

43 - 50 Unintentional Weight Loss

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Defecography (a dynamic barium enema including lateral views obtained during barium expulsion or a magnetic resonance defecogram) measures changes in rectoanal angle, degree of pelvic floor relaxation and perineal descent, as well as anatomic defects of the rectum such as internal mucosal prolapse, intussusception, and enteroceles or rectoceles. Surgically remediable conditions are identified in only a few patients with severe, whole-thickness intussusception or extremely large rectocele that fills preferentially during attempts at defecation instead of expulsion through the anus. Magnetic resonance defecography provides more information about the structure of the pelvic floor, distal colorectum, and anal sphincters and some information about the function during defecatory effort; however, it is performed in supine rather than seated position.

PART 2 Cardinal Manifestations and Presentation of Diseases Neurologic testing (electromyography) is rarely performed in the evaluation of patients with constipation. The absence of neurologic signs in the lower extremities suggests that any documented denervation of the puborectalis results from pelvic (e.g., obstetric) injury or from stretching of the pudendal nerve by chronic, long-standing straining. Constipation is common among patients with spinal cord injuries, neurologic diseases such as Parkinson's disease, multiple sclerosis, and diabetic neuropathy. Spinal-evoked responses during electrical rectal stimulation or stimulation of external anal sphincter contraction by applying magnetic stimulation over the lumbosacral cord identify patients with limited sacral neuropathies with sufficient residual nerve conduction to attempt biofeedback training. In summary, a balloon expulsion test is an important component of anorectal manometry as screening tests for anorectal dysfunction. An anatomic evaluation of the rectum or anal sphincters is rarely required when evaluating patients in whom obstructed defecation is suspected. Indications for anatomic evaluation are symptoms of rectal mucosal prolapse, pressure of the posterior wall of the vagina to facilitate defecation (suggestive of anterior rectocele), or prior pelvic surgery that may be complicated by enterocele.

TREATMENT Constipation After the cause of constipation is characterized, a treatment decision can be made. Slow-transit constipation requires aggressive medical or surgical treatment; conversely, anismus or pelvic floor dysfunction usually responds to biofeedback management (Fig. 49-5). The remaining ~60% of patients with constipation have normal colonic transit and can be treated symptomatically. Patients with spinal cord injuries or other neurologic disorders require a dedicated bowel regimen that often includes rectal stimulation, enema therapy, and carefully timed laxative therapy. Patients with constipation are treated with bulk (fiber, psyllium), osmotic (milk of magnesia, lactulose, polyethylene glycol), secretory (linaclotide, lubiprostone, plecanatide, tenapanor), and prokinetic or stimulant laxatives

(including diphenyl methanes such as bisacodyl and sodium picosulfate, senna alkaloids, and the 5-HT₄ agonist prucalopride). If a 3- to 6-month trial of medical therapies fails, unassociated with obstructed defecation, the patient should be considered for laparoscopic colectomy with ileorectostomy; however, this should not be undertaken for pain or in the presence of continued evidence of an evacuation disorder or a generalized GI dysmotility. Referral to a specialized center for further tests of colonic motor function is warranted. The decision to resort to surgery is facilitated by the presence of megacolon and megarectum or documented sigmoid or cecal volvulus. The complications after surgery include small-bowel obstruction (11%) and fecal soiling, particularly at night during the first postoperative year. Frequency of defecation is 3–8 per day during the first year, dropping to 1–3 per day from the second year after surgery. Patients who have a combined (evacuation and transit/motility) disorder should first pursue pelvic floor retraining (biofeedback and muscle relaxation), psychological counseling, and dietetic advice. If

symptoms are intractable despite biofeedback and optimized medical therapy, colectomy and ileorectostomy could be considered as long as the evacuation disorder is resolved and optimized medical therapy is unsuccessful. In patients with pelvic floor dysfunction alone, bio feedback training for 3 months has a 70–80% success rate, measured by the acquisition of comfortable stool habits. Attempts to manage pelvic floor dysfunction with operations (internal anal sphincter or puborectalis muscle division) or injections with botulinum toxin have achieved only mediocre success and have been largely abandoned. Persistence of the evacuation disorder despite physical therapy with biofeedback may require regular enemas or consideration of a loop- or end-ileostomy to relieve the intractable constipation. ■ ■

FURTHER READING Assi R et al: Sexually transmitted infections of the anus and rectum. *World J Gastroenterol* 20:15262, 2014. Blackett JW et al: Comparison of anorectal manometry, rectal balloon expulsion test, and defecography for diagnosing defecatory disorders. *Gastroenterology* 163:1582, 2022. Boeckstaens G et al: Fundamentals of neurogastroenterology: Physiology/motility—sensation. *Gastroenterology* 150:1292, 2016. BouSaba J et al: Impact of bile acid diarrhea in patients with diarrhea-predominant irritable bowel syndrome on symptoms and quality of life. *Clin Gastro Hepatol* 20:2083, 2022. Camilleri M et al: Chronic constipation. *Nat Rev Dis Primers* 3:17095, 2017. Camilleri M et al: Pathophysiology, evaluation, and management of chronic watery diarrhea. *Gastroenterology* 152:515, 2017. Issaka RB et al: AGA clinical practice update on risk stratification for colorectal cancer screening and post-polypectomy surveillance: Expert review. *Gastroenterology* 165:1280, 2023. Peery AF et al: Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2021. *Gastroenterology* 162:621, 2022. Palsson OS et al: Prevalence and associated factors of disorders of gut-brain interaction in the United States: Comparison of two nationwide internet surveys. *Neurogastro Motil* 35:e14564, 2023. Riddle MS et al: ACG Clinical Guideline: Diagnosis, treatment, and prevention of acute diarrheal infections in adults. *Am J Gastroenterol* 111:602, 2016. Rubio-Tapia A et al: American College of Gastroenterology guidelines update: Diagnosis and management of celiac disease. *Am J Gastroenterol* 118:59, 2023. Sanchez DA et al: Characterization of infectious and non-infectious gastrointestinal disease in common variable immunodeficiency: Analysis of 114 patient cohort. *Front Immunol* 14:1209570, 2023. Smalley W et al: AGA Clinical Practice Guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D). *Gastroenterology* 157:851, 2019. J. Larry Jameson

Unintentional Weight

Loss Involuntary or 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 do those with known causes, particularly when the source is neoplastic. 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. ■ ■PHYSIOLOGY OF WEIGHT REGULATION

WITH AGING (See also Chaps. 413 and 488) 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 lean body mass largely reflect the age-dependent decline in growth hormone secretion and, consequently, circulating levels of insulinlike 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, 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.” As noted below, these physiologic changes with aging may be accompanied by social isolation, poverty, and immobility, further contributing to undernutrition. ■

■CAUSES OF UNINTENTIONAL WEIGHT LOSS 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 (Table 50-1). 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. 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. 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.

TABLE 50-1 Causes of Involuntary Weight Loss

Cancer	Upper gastrointestinal	Lung	Colon	Hepatobiliary	Hematologic	Breast	Genitourinary	Ovarian	Prostate	Gastrointestinal disorders													
Difficulty swallowing	Malabsorption	Peptic ulcer	Inflammatory bowel disease	Pancreatitis	Obstruction/constipation	Pernicious anemia	Endocrine and metabolic	Hyperthyroidism	Diabetes mellitus	Pheochromocytoma	Adrenal insufficiency	Cardiac disorders	Chronic ischemia	Chronic congestive heart failure	Respiratory disorders	Emphysema	Chronic obstructive pulmonary						
Medications	Sedatives	Antibiotics	Nonsteroidal anti-inflammatory drugs	Serotonin reuptake inhibitors	Metformin	Levodopa	Angiotensin-converting enzyme inhibitors	Unintentional Weight Loss	CHAPTER 50 inhibitors	Other drugs	Disorders of the mouth and teeth	Dental caries	Dysgeusia	Age-related factors	Physiologic changes	Visual impairment	Decreased taste and smell	Functional disabilities					
Neurologic	Stroke	Parkinson's disease	Neuromuscular disorders	Dementia	Social Isolation	Poverty	Psychiatric and behavioral	Depression	Anxiety	Paranoia	Bereavement	Alcoholism	Eating disorders	Increased activity or exercise	Idiopathic disease	Renal insufficiency	Rheumatologic disease	Infections	HIV	Tuberculosis	Parasitic infection	Subacute bacterial endocarditis	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. 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 T3 toxicosis (Chap. 394). 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