Weight Loss in the Elderly: What's Normal and What's Not

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INTRODUCTION

Involuntary weight loss (IWL) is commonly observed in the older population, affecting 13% of ambulatory patients and 50% to 60% of nursing-home residents.[1] It is an important indicator of significant decline in health and function, resulting in a higher risk for infection, depression, and death.

Although it is important to recognize that periods of substantially positive or negative energy balance and body weight fluctuation occur as a normal part of life, a weight loss greater than 5% over six months should be investigated.

We can divide the major causes of weight loss in the elderly into three categories:

- psychosocial
- medical
- age-related

The clinical evaluation should include a careful history and physical examination. If these do not provide clues to the weight loss, simple diagnostic tests are indicated. A period of watchful waiting is preferable to blind pursuit of additional diagnostic testing that may yield few useful data if the results of these initial tests are normal. The first steps in managing patients with weight loss are to identify and treat any specific causative or contributing conditions and to provide nutritional support when indicated. Orexigenic (appetite-stimulating) drugs have found an established place in the management of protein-energy malnutrition.

PATHOPHYSIOLOGY

Regulation of food intake changes with increasing age, leading to what has been called a "physiological anorexia of aging." The amount of circulating cholecystokinin, a satiating hormone, increases in the circulation.[2] Other substances are also thought to cause satiety.[3,4]

The interplay between the brain and the gut is gaining increasing attention as a mechanism of anorexia and subsequent weight loss. A highly complex process involving taste sensation, neural and humoral signals from the gastrointestinal tract, and neurotransmitters and peptides in the hypothalamus or other brain regions regulates food intake and, consequently, energy homeostasis.[5] Psychosocial and spiritual distress can also influence the sensation of hunger, appetite, or satiety.[6]

Loss of lean body mass is common in older people.[7] Advancing age is also associated with a decrease in the basal metabolic rate as well as with changes in the senses of taste and smell.

Overly restricted diets, such as those that are low in fat and salt, may cause decreased intake[8]; therefore, a special or restricted diet (low in cholesterol, salt, or concentrated sweets) often reduces food intake without significantly improving the clinical status.

The role of inflammatory cytokines, including tumor necrosis factor (TNF, formerly cachectin), interleukin-1 (IL-1), and interleukin-6, has also been postulated.[9] Physiological changes in the regulation of food intake take place, even in the presence of the increased body fat and the increased rates of obesity that occur with age, some of which can be explained by altered patterns of physical activity.[10]

Generally speaking, individuals aged 65 years and older experience a mild loss of weight, a near doubling of adiposity, and a significant non-fat mass loss of 5% to 15%.[11]

Sarcopenia, the loss of skeletal muscle mass—and thus leading to a loss of protein—may play an important role in IWL. Muscle loss can be the result of negative nitrogen balance that occurs with normal aging and with inadequate protein intake, which is commonly observed among the elderly.[12,13] Age-related changes in anabolic hormones may contribute to non-fat mass loss. Low testosterone levels in men correlate with the loss of lean body mass, and loss of estrogen during menopause is associated with non-fat mass loss in women.[14,15]

Growth hormone appears to play an important role in body composition; growth hormone levels may decrease by 14% per decade.[16] It has been found that replacement of growth hormone in older people results in increased lean body mass and reduced fat mass.[17]

Some of the consequences of IWL include:

- anemia
- decreased cognition
- edema
- falls
- hip fractures
- immune dysfunction
- infections
- muscle loss
- osteoporosis
- pressure sores

HISTORY AND EVALUATION

Clinicians should seek common treatable causes of weight loss in elderly patients. One approach is to distinguish among four basic causes of weight loss: anorexia, dysphagia, socioeconomic factors, and weight loss despite normal intake.[18] Often, these causes are interrelated. Whichever approach is used, the initial evaluation can yield a reason for weight loss in a large number of patients.[19]

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The medical evaluation should begin with a comprehensive history and physical examination, with emphasis on relevant medical, pharmacological, psychological, and functional factors. It is important to determine whether the patient is taking in an adequate number of calories; questioning the caregiver is essential.

The activities of daily living (ADL) and the instrumental activities of daily living (IADL) are important measures of patient function. A higher level of functioning is required to perform IADL. A variety of medical conditions can impair these activities. In addition, cognition, memory, vision, and hearing need to be evaluated.

A change in living habits may also indicate cognitive decline; clinicians should assess for cognitive dysfunction caused by depression and dementia.

Depression not only is an indicator of poor function but also is an independent factor associated with weight loss.[20] It has been found that weight loss precedes the development of Alzheimer's disease in 50% of patients and may be secondary to anosmia (loss of sense of smell).[21]

Using the "Get Up and Go" test to screen for physical function, functional reach, and handgrip may elaborate difficulty with the strength and mobility that patients need to maneuver in the grocery store or kitchen. A thorough review of medications may reveal that patients are experiencing polypharmacy, which is known to interfere with taste and to cause anorexia.[18,22]

Many individual medications have been associated with unintentional weight loss (Table 1).[23] These include some selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac®, Eli Lilly).[24] Other SSRIs may have a lesser anorectic effect, but patients taking those drugs should still be followed closely.

Sedatives and narcotic analgesics may interfere with cognition and the ability to eat.[25] A reduction in the dosage of psychotropic medications may also cause weight loss, possibly by unmasking an underlying disorder such as anxiety or depression.[26]

Table 1 Drugs Associated with Weight Loss

SSRI Antidepressants
- Citalopram hydrobromide (Celexa®, Forest)
- Fluoxetine (Prozac®, Eli Lilly)
- Paroxetine (Paxil®, GlaxoSmithKline)*

Cardiac Agents
- Bepridil (Vascor®, Ortho-McNeil)*
- Digoxin (Lanoxin®, GlaxoSmithKline)
- Furosemide (Lasix®, Aventis)

Stimulants and Appetite Suppressants
- Amphetamine/dextroamphetamine (Adderall®, Shire)
- Dextroamphetamine sulfate (Dexedrine®, GlaxoSmithKline)
- Methylphenidate (Ritalin®, Novartis; Concerta®, Alza)
- Pemoline (Cylert®, Abbott)
- Phentermine (e.g., Ionamin®, Celltech)
- Sibutramine HCl monohydrate (Meridia®, Abbott)

Benzodiazepines
- Clonazepam (Klonopin®, Roche)
- Lorazepam (Ativan®, Wyeth-Ayerst)

Miscellaneous
- Metformin (Glucophage®, Bristol-Myers Squibb)

* Can also cause increased appetite.
From *Drug Facts and Comparisons, 2002*. Micromedex Health Care Series (2002); and *Drug Information Handbook* (1999–2000), 7th ed, LexiComp.

PHYSICAL EXAMINATION

The physical examination of elderly patients with unintentional weight loss is directed by the information gathered during the history-taking process. It is particularly important to evaluate the oral cavity and the respiratory and gastrointestinal systems.

Anthropometric measurements, specifically the patient's height and weight, are of prime importance and should be compared with minimum and maximum adult weights. The patient's body mass index (BMI) can be calculated by dividing the weight in kilograms by the square of the height in meters. In one study,[27] a BMI of less than 22 kg/m^2 in women and less than 23.5 kg/m^2 in men was associated with increased mortality. In another study,[28] the optimal BMI in older adults was 24 to 29 kg/m^2. Because of the difficulty in determining height in some elderly patients (e.g., those who are confined to beds or wheelchairs), the BMI is less commonly used than weight.

Stevens et al. found that after age 75, mortality rates increased with a BMI below 25.[29] Reynolds et al.[30] and Landi et al.[31] demonstrated that a low BMI among community-dwelling elderly adults was associated with increased mortality independently of any pre-existing diseases.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of unintended weight loss in the elderly can be extensive. The most commonly identified causes are summarized with the mnemonic *"Meals on Wheels"*:[32]

Medications (e.g., digoxin, theophylline, antipsychotic agents)
Emotional problems (depression)
Anorexia tardive (nervosa) or alcoholism
Late-life paranoia
Swallowing disorders (dysphagia)
Oral problems (e.g., poorly fitting dentures)
Nosocomial infections (tuberculosis, *Helicobacter pylori*, *Clostridium difficile*)
Wandering and other dementia-related behaviors
Hyperthyroidism, hypercalcemia, hypoadrenalism
Enteric problems (e.g., malabsorption)
Eating problems (e.g., difficulty in self-feeding)
Low-salt, low-cholesterol diet
Stones (cholelithiasis)

Causes of weight loss in residents of long-term-care facilities may differ from those in ambulatory patients. In one study, depression was present in 36% of nursing-home residents with unintentional weight loss.[10] Overall, psychiatric disorders, including depression, account for 58% of the cases of involuntary weight loss in nursing-home patients.[26]

DIAGNOSTIC STUDIES

Although unexplained weight loss in the elderly can have myriad causes, an undirected ("shotgun") approach to labora-

tory tests and other diagnostic studies is rarely fruitful. Initial targeted studies can determine the cause in many patients.[9,19]

The findings of the history and physical examination guide the initial diagnostic assessment. A reasonable initial panel of tests in the elderly patient with unintentional weight loss includes:

- a fecal occult blood test to screen for cancer.
- a complete blood count to assess for infection, iron deficiency anemia, or lymphoproliferative disorder.
- a chemistry profile to check for evidence of diabetes mellitus, renal dysfunction, or dehydration.
- a thyroid-stimulating hormone test to check for hypothyroidism or hyperthyroidism.
- a urinalysis to check for evidence of infection, renal dysfunction, or dehydration.

An upper gastrointestinal (GI) series (radiography or endoscopy) may be warranted in patients with GI-related symptoms or in patients with persistent weight loss.

Serum albumin levels below 3.5 g/dl occur in 6% to 43% of nursing-home residents. Hypoalbuminemia is commonly considered a sign of malnutrition. However, low serum albumin may be a better indication of inflammation than malnutrition caused by cytokine excess. This excess inhibits albumin synthesis in the liver and causes albumin leakage into the extracellular space, making albumin a poor marker of nutritional status.

MANAGEMENT

The treatment of unintentional weight loss is directed at identifying the underlying causes (Figure 1). While the evaluation is proceeding or if a cause is not well defined, the goal is to prevent further weight loss. Initiating nutritional support early may help to avoid some of the complications related to weight loss.[28]

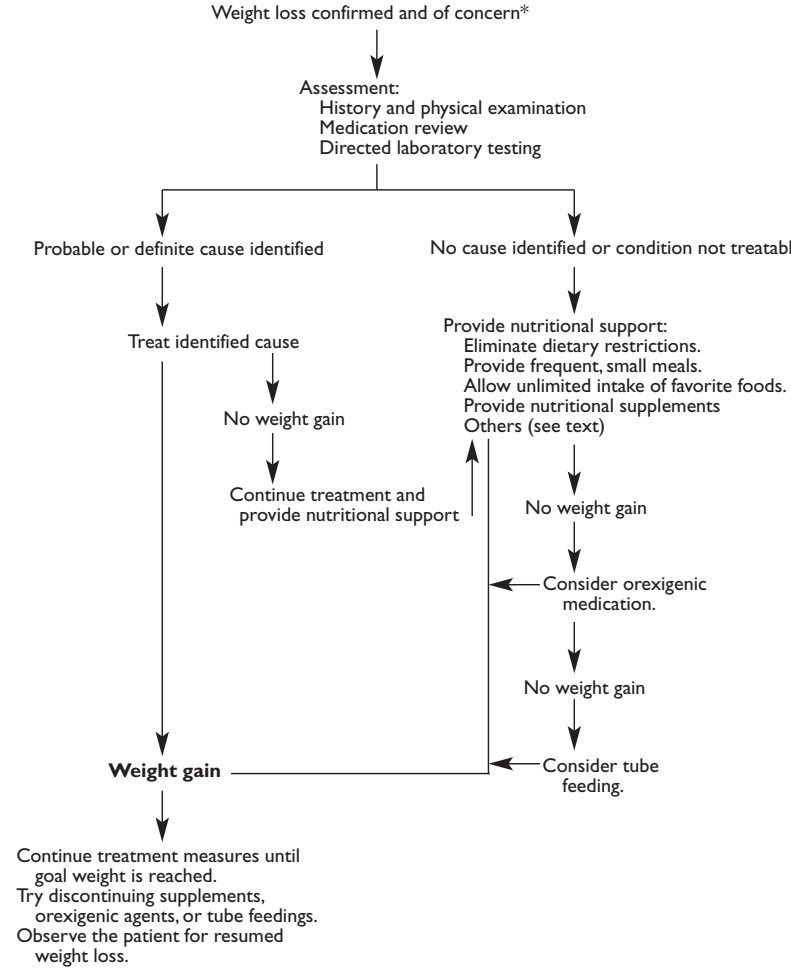
The contributions of dietitians, speech therapists (for oropharyngeal and swallowing evaluations), and social services personnel cannot be overestimated; the efforts of these skilled personnel can improve many strategies to increase food intake. In long-term care facilities, the food service manager and caregivers can often offer individualized suggestions for facilitating food intake.

Because restricted diets are often unpalatable, one early intervention is to remove dietary limitations, such as restrictions on the intake of salty or high-cholesterol foods. Patients with diabetes mellitus may also be given a less restrictive diet; in some instances, weight loss in these patients may reflect overzealous blood glucose control. However, blood sugar and glycosylated hemoglobin levels should continue to be monitored in patients with diabetes mellitus.

Adding flavor enhancers that amplify the intensity of food odors may be useful in patients with hyposmia.[23] Patients with dysphagia may require puréed foods and thickened liquids.

Patients may benefit from simply being offered frequent, small servings of foods that they like. Large portions may be overwhelming and may actually discourage intake.

When possible, physical exercise and even physical therapy should be encouraged, because increased activity has been shown to promote appetite and food intake. One study found that caloric intake was greater in patients who received both



**Weight loss of concern is generally defined in several ways: (1) loss of 5% to 10% of body weight in the previous one to 12 months or (2) loss of 2.25 kg (5 lb) in the previous three months. Nursing-home guidelines require evaluation if there is a 10% loss in the previous six months, a 5% loss in the previous month or a 2% loss in the previous week.*

Figure 1 Management of weight loss in elderly adults. (From Huffman GB. Evaluating and treating unintentional weight loss in the elderly. *Am Acad Fam Physicians* 2002;65:640–650. Copyright © 2002, American Academy of Family Physicians. All rights reserved.)

nutritional supplements and exercise than in patients who received only supplements.[33]

When liquid-calorie supplements are used, they should not be given with meals because total caloric intake does not improve with this method of administration.[34,35] Liquid supplements are preferable to solids.[35] With liquids, the gastric emptying time is quicker, and total caloric intake is more likely to be maximized. Wilson et al.[36] found that the liquid-calorie supplement, when given before meals, increased total caloric intake. Therefore, patients should take caloric supplements *between* meals, not *with* meals.

PHARMACOLOGICAL TREATMENT

The pharmacological treatment of primary anorexia and severe weight loss attempts to alter metabolic, neuroendocrine, and anabolic activities in order to provide symptomatic improvement.[37,38] Although several drugs have been used to promote weight gain (Table 2), none have been specifically indicated to treat weight loss in elderly patients and few have been studied in this population.[35]

Although medications may help to promote appetite and weight gain in older patients with unintentional weight loss, drugs should not be considered the first-line treatment. Even if drugs are successful in inducing weight gain, their long-term effects on quality of life are unknown.

Testosterone

Bakhshi et al. indicated that the administration of testosterone improved functioning in men during rehabilitation following hospitalization.[39] No studies have been conducted in long-term-care institutions. It would be reasonable to study the effects in malnourished men with low testosterone levels; testosterone supplementation might be more useful in sarcopenia but not in anorexia.

Oxandrolone

Another anabolic steroid, oxandrolone (Oxandrin®, Savient), decreased weight loss, nitrogen loss, and the length of hospitalization in elderly burn patients.[40] In patients with chronic obstructive pulmonary disease (COPD), 10 mg of oxandrolone twice daily produced weight gain.[41] Although the U.S. Food and Drug Administration (FDA) has approved oxandrolone for the treatment of IWL, this agent has not yet been studied in the elderly.

Megestrol Acetate

Megestrol acetate (MA) (Megace®, Bristol-Myers Squibb Oncology) 400–800 mg has been used successfully to treat cachexia in patients with AIDS or cancer.[42] Yeh et al. noted significant weight gain by three months after administration of MA.[43]

There have been several studies of MA in geriatric patients. Castle et al. reported weight gain in two of four patients receiving MA. Patients were to receive 400 mg of MA for six weeks.[44] In a randomized, double-blind study, 74% of 27 long-term care patients taking 800 mg of MA over 24 weeks showed a significant increase in weight, with the weight gain being greater in women than in men.[45]

In a small number of nursing-home residents receiving MA, Karcic et al. reported an increase in food intake, BMI, albumin, pre-albumin, hemoglobin, and lymphocyte count.[46] Yeh et al. showed that taking MA decreased IL-6, TNF p75 receptor, and soluble IL-2 receptor levels.[47] In addition, Lambert et al. showed that MA reduced IL-6 levels, suggesting that MA

Table 2 Drugs Associated with Weight Gain

Tricyclic Antidepressants
- Amitriptyline (Elavil®, AstraZeneca)
- Despramine (Norpramin®, Aventis)
- Impramine (Tofranil®, Mallinckrodt)
- Nortriptyline (Aventyl®, Eli Lilly; Pamelor®, Mallinckrodt)

Appetite Stimulants
- Dronabinol (Marinol®, Roxane)
- Megestrol acetate (Megace®, Bristol-Myers Squibb Oncology)

Anabolic Steroids
- Oxandrolone (Oxandrin®, Biotechnology General Corporation [Savient])

Glucocorticoids
- Dexamethasone (e.g., Decadron®, Merck)
- Methylprednisone (e.g., Medrol®, Pharmacia)
- Prednisone (e.g., Orasone®, Solvay)
- Prednisolone: (e.g., Prelone® Syrup, Muro)

Antipsychotic Agents
- Haloperidol (e.g., Haldol®, Ortho-MacNeil) and others in this group
- Olanzapine (Zyprexa®, Eli Lilly)*
- Risperidone (Risperdal®, Janssen)

Miscellaneous
- Cyproheptadine (Periactin®, Merck)
- Lithium (Eskalith®, GlaxoSmithKline; Lithobid®, Solvay)
- Omeprazole (Prilosec®, AstraZeneca)

* Zyprexa® is also associated with weight loss.
From *Drug Facts and Comparisons, 2002*. Micromedex Health Care Series (2002); and *Drug Information Handbook* (1999–2000), 7th ed, LexiComp.

Table 3 Established Pharmacological Treatments of Involuntary Weight Loss

Effect	Corticosteroids*	Progestins†	Prokinetics‡
Weight gain			
Nonfluid	–	+	–
Lean body mass	–	–	–
Anorexia	+	++	+
Chronic nausea	+	+	++
Early satiety	–	?	+
Fatigue or asthenia	+	(+)	–
Performance status	+	+	–
Quality of life or feeling of well-being	+	(+)	–

* Short-term application of prednisolone equivalent 20 to 50 mg for one to two weeks.
† Intermediate- to high-dose megestrol acetate or medroxyprogesterone acetate.
‡ Metoclopramide 10 to 15 mg is administered 30 minutes before meals or every four hours.
Key: – = no effect reported; + = mild effect; ++ = established effect; ? = controversial effect; (+) = possible effect.
Adapted from Strasser F, Bruera ED. Update on anorexia and cachexia. *Hematol Oncol Clin North Am* 2002;16(3):589–617. Copyright 2002, with permission from Elsevier.

might be useful in cytokine excess states, as measured by C-reactive protein values.[48]

One drawback of MA is its tendency to increase fat mass; with an exercise program, however, non-fat mass may increase. The exact duration and optimal dose of MA in geriatric patients are not known. One retrospective study suggested that MA at dosages ranging from 80 mg to 400 mg effectively reversed IWL in nursing-home patients after three months of use.[49]

It is known that MA can cause edema, constipation, delirium, hypogonadism, hyperglycemia, adrenal insufficiency, and possibly deep vein thrombosis. These side effects may limit its usefulness.[46]

Table 3 shows a comparison between the effects and the prokinetics of corticosteroids and those of progestins.[50]

Mirtazapine

The treatment of depression itself may cause weight gain. Mirtazapine (Remeron®, Organon) has been shown to increase appetite and promote weight gain while it also treats the underlying depression.[51] Depressed patients should receive treatment without dietary restriction with orexigenic medications.

Dronabinol

The cannabinoid dronabinol (Marinol®, Roxane) is indicated for the treatment of anorexia accompanied by weight loss; there has been an interest in applying its benefits as an appetite stimulant in patients with cancer[52–54] and acquired immunodeficiency syndrome (AIDS).[55,56]

This drug has also been studied, with some promising results, in patients with Alzheimer's disease.[57] Because of the side effects of dizziness, confusion, and somnolence, however, it should not be used in patients whose cognitive deficits are not well defined. The drug appears to cause weight gain in Alzheimer's patients who are agitated.[57] To avoid delirium, patients should initially take 2.5 mg before bedtime; after one week, patients should take it before the evening meal. If there is no response in two weeks, patients can take 2.5 mg at dinner and before going to bed.

Other potential benefits of dronabinol are its antimemetic and analgesic effects.[58–60]

Growth Hormone

Recombinant human growth hormone, or somatotropin (Serostim®, Serono), can increase lean body mass. However, this hormone is very expensive, and its adverse effects include carpal tunnel syndrome, headache, arthralgias, myalgias, and gynecomastia.[61] Currently, growth hormone cannot be recommended for use in older malnourished patients because data regarding its efficacy are unclear.

Gherelin

Ghrelin, a peptide hormone produced by the fundus of the stomach, increases food intake and releases growth hormone. Ghrelin appears to be a potentially excellent medication for the treatment of anorexia and weight loss.

Cyproheptadine

Cyproheptadine (Periactin®, Merck) is an antihistaminic and antiserotoninergic medication that causes a mild increase in appetite. In one study,[62] patients with a median age of 65 years who received cyproheptadine experienced a decrease in their rate of weight loss but no weight gain. Drowsiness and dizziness are side effects that may make the use of this medication particularly problematic in elderly patients.

Metoclopramide

Metoclopramide (Reglan®, Schwarz Pharma), a prokinetic agent, may relieve nausea-induced anorexia,[63] but it can cause severe dystonia and may precipitate parkinsonian symptoms in these patients.

SUMMARY

Involuntary weight loss is associated with increased morbidity and mortality in older adults. Identifying the multifactorial causes of this condition in these patients poses a challenge to clinicians, and a comprehensive geriatric assessment aids in reviewing the multitude of potential causes. Patients with depression should receive an antidepressant that has orexigenic properties. Orexigenic drugs should be used when no obvious treatable cause of IWL is present and when nonpharmacological interventions are ineffective. Close monitoring for potential side effects is necessary in elderly patients. More studies are needed to define the role of these medications in end-of-life and palliative care.

REFERENCES

1. Bouras EP, Lange SM, Scolapio JS. Rational approach to patients with unintentional weight loss. *Mayo Clin Proc* 2001;76(9):923–929.
2. Smith GP, Gibbs J. The satiating effects of cholecystokinin. *Curr Concepts Nutr* 1988;16:35–40.
3. Levine AS, Morley JE. Peripherally administered somatostatin reduces feeding by a vagal mediated mechanism. *Pharmacol Biochem Behav* 1982;16:897–902.
4. Morley JE, Flood JF, Horowitz M, et al. Modulation of food intake by peripherally administered amylin. *Am J Physiol* 1994;267:R178–R184.
5. Schwartz MW, Woods SC, Porte D Jr, et al. Central nervous system control of food intake. *Nature* 2000;404(6778):661–671.
6. Sanders CM. *The Management of Terminal Illness*. New York: Hospital Medicine Publications; 1967.
7. Fabiny AR, Kiel DP. Assessing and treating weight loss in nursing home patients. *Clin Geriatr Med* 1997;13:737–751.
8. Buckler DA, Kelber ST, Goodwin JS. The use of dietary restriction in malnourished nursing home patients. *J Am Geriatric Soc* 1994;42:1100–1102.
9. Reife CM. Involuntary weight loss. *Med Clin North Am* 1995;79:299–313.
10. Morley JE. Anorexia of aging: Physiologic and pathologic. *Am J Clin Nutr* 1997;66:760–773.
11. Evans WJ, Campbell WW. Sarcopenia and age-related changes in body composition and functional capacity. *J Nutr* 1993;123(2 Suppl):465–468.
12. Monroe HN. Protein. *In:* Hartz SC, Russell RM, Rosenberg IH, eds. *Nutrition in the Elderly.* The Boston Nutritional Status Survey from the USDA Human Research Center on Aging, Tufts University. London: Smith–Gordon and Co., Ltd.; 1992:75–86.
13. Evans WJ. What is sarcopenia? *J Gerontol A Biol Sci Med Sci* 1995;50(Special No.):5–8.
14. Dionne IJ, Kinaman KA, Poehlman ET. Sacropenia and muscle function during menopause and hormone replacement therapy. *J Nutr Health Aging* 2000;4(3):156–161.
15. Mauras N, Hayes V, Welch S, et al. Testosterone deficiency in young men: Marked alterations in whole body protein kinetics,

strength, and adiposity. *J Clin Endocrinol Metab* 1998;83(6):1886–1892.
16. Iranmanesh A, Lizarralde G, Veldhuis JD. Age and relative adiposity are specific negative determinants of the frequency and amplitude of growth hormone (GH) secretory bursts and half-life of endogenous GH in healthy men. *J Clin Endocrinol Metab* 1991;73(5):1081–1088.
17. Cuneo RC, Judd S, Wallace JD, et al. The Australian multicenter trial of growth hormone (GH) treatment in GH-deficient adults. *J Clin Endocrinol Metab* 1998;83(1):107–116.
18. Gazewood JD, Mehr DR. Diagnosis and management of weight loss in the elderly. *J Fam Pract* 1998;47:19–25.
19. Marton KI, Sox HC, Krupp JR. Involuntary weight loss: Diagnostic and prognostic significance. *Ann Intern Med* 1981;95:568–574.
20. Markson EW. Functional, social, and psychological disability as causes of loss of weight and independence in older community-living people. *Clin Geriatr Med* 1997;13(4):639–652.
21. Barrett-Conner E, Edelstein S, Corey-Bloom J, Wiederholt W. Weight loss precedes dementia in community-dwelling older adults. *J Nutr Health Aging* 1998;2(2):113–114.
22. Carr-Lopez SM, Phillips SK. The role of medications in geriatric failure to thrive. *Drugs Aging* 1996;9:221–225.
23. Schiffman SS. Taste and smell losses in normal aging and disease. *JAMA* 1997;278:1357–1362.
24. Brymer C, Winograd CH. Fluoxetine in elderly patients: Is there cause for concern? *J Am Geriatr Soc* 1992;40:902–905.
25. Guigoz Y, Vellas B, Garry PJ. Assessing the nutritional status of the elderly: The Mini Nutritional Assessment as part of the geriatric evaluation. *Nutr Rev* 1996;54:S59–S65.
26. Morley JE, Kraenzle D. Causes of weight loss in a community nursing home. *J Am Geriatr Soc* 1994;42:583–585.
27. Calle EE, Thun MJ, Petrelli JM, Rodriguez C. Body mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999;341:1097–1105.
28. Beck AM, Ovesen L. At which body mass index and degree of weight loss should hospitalized elderly patients be considered at nutritional risk? *Clin Nutr* 1998;17:195–198.
29. Stevens J, Cai J, Pamuk ER, et al. The effect of age on the association between body mass index and mortality. *N Engl J Med* 1998;338(1):1–7.
30. Reynolds MW, Fredman L, Langenberg P, Magaziner J. Weight, weight change, mortality in a random sample of older community-dwelling women. *J Am Geriatr Soc* 1999;47(12):1409–1414.
31. Landi F, Zuccala G, Gambassi G, et al. Body mass index and mortality among older people living in the community. *J Am Geriatr Soc* 1999;47(9):1072–1076.
32. Morley JE, Silver AJ. Nutritional issues in nursing home care. *Ann Intern Med* 1995;123:850–859.
33. Fiatarone MA, O'Neill EF, Ryan ND, et al. Exercise training and nutritional supplements for physical frailty in very elderly people. *N Engl J Med* 1994;330:1769–1775.
34. Lipschitz DA. Approaches to the nutritional support of the older patient. *Clin Geriatr Med* 1995;11:715–724.
35. Morley JE. Anorexia in older persons: Epidemiology and optimal treatment. *Drugs Aging* 1996;8:134–155.
36. Wilson MM, Purushothaman R, Morley JE. Effect of liquid dietary supplements on energy intake in the elderly. *Am J Clin Nutr* 2002;75(5):944–947.38.
37. Bruera E, Sweeney C. Cachexia and asthenia in cancer patients. *Lancet Oncol* 2000;1:138–147.
38. Gagnon B, Bruera E. A review of the drug treatment of cachexia associated with cancer. *Drugs* 1998;55(5):675–688.
39. Bakashi V, Elliot M, Getili A, et al. Testosterone improves rehabilitation outcomes in ill older men. *J Am Geriatr Soc* 2000;48:550–553.
40. Demling R, DeSanti L. The beneficial effects of the anabolic steroid oxandrolone in the geriatric burn population. *Wounds* 2003;15:54–58.
41. Yeh SS, DeGuzman B, Kramer T. Reversal of COPD-associated weight loss using the anabolic agent oxandrolone. *Chest* 2002;122:421–428.
42. Chen HC, Leung SW, Wang CJ, et al. Effect of megestrol acetate and Propulsid on nutritional improvement in patients with head and neck cancers undergoing radiotherapy. *Radiother Oncol* 1997;43:759.
43. Yeh S, Wu S, Lee T, et al. Improvement in quality of life measures and stimulation of weight gain after treatment with megestrol acetate oral suspension in geriatric cachexia: Results of a double-blind, placebo-controlled study. *J Am Geriatr Soc* 2000;48:485–492.
44. Castle S, Nguyen C, Joaquin A, et al. Megestrol acetate suspension therapy in the treatment of geriatric/cachexia in nursing home patients. *J Am Geriatr Soc* 1995;43:835–836.
45. Van Roenn JH, Armstrong D, Katler DP, et al. Magesterol acetate in patients with acquired immunodeficiency syndrome–related cachexia. *Ann Intern Med* 1994;121:393–399.
46. Karcic E, Philpot C, Morley JE. Treating malnutrition with megestrol acetate: Literature review and review of our experience. *J Nutr Health Aging* 2002;6:191–200.
47. Yeh SS, Wu SY, Levine DM, et al. The correlation of cytokine levels with body weight after megestrol acetate treatment in geriatric patients. *J Gerontol A Biol Sci Med Sci* 2001;56:M48–M54.
48. Lambert CP, Sullivan DH, Evan WJ. Effects of testosterone replacement and/or resistance training on interleukin-6, tumor necrosis factor alpha, and leptin in elderly men ingesting megestrol acetate: A randomized control trial. *J Gerontol A Biol Sci* 2003;58:165–170.
49. Lewko MP, Soliman I. Effectiveness of megestrol acetate (MA) in treating involuntary weight loss in nursing home patients (Abstract). *J Am Med Directors Assoc* 2000;1:19.
50. Strasser F, Bruera ED. Update on anorexia and cachexia. *Hematol Oncol Clin North Am* 2002;16(3):589–617.
51. Fawcett J, Barkin RL. Review of the results from clinical studies on the efficacy, safety, and tolerability of mirtazapine for the treatment of patients with major depression. *J Affect Disord* 1998;51:267–285.
52. Jatoi A, Windschitl HE, Loprinzi CL, et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: A North Central Cancer Treatment Group study. *J Clin Oncol* 2002;20:567–573.
53. Berry EM, Mechoulam R. Tetrahydrocannabinol and endocannabinoids in feeding and appetite. *Pharmacol Ther* 2002;95:185–190.
54. Walsh D, Nelson KA, Mahmoud FA. Established and potential therapeutic applications of cannabinoids in oncology. *Support Care Cancer* 2001;11:137–143.
55. Beal JE, Olson R, Lefkowitz I, et al. Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome–associated anorexia. *J Pain Symptom Manage* 1997;14(1):7–14.
56. Beal JE, Olson R, Lefkowitz I, et al. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *J Pain Symptom Manage* 1995;10:89–97.
57. Volicer L, Stelly M, Morris J, et al. Effects of dronabinol on anorexia and disturbed behavior in patients with Alzheimer's disease. *Int J Geriatr Psychiatry* 1997;12:913–919.
58. Gonzales-Rasales F, Walh D. Intractable nausea and vomiting due to gastrointestinal mucosal metastases relieved by tetrahydrocannabinol. *J Pain Symptom Manage* 1997;4:311–314.
59. Glemont-Gnamien S, Atlanti S, et al. The therapeutic use of delta 9 tetrahydrocannabinol in refractory neuropathic pain. *Presse Med* 2002;31:1840–1845.
60. Wallace JI, Schwartz RS. Involuntary weight loss in elderly outpatients: Recognition, etiologies, and treatment. *Clin Geriatr Med* 1997;13:717–735.
61. Schambelan M, Mulligan IK, Grunfeld C, et al. Recombinant human growth hormone in patients with HIV-associated wasting: A randomized, placebo-controlled trial. Serostim Study Group. *Ann Intern Med* 1996;125:873–882.
62. Kardinal CG, Loprinzi CL, Schaid DJ, et al. A controlled trial of cyproheptadine in cancer patients with anorexia and/or cachexia. *Cancer* 1990;65:2657–2662.
63. Gorter R. Management of anorexia–cachexia associated with cancer and HIV infection. *Oncology [Huntingt]* 1991;5:13–17.