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; 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.2 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
Weight Loss in the Elderly

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. 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**

<table>
<thead>
<tr>
<th>SSRI Antidepressants</th>
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<tbody>
<tr>
<td>Citalopram hydrobromide (Celexa®, Forest)</td>
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<tr>
<td>Fluoxetine (Prozac®, Eli Lilly)</td>
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<tr>
<td>Paroxetine (Paxil®, GlaxoSmithKline)*</td>
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<tr>
<td><strong>Cardiac Agents</strong></td>
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<tr>
<td>Bepridil (Vascor®, Ortho-McNeil)*</td>
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<tr>
<td>Digoxin (Lanoxin®, GlaxoSmithKline)</td>
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<tr>
<td>Furosemide (Lasix®, Aventis)</td>
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<tr>
<td><strong>Stimulants and Appetite Suppressants</strong></td>
</tr>
<tr>
<td>Amphetamine/dextroamphetamine (Adderall®, Shire)</td>
</tr>
<tr>
<td>Dextroamphetamine sulfate (Dexedrine®, GlaxoSmithKline)</td>
</tr>
<tr>
<td>Methylphenidate (Ritalin®, Novartis; Concerta®, Alza)</td>
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<tr>
<td>Pemoline (Cylert®, Abbott)</td>
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<tr>
<td>Phentermine (e.g., Ionamin®, Celltech)</td>
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<tr>
<td>Sibutramine HCl monohydrate (Meridia®, Abbott)</td>
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<tr>
<td><strong>Benzodiazepines</strong></td>
</tr>
<tr>
<td>Clonazepam (Klonopin®, Roche)</td>
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<tr>
<td>Lorazepam (Ativan®, Wyeth-Ayerst)</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>Metformin (Glucophage®, Bristol-Myers Squibb)</td>
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</table>


**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/m² in women and less than 23.5 kg/m² in men was associated with increased mortality. In another study,28 the optimal BMI in older adults was 24 to 29 kg/m². 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.20

**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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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...
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 supplementation might be more useful in sarcopenia but not in anorexia.

**Table 2** Drugs Associated with Weight Gain

<table>
<thead>
<tr>
<th>Tricyclic Antidepressants</th>
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<tbody>
<tr>
<td>* Amitriptyline (Elavil®, AstraZeneca)</td>
<td></td>
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<tr>
<td>* Desipramine (Norpramin®, Aventis)</td>
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<td></td>
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<tr>
<td>* Imipramine (Tofranil®, Mallinckrodt)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Nortriptiline (Aventyl®, Eli Lilly; Pamelor®, Mallinckrodt)</td>
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</table>

**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., Prealone® Syrup, Muro) | | |

**Antipsychotic Agents**

| Haloperidol (e.g., Haldol®, Ortho-MacNeil) and others in this group | | |
| Olanzapine (Zyprexa®, Eli Lilly) \(^{45}\) | | |
| Risperidone (Risperdal®, Janssen) | | |

**Miscellaneous**

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

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\(^{45}\) Zyprexa® is also associated with weight loss.


**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 3** Established Pharmacological Treatments of Involuntary Weight Loss

<table>
<thead>
<tr>
<th>Effect</th>
<th>Corticosteroids*</th>
<th>Progestins†</th>
<th>Prokinetics‡</th>
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</thead>
<tbody>
<tr>
<td>Weight gain</td>
<td>−</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Nonfluid</td>
<td>Lean body mass</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Anorexia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic nausea</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Early satiety</td>
<td>−</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Fatigue or asthenia</td>
<td>+</td>
<td>(+)</td>
<td>−</td>
</tr>
<tr>
<td>Performance status</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Quality of life or feeling of well-being</td>
<td>+</td>
<td>(+)</td>
<td>−</td>
</tr>
</tbody>
</table>

* 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.

might be useful in cytokine excess states, as measured by 
C-reactive protein values.58

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 possi-
ibly deep vein thrombosis. These side effects may limit its use-
fulness.46

Table 3 shows a comparison between the effects and the pro-
kinetics of corticosteroids and those of progestins.56

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 
apetite stimulant in patients with cancer52–54 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, how-
ever, 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 din-
nner and before going to bed.

Other potential benefits of dronabinol are its antinmectic 
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.51 Currently, growth hormone cannot be rec-
commended for use in older malnourished patients because 
data regarding its efficacy are unclear.

Ghrelin

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 antiserotonergic medication that causes a mild increase 
in appetite. In one study,52 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 mor-
bidity and mortality in older adults. Identifying the multi-
factorial causes of this condition in these patients poses a 
challenge to clinicians, and a comprehensive geriatric assess-
ment 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.

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