

Chapter 50 | Unintentional Weight Loss

Cardinal Manifestations and Presentation of Diseases | Part 2 – Cardinal Manifestations & Presentation | DETAILED EDITION

KEY CLINICAL POINTS

1. Clinically important weight loss is defined as the loss of >5% of body weight over a period of 6–12 months.
2. In patients with no known cause of weight loss, prognosis is generally better than those with known causes, particularly when the source is neoplastic.
3. Significant weight loss is associated with increased mortality within 1–2 years.
4. Up to one-quarter of patients have no identifiable cause despite extensive investigation.
5. One-third of UWL cases are due to organic disease, and one-quarter are due to malignant neoplasms.
6. The 'anorexia of aging' is caused by declining chemosensory function, reduced chewing efficiency, slowed gastric emptying, and alterations in the neuroendocrine axis.
7. Malignancy that reveals itself through significant weight loss usually has a very poor prognosis.
8. Up to 20% of all cancer deaths are caused directly by cachexia (through immobility and/or cardiac/respiratory failure).
9. Risk factors for undiagnosed cancer include a history of smoking (particularly for men), localizing symptoms, and abnormal laboratory tests.
10. Table 50-1 categorizes causes into: Malignant neoplasms, Chronic inflammatory/infectious diseases, Metabolic disorders, and Psychiatric disorders.

FIGURES IN THIS CHAPTER

No figures extracted.

1. DEFINITION & OVERVIEW

- Unintentional weight loss (UWL) is frequently insidious and can have important implications, often serving as a harbinger of serious underlying disease.
- Clinically important weight loss is defined as the loss of >5% of body weight over a period of 6–12 months.
- UWL is not uncommon in individuals aged ≥ 65 years.
- It can be challenging to recognize in patients with preexisting obesity or inadequate documentation of previous weights.

- There is no identifiable cause in up to one-quarter of patients despite extensive investigation.
- People with no known cause of weight loss generally have a better prognosis than those with known causes, particularly when the source is neoplastic.

1.1 Epidemiology & Prognosis

- Weight loss in older persons is associated with a variety of deleterious effects, including falls and fractures, pressure ulcers, impaired immune function, and decreased functional status.
- Not surprisingly, significant weight loss is associated with increased mortality within 1–2 years.
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2. EPIDEMIOLOGY

- UWL is frequently insidious and can have important implications, often serving as a harbinger of serious underlying disease.
- UWL is not uncommon in individuals aged ≥ 65 years.
- There is no identifiable cause in up to one-quarter of patients despite extensive investigation.
- People with no known cause of weight loss generally have a better prognosis than those with known causes, particularly when the source is neoplastic.

2.1 Age Distribution & Mortality

- UWL is not uncommon in individuals aged ≥ 65 years.
- Significant weight loss is associated with increased mortality within 1–2 years.
- Weight loss in older persons is associated with a variety of deleterious effects, including falls and fractures, pressure ulcers, impaired immune function, and decreased functional status.

3. ETIOLOGY & PATHOPHYSIOLOGY

- Most causes of UWL belong to one of four categories: (1) malignant neoplasms, (2) chronic inflammatory or infectious diseases, (3) metabolic disorders (e.g., hyperthyroidism and diabetes), or (4) psychiatric disorders.
- Not infrequently, more than one of these causes can be responsible for UWL.
- Depending upon patient populations, UWL is caused by malignant disease in a quarter of patients and by organic disease in one-third, with the remainder due to psychiatric disease, medications, or uncertain causes.
- Risk factors for undiagnosed cancer include a history of smoking, particularly for men, localizing symptoms, and abnormal laboratory tests.

3.1 Physiology of Weight Regulation with Aging

- Among healthy aging people, total body weight peaks in the sixth decade of life and generally remains stable until the ninth decade, after which it gradually falls.
- In contrast, lean body mass (fat-free mass) begins to decline at a rate of 0.3 kg per year in the third decade, and the rate of decline increases further beginning at age 60 in men and age 65 in women.
- These changes in body composition largely reflect the age-dependent decline in growth hormone secretion and, consequently, circulating levels of insulin-like growth factor type I (IGF-I) that occur with normal aging.

- Loss of sex steroids, at menopause in women and more gradually in men, also contributes to these changes in body composition.
- In the healthy elderly, an increase in fat tissue balances the loss in lean body mass until very old age, when loss of both fat and skeletal muscle occurs.
- Age-dependent changes also occur at the cellular level. Telomeres shorten, and body cell mass—the fat-free portion of cells—declines steadily with aging.
- Between ages 20 and 80, mean energy intake is reduced by up to 1200 kcal/d in men and 800 kcal/d in women.
- Decreased hunger is a reflection of reduced physical activity and loss of lean body mass, producing lower demand for calories and food intake.
- Several important age-associated physiologic changes also predispose elderly persons to weight loss, such as declining chemosensory function (smell and taste), reduced efficiency of chewing, slowed gastric emptying, and alterations in the neuroendocrine axis, including changes in levels of leptin, cholecystikinin, neuropeptide Y, and other hormones and peptides.
- These changes are associated with early satiety and a decline in both appetite and the hedonistic appreciation of food.
- Collectively, they contribute to the 'anorexia of aging.'
- As noted below, these physiologic changes with aging may be accompanied by social isolation, poverty, and immobility, further contributing to undernutrition.

3.2 Mechanisms of Weight Loss

- Malignant neoplasms, chronic inflammatory or infectious diseases, metabolic disorders, and psychiatric disorders are the primary categories.
- Cardiovascular and pulmonary diseases cause UWL through increased metabolic demand and decreased appetite and caloric intake.
- Repeated surgeries may lead to weight loss because of reduced caloric intake and increased metabolic demands resulting from a systemic inflammatory response.
- Uremia produces nausea, anorexia, and vomiting.
- Connective tissue diseases may increase metabolic demand and disrupt nutritional balance.
- As the incidence of diabetes mellitus increases with aging, the associated glucosuria can contribute to weight loss.
- Hyperthyroidism in the elderly may have less prominent sympathomimetic features and may present as 'apathetic hyperthyroidism' or T toxicosis.
- Neurologic injuries such as stroke, quadriplegia, and multiple sclerosis may lead to visceral and autonomic dysfunction that can impair caloric intake.
- Dysphagia from these neurologic insults is a common mechanism.
- Functional disability that compromises activities of daily living (ADLs) is a common cause of undernutrition in the elderly.
- Visual impairment from ophthalmic or central nervous system disorders such as a tremor can limit the ability of people to prepare and eat meals.
- UWL may be one of the earliest manifestations of Alzheimer's dementia.
- Isolation and depression are significant causes of UWL that may manifest as an inability to care for oneself, including nutritional needs.
- A cytokine-mediated inflammatory metabolic cascade can be both a cause of and a manifestation of depression.
- Bereavement can be a cause.

4. CLINICAL FEATURES

- UWL is frequently insidious and can have important implications, often serving as a harbinger of serious underlying disease.
- Clinically important weight loss is defined as the loss of >5% of body weight over a period of 6–12 months.
- UWL is not uncommon in individuals aged ≥65 years.
- It can be challenging to recognize in patients with preexisting obesity or inadequate documentation of previous weights.

4.1 Complications & Deleterious Effects

- Weight loss in older persons is associated with a variety of deleterious effects, including falls and fractures, pressure ulcers, impaired immune function, and decreased functional status.
- Not surprisingly, significant weight loss is associated with increased mortality within 1–2 years.
- Oral and dental problems are easily overlooked and may manifest with halitosis, poor oral hygiene, xerostomia, inability to chew, reduced masticatory force, nonocclusion, temporomandibular joint syndrome, edentulousness, and pain due to caries or abscesses.
- Visual impairment from ophthalmic or central nervous system disorders such as a tremor can limit the ability of people to prepare and eat meals.
- UWL may be one of the earliest manifestations of Alzheimer's dementia.
- Isolation and depression are significant causes of UWL that may manifest as an inability to care for oneself, including nutritional needs.

5. DIFFERENTIAL DIAGNOSIS

- Most causes of UWL belong to one of four categories: (1) malignant neoplasms, (2) chronic inflammatory or infectious diseases, (3) metabolic disorders (e.g., hyperthyroidism and diabetes), or (4) psychiatric disorders.
- Not infrequently, more than one of these causes can be responsible for UWL.
- Depending upon patient populations, UWL is caused by malignant disease in a quarter of patients and by organic disease in one-third, with the remainder due to psychiatric disease, medications, or uncertain causes.

5.1 Malignant Neoplasms

- The most common malignant causes of UWL are gastrointestinal, hepatobiliary, hematologic, lung, breast, genitourinary, ovarian, and prostate.
- Half of all patients with cancer lose some body weight; one-third lose more than 5% of their original body weight, and up to 20% of all cancer deaths are caused directly by cachexia (through immobility and/or cardiac/respiratory failure).
- The greatest incidence of weight loss is seen among patients with solid tumors.
- Malignancy that reveals itself through significant weight loss usually has a very poor prognosis.
- Risk factors for undiagnosed cancer include a history of smoking, particularly for men, localizing symptoms, and abnormal laboratory tests.

5.2 Gastrointestinal Disorders

- In addition to malignancies, gastrointestinal diseases are among the most prominent causes of UWL.

- Peptic ulcer disease, inflammatory bowel disease, dysmotility syndromes, chronic pancreatitis, celiac disease, constipation, and atrophic gastritis are some of the more common entities.
- Oral and dental problems are easily overlooked and may manifest with halitosis, poor oral hygiene, xerostomia, inability to chew, reduced masticatory force, nonocclusion, temporomandibular joint syndrome, edentulousness, and pain due to caries or abscesses.

5.3 Endocrine and Metabolic

- Hyperthyroidism in the elderly may have less prominent sympathomimetic features and may present as 'apathetic hyperthyroidism' or T toxicosis.
- As the incidence of diabetes mellitus increases with aging, the associated glucosuria can contribute to weight loss.
- Pheochromocytoma and adrenal insufficiency are also listed causes.

5.4 Cardiac, Respiratory, and Renal

- Cardiovascular and pulmonary diseases cause UWL through increased metabolic demand and decreased appetite and caloric intake.
- Chronic ischemia, chronic congestive heart failure, emphysema, and chronic obstructive pulmonary disease are listed causes.
- Renal insufficiency is listed as a cause.

5.5 Infections

- Tuberculosis, fungal diseases, parasites, subacute bacterial endocarditis, and HIV are well-documented causes of UWL.
- Cardiovascular and pulmonary diseases cause UWL through increased metabolic demand and decreased appetite and caloric intake.

5.6 Medications

- Sedatives, antibiotics, nonsteroidal anti-inflammatory drugs, serotonin reuptake inhibitors, metformin, levodopa, angiotensin-converting enzyme inhibitors, and other drugs are listed causes.

5.7 Age-Related, Neurologic, and Social Factors

- Age-related factors include physiologic changes, visual impairment, decreased taste and smell, and functional disabilities.
- Neurologic factors include stroke, Parkinson's disease, neuromuscular disorders, and dementia.
- Social factors include isolation and poverty.
- Psychiatric and behavioral factors include depression, anxiety, paranoia, bereavement, alcoholism, and eating disorders.
- Increased activity or exercise is listed as a cause.
- Idiopathic causes are listed.

6. INVESTIGATIONS & DIAGNOSIS

- There is no identifiable cause in up to one-quarter of patients despite extensive investigation.
- People with no known cause of weight loss generally have a better prognosis than those with known causes, particularly when the source is neoplastic.

6.1 Diagnostic Criteria

- Clinically important weight loss is defined as the loss of >5% of body weight over a period of 6–12 months.
- UWL is not uncommon in individuals aged ≥ 65 years.

6.2 Risk Factors for Undiagnosed Cancer

- Risk factors for undiagnosed cancer include a history of smoking, particularly for men, localizing symptoms, and abnormal laboratory tests.

7. MANAGEMENT & TREATMENT

- Management focuses on treating the underlying cause.
- There is no identifiable cause in up to one-quarter of patients despite extensive investigation.
- People with no known cause of weight loss generally have a better prognosis than those with known causes, particularly when the source is neoplastic.

7.1 General Approach

- Management focuses on treating the underlying cause.
- There is no identifiable cause in up to one-quarter of patients despite extensive investigation.
- People with no known cause of weight loss generally have a better prognosis than those with known causes, particularly when the source is neoplastic.

8. PROGNOSIS & COMPLICATIONS

- Weight loss in older persons is associated with a variety of deleterious effects, including falls and fractures, pressure ulcers, impaired immune function, and decreased functional status.
- Not surprisingly, significant weight loss is associated with increased mortality within 1–2 years.
- Half of all patients with cancer lose some body weight; one-third lose more than 5% of their original body weight, and up to 20% of all cancer deaths are caused directly by cachexia (through immobility and/or cardiac/respiratory failure).
- Malignancy that reveals itself through significant weight loss usually has a very poor prognosis.

8.1 Mortality & Cachexia

- Significant weight loss is associated with increased mortality within 1–2 years.
- Up to 20% of all cancer deaths are caused directly by cachexia (through immobility and/or cardiac/respiratory failure).
- Malignancy that reveals itself through significant weight loss usually has a very poor prognosis.

9. SPECIAL CONSIDERATIONS

- Age-dependent changes also occur at the cellular level. Telomeres shorten, and body cell mass—the fat-free portion of cells—declines steadily with aging.
- Between ages 20 and 80, mean energy intake is reduced by up to 1200 kcal/d in men and 800 kcal/d in women.
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- Several important age-associated physiologic changes also predispose elderly persons to weight loss, such as declining chemosensory function (smell and taste), reduced efficiency of chewing, slowed gastric emptying, and alterations in the neuroendocrine axis, including changes in levels of leptin,

cholecystokinin, neuropeptide Y, and other hormones and peptides.

- These changes are associated with early satiety and a decline in both appetite and the hedonistic appreciation of food.
- Collectively, they contribute to the 'anorexia of aging.'
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9.1 Aging Physiology

- Among healthy aging people, total body weight peaks in the sixth decade of life and generally remains stable until the ninth decade, after which it gradually falls.
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- Loss of sex steroids, at menopause in women and more gradually in men, also contributes to these changes in body composition.
- In the healthy elderly, an increase in fat tissue balances the loss in lean body mass until very old age, when loss of both fat and skeletal muscle occurs.

9.2 Social & Psychiatric Factors

- Social factors include isolation and poverty.
- Psychiatric and behavioral factors include depression, anxiety, paranoia, bereavement, alcoholism, and eating disorders.
- Isolation and depression are significant causes of UWL that may manifest as an inability to care for oneself, including nutritional needs.
- A cytokine-mediated inflammatory metabolic cascade can be both a cause of and a manifestation of depression.
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10. KEY PEARLS & CLINICAL TRAPS

- 'Anorexia of aging' is caused by declining chemosensory function, reduced chewing efficiency, slowed gastric emptying, and alterations in the neuroendocrine axis.
- 'Apathetic hyperthyroidism' or T toxicosis may present in the elderly with less prominent sympathomimetic features.
- UWL may be one of the earliest manifestations of Alzheimer's dementia.
- Malignancy that reveals itself through significant weight loss usually has a very poor prognosis.
- Up to 20% of all cancer deaths are caused directly by cachexia (through immobility and/or cardiac/respiratory failure).