ANOREXIA NERVOSA

EPIDEMIOLOGY

Among women, the lifetime prevalence of the full syndrome of AN is approximately 1%. AN is much less common in males. AN is more prevalent in cultures where food is plentiful and in which being thin is associated with attractiveness. Individuals who pursue interests that place a premium on thinness, such as ballet and modeling, are at greater risk. The incidence of AN has increased in recent decades.

ETIOLOGY

The etiology of AN is unknown but appears to involve a combination of psychological, biologic, and cultural risk factors. Risk factors, such as sexual or physical abuse and a family history of mood disturbance, are best viewed as nonspecific risk factors that increase vulnerability to a range of psychiatric disorders, including AN.

Patients who develop AN are inclined to be more obsessional and perfectionist than their peers. The disorder often begins as a diet not distinguishable at the outset from those undertaken by many adolescents and young women. As weight loss progresses, the fear of gaining weight grows; dieting becomes stricter; and psychological, behavioral, and medical aberrations increase. Eating disorders, including AN, may develop among individuals with type 1 diabetes mellitus and are associated with poorer glycemic control and an increased frequency of complications (Chap. 338).

Numerous physiologic disturbances, including abnormalities in a variety of neurotransmitter systems, have been described in AN (see below). It is difficult to distinguish neurochemical, metabolic, and hormonal changes that may have a role in the initiation or perpetuation of the syndrome from those that are secondary to the disorder. The resolution of most of these abnormalities with weight restoration argues against an etiologic role.

Genetic factors contribute to the risk of development of AN, as its incidence is greater in families with one affected member and the concordance in monozygotic twins is greater than in dizygotic twins. However, specific genes have not been identified.

CLINICAL FEATURES

AN typically begins in mid to late adolescence, sometimes in association with a stressful life event such as leaving home for school (Table 76-1). The disorder occasionally develops in early puberty, before menarche, but seldom begins after age 40. Despite being underweight, patients with AN are irrationally afraid of gaining weight, often out of a concern that weight gain will get "out of control." They also exhibit a distortion of body image, which may express itself in several ways. For example, despite being emaciated, patients with AN may believe that their body as a whole, or some part of their body, is too fat. Further weight loss is viewed by the patient as a fulfilling accomplishment, while weight gain is seen as a personal failure. Patients with AN rarely complain of hunger or fatigue and often exercise extensively. Despite the denial of hunger, one-quarter to one-half of patients with AN engage in eating binges. Patients tend to become socially withdrawn and increasingly committed to work or study, dieting, and exercise. As weight loss progresses, thoughts of food dominate mental life and idiosyncratic rules develop around eating. Patients with AN may obsessively collect cookbooks and recipes and be drawn to food-related occupations.

Physical Features Patients with AN typically have few physical complaints but may note cold intolerance. Gastrointestinal motility is diminished, leading to reduced gastric emptying and constipation. Some women who develop AN after menarche report that their menses ceased before significant weight loss occurred. Weight and height should be measured to allow calculation of body mass index (BMI; kg/m^2). Vital signs may reveal bradycardia, hypotension, and mild hypothermia. Soft, downy hair growth (lanugo) sometimes occurs, and alopecia may be seen. Salivary gland enlargement, which is associated with starvation as well as with binge eating and vomiting, may make the face appear surprisingly full in contrast to the marked general wasting. Acrocyanosis of the digits is common, and peripheral edema can be seen in the absence of hypoalbuminemia, particularly when the patient begins to regain weight. Consumption of large amounts of vegetables containing vitamin A can result in a yellow tint to the skin (*hypercarotenemia*), which is especially notable on the palms.

Laboratory Abnormalities Mild normochromic, normocytic anemia is frequent, as is mild to moderate leukopenia, with a disproportionate reduction of polymorphonuclear leukocytes. Dehydration may result in slightly increased levels of blood urea nitrogen and creatinine. Serum transaminase levels may increase, especially during the early phases of refeeding. The level of serum proteins is usually normal. Blood sugar is often low and serum cholesterol may be moderately elevated. Hypokalemic alkalosis suggests self-induced vomiting or the use

TABLE 76-1 COMMON CHARACTERISTICS OF ANOREXIA NERVOSA AND BULIMIA NERVOSA

	Anorexia Nervosa[a]	Bulimia Nervosa
Clinical Characteristics		
Onset	Mid-adolescence	Late adolescence/early adulthood
Female:male	10:1	10:1
Lifetime prevalence in women	1%	1–3%
Weight	Markedly decreased	Usually normal
Menstruation	Absent	Usually normal
Binge eating	25–50%	Required for diagnosis
Mortality	~5% per decade	Low
Physical and Laboratory Findings[a]		
Skin/extremities	Lanugo	
	Acrocyanosis	
	Edema	
Cardiovascular	Bradycardia	
	Hypotension	
Gastrointestinal	Salivary gland enlargement	Salivary gland enlargement
	Slow gastric emptying	Dental erosion
	Constipation	
	Elevated liver enzymes	
Hematopoietic	Normochromic, normocytic anemia	
	Leukopenia	
Fluid/Electrolyte	Increased BUN, creatinine	Hypokalemia
	Hypokalemia	Hypochloremia
		Alkalosis
Endocrine	Hypoglycemia	
	Low estrogen or testosterone	
	Low LH and FSH	
	Low-normal thyroxine	
	Normal TSH	
	Increased cortisol	
Bone	Osteopenia	

[a]Patients with the binge-eating/purging subtype of anorexia nervosa may also exhibit the physical and laboratory findings associated with bulimia nervosa.

Abbreviations: BUN, blood urea nitrogen; LH, luteinizing hormone; FSH, follicle stimulating hormone; TSH, thyroid stimulating hormone

of diuretics. Hyponatremia is common and may result from excess fluid intake and disturbances in the secretion of antidiuretic hormone.

Endocrine Abnormalities The regulation of virtually every endocrine system is altered in AN, but the most striking changes occur in the reproductive system. Amenorrhea is hypothalamic in origin and reflects diminished production of gonadotropin-releasing hormone (GnRH). When exogenous GnRH is administered in a pulsatile manner, pituitary responses of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are normalized, indicating the absence of a primary pituitary abnormality. The resulting gonadotropin deficiency causes low plasma estrogen in women and reduced testosterone in men. The hypothalamic GnRH pulse generator is exquisitely sensitive, particularly in women, to body weight, stress, and exercise, each of which may contribute to *hypothalamic amenorrhea* in AN (Chap. 341).

Serum leptin levels are markedly reduced in AN as a result of undernutrition and decreased body fat mass. The reduction in leptin appears to be the primary factor responsible for the disturbances of the hypothalamic-pituitary-gonadal axis, and to be an important mediator of the other neuroendocrine abnormalities characteristic of AN (Chap. 74).

Serum cortisol and 24-h urine free cortisol levels are generally elevated but without characteristic clinical signs of cortisol excess. Thyroid function tests resemble the pattern seen in euthyroid sick syndrome (Chap. 335). Thyroxine (T_4) and free T_4 levels are usually in the low-normal range, triiodothyronine (T_3) levels are reduced, and reverse T_3 (rT_3) is elevated. The level of thyroid-stimulating hormone (TSH) is normal or partially suppressed. Growth hormone is increased, but insulin-like growth factor 1 (IGF-1), which is produced mainly by the liver, is reduced, as in other conditions of starvation. Diminished bone density is routinely observed in AN and reflects the effects of multiple nutritional deficiencies, reduced gonadal steroids, and increased cortisol. The degree of bone density reduction is proportional to the length of the illness, and patients are at risk for the development of symptomatic fractures. The occurrence of AN during adolescence may lead to the premature cessation of linear bone growth and a failure to achieve expected adult height.

Cardiac Abnormalities Cardiac output is reduced, and congestive heart failure occurs rarely during rapid refeeding. The electrocardiogram usually shows sinus bradycardia, reduced QRS voltage, and nonspecific ST-T-wave abnormalities. Some patients develop a prolonged QT_c interval, which may predispose to serious arrhythmias, particularly when electrolyte abnormalities also are present.

DIAGNOSIS

The diagnosis of AN is based on the presence of characteristic behavioral, psychological, and physical attributes (Table 76-2). Widely accepted diagnostic criteria are provided by the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV). These criteria include weight <85% of that expected for age and height, which is roughly equivalent to a BMI of 18.5 kg/m^2 for adult women. This weight criterion is somewhat arbitrary, so that a patient who meets all other diagnostic criteria but weighs between 85 and 90% of expected would still merit the diagnosis of AN. The current diagnostic criteria require that women with AN not have spontaneous menses, but occasional patients with the characteristics and complications of AN describe regular menstruation. Two mutually exclusive subtypes of AN are specified in DSM-IV. Patients whose weight loss is maintained primarily by caloric restriction, perhaps augmented by excessive exercise, are considered to have the "restricting" subtype of AN. The "binge eating/purging" subtype is characterized by binge eating and self-induced vomiting and/or laxative abuse. Patients with the binge/purge subtype are more prone to develop electrolyte imbalances, are more emotionally labile, and are more likely to have other problems with impulse control, such as drug abuse.

The diagnosis of AN can usually be made confidently in a patient with a history of weight loss accomplished by restrictive dieting and excessive exercise, accompanied by a marked reluctance to gain weight. Patients with AN often deny that they have a serious problem and may be brought to medical attention by concerned family or friends. In atypical presentations, other causes of significant weight loss in previously healthy young people should be considered, including inflammatory bowel disease, gastric outlet obstruction, diabetes mellitus, central nervous system (CNS) tumors, or neoplasm (Chap. 41).

TABLE 76-2 DIAGNOSTIC FEATURES OF ANOREXIA NERVOSA

Refusal to maintain body weight at or above a minimally normal weight for age and height. (This includes a failure to achieve weight gain expected during a period of growth leading to an abnormally low body weight.)
Intense fear of weight gain or becoming fat.
Distortion of body image (e.g., feeling fat despite an objectively low weight or minimizing the seriousness of low weight).
Amenorrhea. (This criterion is met if menstrual periods occur only following hormone—e.g., estrogen—administration.)

PROGNOSIS

The course and outcome of AN are highly variable. One-quarter to one-half of patients eventually recover fully, with few psychological or physical sequelae. However, many patients have persistent difficulties with weight maintenance, depression, and eating disturbances, including BN. The development of obesity following AN is rare. The long-term mortality of AN is among the highest associated with any psychiatric disorder. Approximately 5% of patients die per decade of follow-up, primarily due to the physical effects of chronic starvation or by suicide.

Virtually all of the physiologic abnormalities associated with AN are observed in other forms of starvation and markedly improve or disappear with weight gain. A worrisome exception is the reduction in bone mass, which may not recover fully, particularly when AN occurs during adolescence when peak bone mass is normally achieved.

Rx ANOREXIA NERVOSA

Because of the profound physiologic and psychological effects of starvation, there is a broad consensus that weight restoration to at least 90% of predicted weight is the primary goal in the treatment of AN. Unfortunately, because most patients resist this goal, the management of AN is often accompanied by frustration for the patient, the family, and the physician. Patients typically exaggerate their food intake and minimize their symptoms. Some patients resort to subterfuge to make their weights appear higher, for example, by water-loading before they are weighed. In attempting to engage the patient in treatment, it may be useful for the physician to elicit the patient's physical concerns (e.g., about osteoporosis, weakness, or fertility) and, provide education about the importance of normalizing nutritional status in order to address those concerns. The physician should reassure the patient that weight gain will not be permitted to get "out of control" but simultaneously emphasize that weight restoration is medically and psychologically imperative.

The intensity of the initial treatment, including the need for hospitalization, is determined by the patient's current weight, the rapidity of recent weight loss, and the severity of medical and psychological complications (Fig. 76-1). Hospitalization should be strongly considered for patients weighing <75% of expected, even if the results of routine blood studies are within normal limits. Acute medical problems, such as severe electrolyte imbalances, should be identified and addressed. Nutritional restoration can almost always be successfully accomplished by oral feeding, and parenteral methods are rarely required. For severely underweight patients, sufficient calories (approximately 1200–1800 kcal/d) should be provided initially in divided meals as food or liquid supplements to maintain weight and to permit stabilization of fluid and electrolyte balance. Calories can then be gradually increased to achieve a weight gain of 1–2 kg (2–4 lb) per week, typically requiring an intake of 3000–4000 kcal/d. Meals must be supervised, ideally by personnel who are firm regarding the necessity of food consumption, empathic regarding the challenges entailed, and reassuring about the patient's eventual recovery. Patients have great psychological difficulty complying with the need for increased caloric consumption, and the assistance of psychiatrists or psychologists experienced in the treatment of AN is usually necessary.

Less severely affected patients may be treated in a partial hospitalization program where medical and psychiatric supervision is available and

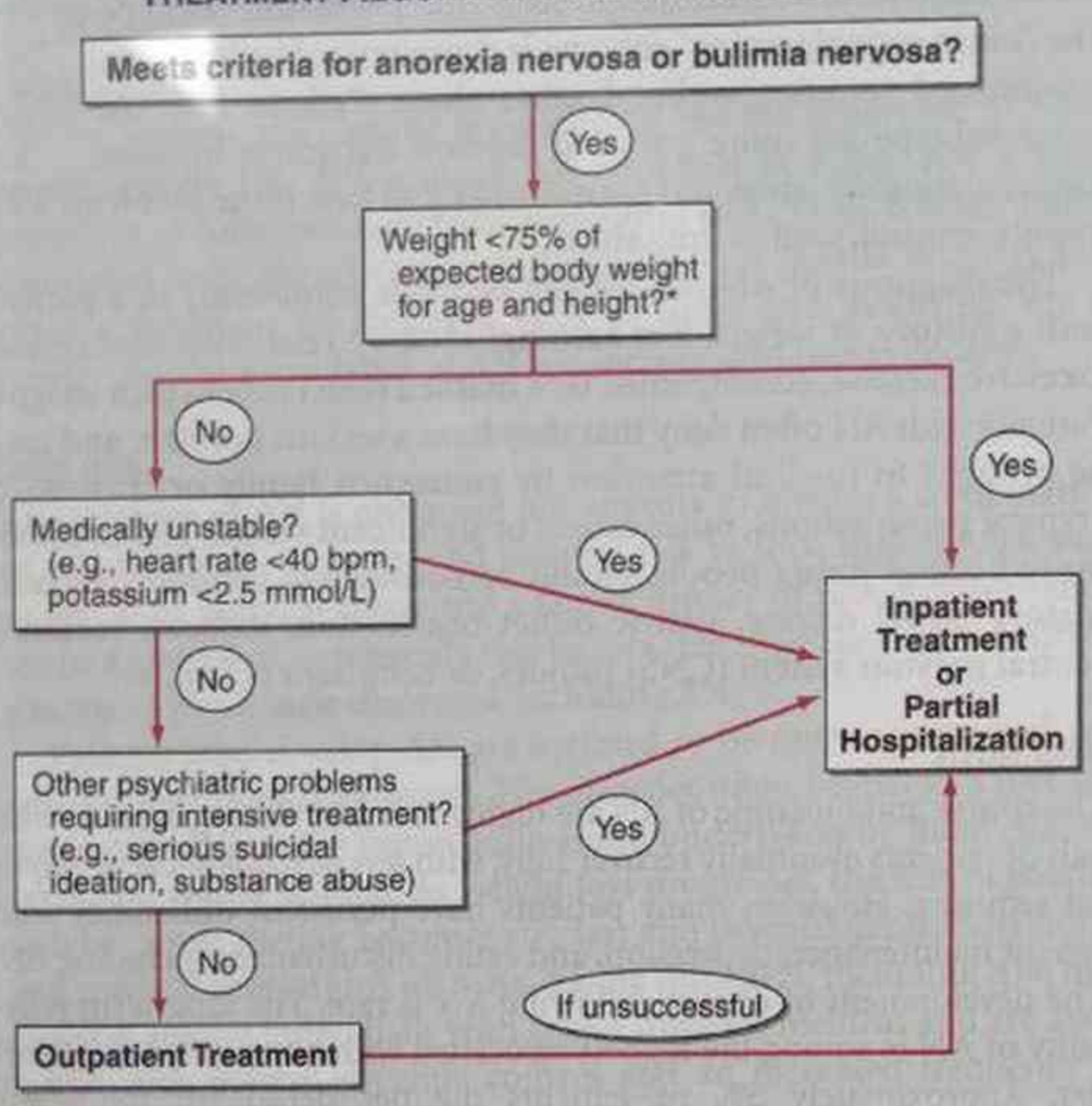

FIGURE 76-1 An algorithm for basic treatment decisions regarding patients with anorexia nervosa or bulimia nervosa. Based on the American Psychiatric Association's practice guidelines for the treatment of patients with eating disorders. *Although outpatient management may be considered for patients with anorexia nervosa weighing more than 75% of expected, there should be a low threshold for using more intensive interventions if the weight loss has been rapid or if current weight is <80% of expected.

several meals can be monitored each day. Outpatient treatment may suffice for mildly ill patients. Weight must be monitored at frequent intervals, and explicit goals agreed on for weight gain, with the understanding that more intensive treatment will be required if the level of care initially employed is not successful. For younger patients, the active involvement of the family in treatment is crucial regardless of the treatment venue.

Psychiatric treatment focuses primarily on two issues. First, patients require much emotional support during the period of weight gain. Patients often intellectually agree with the need to gain weight, but strenuously resist increases in caloric intake, and often surreptitiously discard food that is provided. Second, patients must learn to base their self-esteem not on the achievement of an inappropriately low weight, but on the development of satisfying personal relationships and the attainment of reasonable academic and occupational goals. While this is often possible, some patients with AN develop other serious emotional and behavioral symptoms such as depression, self-mutilation, obsessive-compulsive behavior, and suicidal ideation. These symptoms may require additional therapeutic interventions, in the form of psychotherapy, medication, or hospitalization.

Medical complications occasionally occur during refeeding. Especially in the early stages of treatment, severely malnourished patients may develop a "refeeding syndrome" characterized by hypophosphatemia, hypomagnesemia, and cardiovascular instability. Acute gastric dilatation has been described when refeeding is rapid. As in other forms of malnutrition, fluid retention and peripheral edema may occur, but they generally do not require specific treatment in the absence of cardiac, renal, or hepatic dysfunction. Transient modest elevations in serum liver enzyme levels occasionally occur. Multivitamins should be given, and an adequate intake of vitamin D (400 IU/d) and calcium (1500 mg/d) should be provided to minimize bone loss.

No psychotropic medications are of established value in the treatment of AN; tricyclic antidepressants are contraindicated when there is prolongation of the QT_c interval. The alterations of cortisol and thyroid hormone metabolism do not require specific treatment and are corrected by weight gain. Estrogen treatment appears to have minimal impact on bone density in underweight patients and [illegible]

appears to be outweighed by the potential risks of such agents in young women.

BULIMIA NERVOSA

EPIDEMIOLOGY

In women, the full syndrome of BN occurs with a lifetime prevalence of 1–3%. Variants of the disorder, such as occasional binge eating or purging, are much more common and occur in 5–10% of young women. The frequency of BN among men is less than one-tenth of that among women. The prevalence of BN increased dramatically in the early 1970s and 1980s but may have leveled off or declined somewhat in recent years.

ETIOLOGY

As with AN, the etiology of BN is likely to be multifactorial. Patients who develop BN describe a higher-than-expected prevalence of childhood and parental obesity, suggesting that a predisposition toward obesity may increase vulnerability to this eating disorder. The marked increase in the number of cases of BN during the past 25 years and the rarity of BN in underdeveloped countries suggest that cultural factors are important. Several biologic abnormalities in patients with BN may perpetuate this disorder once it has begun. These include abnormalities of CNS serotonergic function, which is involved in eating behavior, and disruption of peripheral satiety mechanisms, including the release of cholecystokinin (CCK) from the small intestine.

CLINICAL FEATURES

The typical patient presenting for treatment of BN is a woman of normal weight in her mid-twenties who reports binge eating and purging 5–10 times a week for 5–10 years (Table 76-3). The disorder usually begins in late adolescence or early adulthood during or following a diet, often in association with depressed mood. The self-imposed caloric restriction leads to increased hunger and to overeating. In an attempt to avoid weight gain, the patient induces vomiting, takes laxatives or diuretics, or engages in some other form of compensatory behavior. During binges, patients with this disorder tend to consume large amounts of sweet foods with a high fat content, such as dessert items. The most frequent compensatory behaviors are self-induced vomiting and laxative abuse, but a wide variety of techniques have been described, including the omission of insulin injections by individuals with type I diabetes mellitus. Initially, patients may experience a sense of satisfaction that appealing food can be eaten without weight gain. However, as the disorder progresses, patients perceive diminished control over eating. Binges increase in size and frequency and are provoked by a variety of stimuli, such as transient depression, anxiety, or a sense that too much food has been consumed in a normal meal. Between binges, patients restrict caloric intake, which increases hunger and sets the stage for the next binge. Typically, patients with BN are ashamed of their behavior and endeavor to keep their disorder hidden from family and friends. Like patients with AN, those with BN place an unusual emphasis on weight and shape as a basis for their self-esteem. Many patients with BN have mild symptoms of depression. Some patients exhibit serious mood and behavioral disturbances, such as suicide attempts, sexual promiscuity, and drug and alcohol abuse. Although vomiting may be

TABLE 76-3 DIAGNOSTIC FEATURES OF BULIMIA NERVOSA

Recurrent episodes of binge eating, which is characterized by the consumption of a large amount of food in a short period of time and a feeling that the eating is out of control.
Recurrent inappropriate behavior to compensate for the binge eating, such as self-induced vomiting.
The occurrence of both the binge eating and the inappropriate compensatory behavior at least twice weekly, on average, for 3 months.
Overconcern with body shape and weight.

Note: If the diagnostic criteria for anorexia nervosa are simultaneously met, only the