusion, or edema.

The subjective global assessment of a nutrition questionnaire (SGA) combines information on weight change, dietary intake, gastrointestinal symptoms, and functional impairment with information on body composition. Three groups are defined: well nourished, mildly or moderately malnourished, or severely malnourished.^{5,8,10} The SGA has value mainly for the physical examination of body composition (i.e., estimation of fat and muscle mass). The secondary anorexia checklist may inform the clinician more than gastrointestinal symptoms of the SGA. Anthropometric tests (in addition to weight) include skin fold thickness (i.e., body fat) and middle upper arm circumference (i.e., indicator of muscle mass), and it can be used for longitudinal follow-up studies.

Whole-body bioimpedance analysis (BIA) is an easy to administer assessment of body composition, but body water content has to be estimated by the examiner, which may introduce a large degree of variability. Dual-photon absorptiometry or dual x-ray absorptiometry (DEXA) is reliable, but access is limited.

Measurement of muscle mass or visceral tissue mass by computed tomography (CT) or magnetic resonance imaging (MRI) is promising. This approach can take advantage of the regular monitoring of cancer patients (see Fig. 150-1).

Essential nutrients such as vitamins, amino acids, and trace elements are not routinely assessed. However, patients suffering from chronic disease may be deficient in substances such as vitamins D and E or zinc (blood levels of zinc correlate inconsistently with body reserve).

The fifth step is assessment of the patient's physical function, physical activity, and energy expenditure. Performance status (e.g., Karnofsky Performance Status, Eastern Cooperative Oncology Group [ECOG]) can approximate and monitor global function. For muscle function, grip and thigh strength monitoring is simple to administer, as is the sit-up-and-go time. Body sensors can

estimate type, duration, frequency, and intensity of physical activities for indirect calculation of energy expenditure, and they may replace the laborious and expensive double-labeled water technique or indirect calorimetry.

The sixth step in the assessment of ACS is evaluation of its psychosocial impact on the patient and family members. In addition to somatic parameters, psychological characteristics, social and family concerns, and spiritual or existential distress must be included. Emotional, social, and spiritual distresses are first estimated by common symptom screening instruments. The interdisciplinary team then explores how ACS affects distress and quality of life. The Functional Assessment of Anorexia/Cachexia Treatment (FAACT) has 12 questions that ask about pressure by family members and concerns about body appearance and weight.^{10,14}

The seventh step is assessment of associated symptoms. No widely accepted symptom checklist is available for ACS symptoms, and current symptom screening lists are not designed to differentiate the consequences of ACS from concurrent symptoms, which may also cause secondary ACS. FAACT includes key symptoms but does not cover the full clinical experience. In practice, we use the Edmonton Symptom Assessment Scale, the FAACT, screening for fatigue (i.e., cognitive, emotional, and physical dimensions), and questions about eating-related distress among patients and family.

DIFFERENTIAL DIAGNOSIS

The ACS has many causes (see Fig. 150-2).

TREATMENT

Plan of Care

Five common and potentially reversible factors of secondary ACS are assessed and treated (see Fig. 150-2). Priorities should be negotiated with the patient and family, because patients' priorities often are different from those of the physicians. Treatment goals and outcome measures then are discussed with the patient, family, and interdisciplinary team. For instance, control of predominant symptoms (e.g., anorexia, chronic nausea) may be the priority for some, whereas the focus is physical activity for others.

Decision making includes the definition of an intervention goal and agreement on a re-evaluation time and symptom measurement (see Chapters 116 and 120). It is important to ensure understanding of these goals and methods by the patients and family. The 7-P model is helpful in (Box 150-3) decision making (Box 150-4).

The first step in the plan of care is to treat the primary causes of ACS. Treatment of the causative underlying illness is essential. Carefully chosen and monitored anti-neoplastic treatments can offer symptomatic benefit. Anti-inflammatory cytokines (e.g., tumor necrosis factor- α , interleukin-6 inhibitors, thalidomide-like agents), ghrelin, or melanocortin receptor antagonists may provide novel therapeutic approaches.^{5,7,8}

The second component of the care plan is to treat the often-reversible secondary causes of ACS: stomatitis, con-

Box 150-3 Decision Making Based on the 7-P Model

1. What is the *priority* of the clinical problem or syndrome compared with other concurrent problems (e.g., patient's view, doctor's view)?
- 2/3. What is the *price* of the intervention (e.g., side effects, time expenditure), and what is the *probability* that the intervention is going to change or improve the condition?
- 4/5. What is the *prognosis* of the patient, how much lifetime is left, and how fast will the disease *progress*?
6. What can be done to *prevent* suffering (i.e., quaternary prevention) from future complications associated with the clinical problem or syndrome?
7. What is the patient's *preference*?

Box 150-4 Therapeutic Options for the Management of Anorexia-Cachexia Syndrome

1. Treat the primary causes of anorexia-cachexia syndrome (ACS).
2. Treat the secondary causes of ACS.
3. Provide appropriate nutritional support.
4. Provide measures to stabilize or improve body composition, and supply conditional essential nutrients.
5. Increase physical activity and exercise.
6. Provide psycho-social-existential counseling and support.
7. Treat associated symptoms according to guidelines.

stipation, pain and dyspnea, delirium, and nausea or vomiting. Interdisciplinary management is advisable for many secondary causes.

The third component of management is to provide appropriate nutritional support. Nutritional counseling is a cornerstone of ACS management, whereas the use of artificial nutrition in managing patients with advanced cancer is controversial. There is no evidence that increased caloric intake in all cancer patients with ACS can increase muscle mass or produce a survival advantage (see Chapters 104, 105, 108, and 109). The main reason is that primary ACS impedes effective caloric intake.^{8,15} Patients with dominant starvation cachexia (i.e., most secondary ACS factors excluding catabolism) and with minimally controlled primary ACS may represent a subgroup of ACS who can profit from artificial nutrition.

Starvation is characterized as hypometabolism with reduced protein and glucose turnover but increased lipolysis without an underlying pro-inflammatory condition. Starvation is often seen in patients with bowel obstruction, those undergoing radiotherapy for head and neck cancers, and surgical patients.

Both the assessment and intervention parts of dietary counseling are essential in management (see Chapter 51). Assessment includes calculation of nutritional intake considering the relative composition of nutrients (e.g., kcal, proteins, vitamins), estimation of nutritional status to define the goals of intervention, and analysis of physical activity and underlying disease activity. Clinicians must assess eating habits, screen for family distress, and explore educational needs. Interventions include counseling to alleviate anxiety and conflict about the inability to consume a normal diet and educate cancer patients about the role

of high-protein and high-fat diets (i.e., that eating “unhealthy” food is a response to their needs). Comfort-centered counseling may produce more stress reduction than achieving certain caloric and protein goals.

Enteral nutrition should be favored over parenteral nutrition, although it is important to identify the few who may profit from parenteral nutrition. Before instituting parenteral nutrition, clear time goals should be set for re-evaluation of its effectiveness and potential withdrawal.

The fourth component of the care plan is to provide measures to stabilize or improve body composition by means of combined interventions tackling nutritional intake, muscle function, and reversal of catabolism (e.g., inflammation, disease). Evidence from animal models or specific diseases suggests that vitamins, trace elements, and specific amino acids can ameliorate ACS. Extrapolation of this evidence to clinical management is controversial.

The fifth component of the management plan is to increase physical activity and exercise. Overall anabolism and especially muscle anabolism are maximized with frequent contractile exercise, particularly resistance-type activity (e.g., weightlifting) in elderly patients, and with nutritional and pharmacological support.¹¹ Exercise intervention studies (e.g., cancer survivors) reported improved quality of life and improved nutritional status, symptoms (e.g., nausea, fatigue, anxiety), muscle strength, and functional capacity. It is unclear which subgroups of patients with advanced incurable diseases benefit.

The sixth component of management is psychosocial-existential counseling and support. “Starving to death” is a common concern of patients with ACS and their families. Because of the high frequency and impact of eating-related distress of patients, family members, and caregivers, adequate education and counseling (including practical acts of friendship and caring) deserve high priority.

The seventh component of the care plan is treatment of associated symptoms. Associated symptoms may be the cause of ACS or may result from it. Depression may lead to reduced oral intake, and weight loss and anorexia may result in depression.

Drugs

Progestins, short-term corticosteroids, and prokinetics alleviate selected aspects of ACS. Several agents targeting appetite stimulation or secondary anorexia have been investigated with negative results. However, limited trial and preclinical data have been reported for some promising drugs (e.g., ghrelin, ATP, thalidomide, MC4-receptor antagonists, β_2 -mimetics) (see Chapter 133).

Supportive Care

Evidence is growing for many pharmacological and non-pharmacological interventions. The use of progestational drugs, short-term corticosteroids, and metoclopramide for anorexia is supported by the results of randomized, controlled trials and meta-analysis.^{2,5,6} However, evidence for consistent effects on weight loss or quality of life is lacking.

Studies of nutritional counseling or oral supplements have reported increased food intake, but no consistent

evidence exists for improvements in body composition, function, tumor treatment response, or survival.

RESEARCH OPPORTUNITIES

Several phenotypes of primary ACS with different underlying pathophysiological mechanisms are suspected, and they should be characterized for targeted therapy. A systematic approach to assessment and classification of ACS is important for improved clinical practice.

Combined pharmacological treatments of various targets (i.e., appetite and others) and individualized interventions (e.g., nutritional support) should be evaluated. To tailor ACS treatment, research should focus on genetic variability, such as altered leptin, neuropeptide Y, melanocortin, ghrelin, and ubiquitin-proteasome pathways. The importance of the cancer cachectic factor (i.e., proteolysis-inducing factor) is controversial, but it may hold promise as a novel therapeutic target.^{2,5,6,9,12}

REFERENCES

- Morley JE, Thomas DR, Wilson MM. Cachexia: pathophysiology and clinical relevance. *Am J Clin Nutr* 2006;83:735-743.
- Inui A: Cancer anorexia-cachexia syndrome: current issues in research and management. *CA Cancer Clin* 2002;52:72-91.
- Davis MP, Dickerson D. Cachexia and anorexia: cancer's covert killer. *Support Care Cancer* 2000;8:180-187.
- Fearon KC, Voss AC, Hustead DS, for the Cancer Cachexia Study Group. Definition of cancer cachexia: Effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. *Am J Clin Nutr* 2006;83:1345-1350.
- Strasser F: Pathophysiology of the anorexia/cachexia syndrome. In Doyle D, Hanks G, Cherny N, Calman K (eds). *Oxford Textbook of Palliative Medicine*. New York: Oxford University Press, 2005.
- Yavuzsen T, Mellar PD, Walsh D, et al. Systematic review of the treatment of cancer-associated anorexia and weight loss. *J Clin Oncol* 2005;85:8500-8511.
- Strasser F: Eating-related disorders in patients with advanced cancer. *Support Care Cancer* 2003;11:11-20.
- Strasser F, Bruera ED. Update on anorexia and cachexia. *Hematol Oncol Clin North Am* 2002;16:589-617.
- MacDonald N, Easson AM, Mazurak VC, et al. Understanding and managing cancer cachexia. *J Am Coll Surg* 2003;197:143-161.
- Strasser F, Bruera E. Cancer anorexia/cachexia syndrome: Epidemiology, pathogenesis, and assessment. In Ripamonti C, Bruera E (eds). *Gastrointestinal Symptoms in Advanced Cancer Patients*. New York: Oxford University Press, 2002.
- Baracos VE. Cancer-associated cachexia and underlying biological mechanisms. *Annu Rev Nutr* 2006;26:435-461.
- Giordano KF, Jatoi A: The cancer anorexia/weight loss syndrome: Therapeutic challenges. *Curr Oncol Rep* 2005;7:271-276.
- Stewart GD, Skipworth RJ, Fearon KC. Cancer cachexia and fatigue. *Clin Med* 2006;6:140-143.
- Strasser F, Binswanger J, Cerny T, Kesselring A. Fighting a losing battle: Eating-related distress of men with advanced cancer and their female partners. A mixed-methods study. *Palliat Med* 2007;21:129-137.
- Bruera E. ABC of palliative care. Anorexia, cachexia, and nutrition. *BMJ* 1997;315:1219-1222.

SUGGESTED READING

- Baracos VE. Cancer-associated cachexia and underlying biological mechanisms. *Annu Rev Nutr* 2006;26:435-461.
- Inui A. Cancer anorexia-cachexia syndrome: current issues in research and management. *CA Cancer Clin* 2002;52:72-91.
- Strasser F, Bruera ED. Update on anorexia and cachexia. *Hematol Oncol Clin North Am* 2002;16:589-617.

CHAPTER 151

Anxiety

Susan B. LeGrand

KEY POINTS

- There is little specific palliative medicine evidence on the diagnosis and management of anxiety.
- The prevalence is about 25%, but it is higher among younger women.
- Anxiety may be a primary symptom, a sign of other medical illnesses or complications, or a medication side effect, and the source should be considered before initiating therapy.
- Psychotherapeutic interventions are recommended even in patients with advanced disease.
- Benzodiazepines and selective serotonin reuptake inhibitors are useful agents for treating anxiety.

Although anxiety is common in patients with advanced illness, there is little research on the symptom specific to palliative medicine. What exists is typically expert opinion extrapolated from the general psychiatric literature. *Anxiety* is defined as “the presence of fear or apprehension that is out of proportion to the context of the life situations.”¹ However, for patients facing death, what is proportional to the context? As in many situations in advanced illness, the level of distress should prompt intervention rather than strict diagnostic criteria.

Anxiety may be a symptom of other conditions, and the contribution of each to the incidence of anxiety is unknown:

- A preexisting psychiatric illness exacerbated by advanced disease, such as adjustment disorders, panic disorders, depression, and generalized anxiety disorders
- A medical complication, such as sepsis, pulmonary embolus, hypoxia, delirium, or medication withdrawal
- A medication side effect, such as those of corticosteroids or metoclopramide
- Existential fears about dying or burial^{2,3}

BASIC SCIENCE

Humans have the ability to react to threat by means of the neurochemical systems (e.g., cortisol, catecholamines) that govern the fight-or-flight response. Just as an unrelieved pain stimulus may lead to long-term changes in the spinal cord and chronic pain, chronic activation of these systems and possibly early exposure to high levels of stress may fundamentally change a person, leading to chronic anxiety disorders, learned helplessness, or increased sensitivity to stress.⁴