

## Diagnosis and Care of Patients with Anorexia Nervosa in Primary Care Settings

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Anorexia nervosa is a psychiatric disorder characterized by abnormal eating behaviors that results in weight loss and has serious potential medical consequences. Most of these complications are readily treatable if diagnosed and attended to early in the course of the illness. In caring for patients with anorexia nervosa, the primary care physician has several critical roles. Because patients deny the severity of their illness, they delay seeking psychiatric treatment. The primary care physician must be skilled in recognizing this disorder, as well as in diagnosing and effectively treating the medical complications while educating the patient about them. The primary care physician is also involved with arranging and coordinating a comprehensive and multidisciplinary program, including dietary and mental health treatment. The multidisciplinary

team is responsible for ensuring safe weight restoration and a judicious refeeding treatment plan. In addition to establishing the diagnosis and treating the multiple medical complications associated with anorexia nervosa, the primary care physician plays a central role in maintaining continuity of care despite the fact that successful care may require a variety of treatment settings. Factors that foster good prognoses for this increasingly common and often protracted eating disorder include early diagnosis and skilled medical intervention to prevent the inexorable physical decline that marked weight loss can cause.

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**A** 20-year-old woman presents to her internist because her mother is concerned about her amenorrhea, which has lasted for 5 months; before this, her periods were normal. The patient reports no headaches, hirsutism, change in vision, or medications. On examination, she is 69 inches (175.26 cm) tall and weighs 117 pounds (52.65 kg). Her blood pressure is 96/58 mm Hg, and her heart rate is 46 beats/min. The thyroid gland is normal, there are no signs of virilization, and results of visual field testing are normal.

### COULD THIS PATIENT HAVE ANOREXIA NERVOSA?

The clinical diagnosis of anorexia nervosa is often obscured (1). Clinicians must be extremely vigilant for this diagnosis, since patients with mild cases usually seek help for nonspecific symptoms, such as asthenia, dizziness, and a lack of energy (2). Often, family members bring patients to the physician because they are concerned about amenorrhea or substantial weight loss. Patients with anorexia nervosa, in contrast to medically ill patients, are unconcerned about their weight loss; presentation is remarkable for its lack of complaints. Although some patients exhibit obvious indicators, such as potentially unhealthy weight-control practices, such features may be absent (3).

Menstrual disorders are among the most common reasons that women seek medical attention (4). Secondary amenorrhea is a symptom, not a diagnosis, and a

thorough history and physical examination are required to define its cause (5). Hypothalamic dysfunction and polycystic ovarian disease each account for 30% of cases, pituitary prolactinomas and ovarian failure each account for 15%, and uterine problems account for 5% (6). Since hypothalamic-induced amenorrhea is a universal feature of anorexia nervosa, it should be determined whether the amenorrheic patient has a history of recent moderate to marked weight loss.

Other presenting symptoms and signs of anorexia nervosa depend on the disease's severity. Many patients with moderate and severe anorexia have fine lanugo-type hair on the sides of their faces and their arms, brittle nails, thinning hair, sensitivity to cold, abdominal pain, lightheadedness, and fatigue.

*The patient returns to discuss her blood tests results, all of which are normal. Results of a pregnancy test are negative. Further history reveals that she has lost 25 pounds (11.25 kg) over the previous 6 months, a fact she relishes. Her father's comments about her weight motivated her to begin dieting. The patient lost weight by restricting her caloric intake and does not report purging behaviors.*

### DOES THIS PATIENT MEET THE CRITERIA FOR ANOREXIA NERVOSA?

The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) defines anorexia nervosa as having an

**Table 1. Criteria for Anorexia Nervosa**

Intense fear of weight gain Undue emphasis on body shape Body weight < 85% of predicted Amenorrhea for 3 consecutive months
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intense fear of gaining weight, putting undue emphasis on body shape, having a body weight that is less than 85% of the predicted weight, and missing three consecutive periods (7) (Table 1). Anorexia nervosa is further divided into restricting and purging subtypes. Patients with the more common restricting subtype drastically limit their food intakes, whereas patients with the purging subtype also engage in purging behaviors. In contrast to the bulimic patient, whose appearance is often unremarkable and whose disease may therefore initially go unrecognized in clinical settings (8, 9), the cachectic appearance of the patient with severe anorexia is readily noticeable. Although the differential diagnosis for weight loss is extensive (10, 11), the young age of most patients with anorexia nervosa simplifies the evaluation. Malabsorption and catabolic states can easily be excluded with a careful history and physical examination and judicious laboratory testing, including tests for levels of thyroid-stimulating hormone and serum albumin.

Anorexia nervosa is common, with a prevalence of 1% to 2% (12). The yearly incidence has increased to a range of 17 to 20 cases per 100 000 (13). Bulimia is more common (14), and almost half of patients with anorexia eventually develop bulimic symptoms (15, 16). The female-to-male ratio for anorexia is 20:1, and homosexuality may be an associated factor in men (17). Anorexia nervosa is more common in industrialized nations (18, 19) and among white women of higher socioeconomic classes (20). Participation in activities that promote thinness, such as modeling and athletics, and type 1 diabetes mellitus in young women are associated with a higher prevalence of anorexia nervosa (21–24). Other proposed risk factors are perfectionism and negative comments from others about body appearance (25, 26). A recent controlled study suggests that overprotective parenting, linked to unresolved grief about a previous life event, is associated with development of anorexia nervosa (27). In addition, new evidence has established a genetic basis for increased risk (28). Adolescence and its rapid period of physical change are also

commonly associated with anorexia nervosa (29), as is depression (30). In addition, young adults who strive for unhealthy weight loss are more likely to engage in other harmful behaviors, such as substance abuse (31).

### CAN ANY DIAGNOSTIC TOOLS HELP IN THE IDENTIFICATION OF ANOREXIA NERVOSA?

Early detection and treatment improve prognosis (32). Questionnaires designed to screen for eating disorders, such as the Eating Attitude Test (EAT), have a variable performance record (33, 34). Recently, a new screening tool, SCOFF, has been developed (35) (Table 2). However, there are concerns about its applicability and reliability (36).

### HOW DOES THE CLINICIAN RULE OUT BULIMIA?

Diagnostic criteria for bulimia are found in Table 3. Bulimia should be distinguished from anorexia nervosa not by a weight threshold but by the presence of binge eating and purging. Bulimic patients may purge through self-induced vomiting, abuse of laxatives or diuretics, or excessive exercise. Both bulimic and anorectic patients frequently engage in excessive amounts of exercise. Compulsive exercise training is associated with weight obsession (37). Abnormal eating behaviors are associated with a specific negative attitude toward running independent of the weekly mileage (38); runners experience “withdrawal” symptoms if they cannot run and are unable to stop running if they are sick or injured. In fact, excessive exercise often precedes the development of the formal eating disorder (39). One other eating disorder that could be considered is the “night-eating syndrome,” which is characterized by nocturnal bingeing, daytime anorexia, and insomnia (40) and is distinct from the established disorders of anorexia and bulimia.

Bulimia is more common than anorexia, affecting up to 2% to 3% of adult women (41). Bulimic patients

**Table 2. SCOFF Questions\***

Do you make yourself sick because you feel uncomfortably full? Do you worry that you have lost control over how much you eat? Have you recently lost more than one stone (14 pounds [6.3 kg]) in a 3-month period? Do you believe yourself to be fat when others say you are too thin? Would you say that food dominates your life?
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\* Each “yes” = 1 point; a score of 2 points indicates a likely diagnosis of anorexia nervosa.

**Table 3. Criteria for Bulimia Nervosa**

<p>Recurrent episodes of binge eating characterized by either a larger amount of food than most people would eat in a discrete period or a sense of having no control over eating during the episode</p> <p>Recurrent, inappropriate, compulsive behavior to prevent weight gain, such as self-induced vomiting; abuse of laxatives, diuretics, or other medications; or excessive exercise</p> <p>Binging and purging at least twice per week for 3 months</p> <p>Self-evaluation unduly influenced by body shape and weight</p>
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who purge through self-induced vomiting may present with sialadenosis, perimyolysis, or symptoms of reflux esophagitis. Persons who abuse laxatives may report abdominal cramping, diarrhea, or rectal bleeding. Laboratory studies are the most useful tool in evaluating bulimia. The specific pattern of serum and urine electrolytes helps to define the mode of purging. Metabolic alkalosis and hypokalemia are the most common abnormalities encountered and can be seen in patients who purge through self-induced vomiting or diuretic abuse (42). In contrast, anorectic patients who lose weight exclusively by restricting caloric intake usually have normal electrolyte levels.

*One week later, the patient has lost 2 pounds (0.9 kg). She denies dizziness, and vital signs are stable. Physical examination is unremarkable. The patient minimizes her obsession with weight loss but admits that she fears gaining weight.*

**WOULD ADDITIONAL LABORATORY TESTS BE HELPFUL IN DIAGNOSING ANOREXIA NERVOSA?**

One of the remarkable characteristics of anorexia is the consistent finding of normal results on blood chemistry tests despite extensive weight loss. On occasion, leukopenia and anemia may be present (43, 44), but these conditions invariably resolve with weight gain and have little clinical significance. In addition, hypoglycemia may be found and is indicative of a poor prognosis (45). The presence of hypokalemia or metabolic alkalosis should raise concern that the anorectic patient may be surreptitiously purging through vomiting or diuretic abuse (46, 47). Abnormalities on thyroid function tests are often present in the form of the euthyroid sick syndrome. Serum levels of L-thyroxine are normal to low, as are levels of triiodothyronine. Levels of thyroid-stimulating hormone seem normal, but levels of reverse triiodothyronine (reverse T<sub>3</sub>) are increased. With resolu-

tion of anorexia nervosa, all of these indicators return to normal. The important clinical point is that laboratory values generally remain normal until the very late stages of illness in anorectic patients who restrict their dietary intake; therefore, these values should not in any way independently influence decisions about the necessary intensity of treatment.

**WHAT CRITERIA ARE USED TO DECIDE ON THE APPROPRIATE INITIAL COURSE OF TREATMENT FOR A PATIENT WITH ANOREXIA NERVOSA?**

Clinicians must first decide what level of treatment is appropriate. Treatment can range from outpatient care to acute medical or psychiatric hospitalization. However, outpatient treatment is adequate for most patients. Anorexia nervosa can be classified as mild, moderate, or severe on the basis of the combination of the severity of body image distortion, the presence of physical complications, and the percentage of ideal body weight (48). Patients who are within 10% of ideal body weight and have only minimal distortion of body image are considered to have mild cases. Technically, because this degree of weight loss does not qualify as anorexia nervosa, these patients are classified as having a not-otherwise-specified eating disorder. This diagnosis is given to patients who do not meet all of the criteria for anorexia nervosa.

No controlled trials have been performed to define when inpatient hospitalization is indicated. Commonly accepted indications include a weight that is more than 25% to 30% below ideal body weight, rapid and severe weight loss refractory to outpatient treatment, marked symptomatic hypotension or syncope, a pulse rate less than 35 to 40 beats/min, arrhythmias, or a prolonged QT interval (Table 4) (49). A lower weight at referral is consistently associated with less frequent attainment of normal weight and a greater risk for chronic anorexia and death (50, 51). However, the decision to hospitalize patients must be carefully deliberated because lengthy

**Table 4. Indications for Inpatient Treatment**

<p>Markedly abnormal vital signs (heart rate &lt; 35–40 beats/min, symptomatic hypotension)</p> <p>Weight &lt; 70%–75% of ideal body weight</p> <p>Rapid and severe weight loss unresponsive to outpatient treatment</p> <p>Cardiac arrhythmias</p>
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admissions might interfere with the potential for long-term recovery (52). A randomized, controlled trial is needed to clarify the merits of inpatient compared with outpatient treatment for patients with severe anorexia.

### HOW AND WHEN SHOULD A MENTAL HEALTH SPECIALIST AND A DIETITIAN BE INVOLVED?

After the decision is made to initially manage the patient as an outpatient, the next issue is choosing the specific treatment plan. Patients who are within 85% to 90% of healthy body weight and are considered medically stable require regular visits to the primary provider and to a mental health professional with expertise in this area. The mental health professional monitors the anorectic patient to promote weight gain by changing faulty thought processes. Cognitive psychotherapy, which attempts to help patients recognize the connection between their dysfunctional thoughts and maladaptive behaviors, is frequently used. Because anorexia nervosa is often chronic and very complicated, an expert in dealing with patients who have eating disorders should handle psychiatric management.

The psychiatrist or psychologist usually leads a multidisciplinary team that includes representatives of the necessary clinical specialties, including an internist and a dietitian. This multidisciplinary approach is particularly relevant to patients with more severe disease or to patients who receive care at a specialty unit for eating disorders. The mental health professional must be able to intervene, achieve patient adherence, integrate and prioritize treatments, and effectively treat comorbid psychiatric illnesses. He or she must work with ancillary staff to educate and support patients so that the terror accompanying their fears of becoming fat are attenuated. In addition, the psychiatrist must work with the internist to facilitate and coordinate maximum cooperation and collaboration.

The primary care physician's role is to regularly assess and monitor the patient's physical status and body weight while setting a weight loss limit past which the patient will be referred for more intensive and structured treatment. The primary care physician should see the patient for follow-up visits at 3- or 4-week intervals, which can be lengthened as the patient improves. In general, regular participation in athletics is discouraged until the patient achieves her target weight. If the pa-

tient's weight decreases to a lower range (75% to 85% of ideal body weight), the need for the formalized multifaceted approach is much more compelling (53). The components of this treatment plan include general medical care, formal dietary counseling, and pertinent psychotherapy. For patients with more severe anorexia nervosa, the psychiatrist often directs the necessary collaboration with other clinicians.

*Four weeks later, the patient claims that she is ingesting 1500 kcal/d but is still losing weight. She denies excessive exercise. Her weight is noted to be 114 pounds (51.3 kg). Vital signs remain stable, and there is no physical or laboratory evidence of purging behaviors. You recommend having a dietitian and a psychiatrist involved in her care.*

### HOW ARE CALORIC NEEDS CALCULATED?

Another important component of the treatment plan, especially for the patient with more severe disease, is the invaluable expertise of a dietitian. Sir William Withey Gull accurately emphasized this in his classic 1874 description of anorexia nervosa: "I don't prescribe medicine because nursing and the food are more important" (54). Although the specifics of the dietary issues are beyond the intended scope of this article, a few general comments are worth noting. It is important that all members of the treatment team agree on a target weight. The time-honored method for calculating target weight assumes that the ideal weight for a person who is 5 feet tall (150 cm) is 100 pounds (45 kg); 5 pounds (2.25 kg) should be added for each additional inch of height. Generally, the target goal weight should be within 90% of this ideal body weight. During treatment, the dietitian should weigh the patient once or twice per week with the patient's back to the numbers on the scale, monitor the progress of weight gain and meal plans, and disseminate this information to the other team members. This is important because patients with anorexia nervosa often unrealistically assess their caloric intakes.

Clinicians aim for a weight gain of 1 pound (0.45 kg) per week for outpatients and 2 to 3 pounds (0.9 to 1.35 kg) per week for inpatients. Early in the refeeding process, despite low caloric intake, patients may gain weight rapidly because of fluid retention and because the resting metabolic rate is reduced (55). However, the number of ingested kilocalories required for weight gain rapidly increases as body weight increases. This can be

very frustrating for anorectic patients (56–58). Increases in resting energy expenditure are noticeable after just 1 week of refeeding (59).

Generally, patients receiving refeeding require diets of 800 to 1000 kcal/d initially, with incremental increases of 200 to 300 kcal every 3 to 4 days as tolerated and as determined by individual weight gain. As patients near their target weight, they frequently require 3000 to 3500 kcal/d. For extremely refractory cases, total parenteral nutrition or nocturnal enteral feedings should be judiciously considered (60, 61). Careful clinical monitoring and a gradual refeeding program are crucial to avoid the refeeding syndrome in this high-risk population (62).

*The patient reluctantly follows up with the dietitian, who reports that she was ingesting only 500 kcal/d. Her current meal plan is set at 1000 kcal/d, to be increased by 300 kcal/d every 4 days. Two weeks later, she is ingesting 2200 kcal/d. She reports that she is required to eat too much food and that she has swelling in her legs. Examination reveals that she has gained 5 pounds (2.25 kg), her pulse is 54 beats/min, her lungs are clear, and she has trace pitting edema in her legs.*

#### WHAT ARE THE ADVERSE EFFECTS OF REFEEDING?

The clinical entity known as the refeeding syndrome is a potentially catastrophic complication that may occur during the initial nutritional rehabilitation of patients with moderate and severe anorexia nervosa (63). Patients are at greatest risk for this syndrome during the first 2 to 3 weeks of refeeding. The refeeding syndrome is manifested by cardiovascular collapse in a malnourished person after oral, enteral, or parenteral intake of highly caloric nutrients. The classic definition of the syndrome refers to the potentiation of refeeding-induced hypophosphatemia, but it can also involve other electrolytes. Phosphate depletion, in turn, produces widespread abnormalities, including cardiac arrest and delirium (64). The two primary biochemical abnormalities responsible for many of the clinical manifestations of hypophosphatemia are impaired cellular energy stores, caused by depletion of intracellular adenosine triphosphate, and tissue hypoxia, the result of decreased levels of erythrocyte 2,3 diphosphoglycerate (2,3-DPG) (65). The patient's serum electrolyte levels, especially phosphorus, must be assiduously monitored every few days

during the early phases of weight restoration to avoiding refeeding problems (66, 67). Less frequent monitoring is appropriate after the patient has steadily gained weight for a few weeks.

The refeeding syndrome also affects the cardiac muscle. Because patients with anorexia nervosa have lost a substantial amount of weight, they also experience an absolute decrease in stroke volume caused by a decrease in ventricular mass and myofibrillar atrophy (68, 69). During refeeding, the sudden ingestion of large amounts of nutrients can overwhelm the diminished capacity of the cardiovascular system and result in heart failure.

*The patient's electrolyte and phosphorus levels are found to be normal. The dietitian decides to delay any caloric increases until a follow-up visit. One week later, the patient continues to struggle with her meal plan. The dietitian and the psychiatrist have been seeing her twice weekly. Her weight has decreased by 1 pound (0.45 kg), her pulse is 42 beats/min, and her edema has resolved.*

#### IS THE PATIENT'S BRADYCARDIA A CAUSE FOR CONCERN?

Marked bradycardia (with rates between 40 and 50 beats/min) and reduced systolic blood pressure are common energy-conserving mechanisms. Cardiac vagal hyperactivity also contributes to bradycardia (70, 71). Although no clear evidence supports it, some clinicians recommend cardiac monitoring whenever the heart rate is below 40 beats/min. However, if patients are asymptomatic, heart rates as low as 30 beats/min that are sinus rhythm might still be considered within the normal range (72). Therefore, frequent individualized clinical assessments and clinical judgment are very important in each case of anorexia nervosa, especially during the first few weeks of refeeding. Specifically, pulse and respiratory rate should be monitored for unexpected increases and patients should be monitored for edema, rapid weight gain, or abdominal distension.

Other cardiac changes include an increased incidence of mitral valve prolapse (73, 74), which often remits with weight gain. Although chest pain has been reported in anorexia nervosa (75), autopsy studies have not shown substantial atherosclerosis (76); in addition, a recent series did not find increased low-density lipoprotein cholesterol levels in patients with this disorder (77).

Anorexia has the highest mortality rate of all mental disorders (78). Most deaths in patients with anorexia nervosa are caused by cardiac arrest secondary to arrhythmias. A prolonged QT interval, which is common in patients with this disorder (79–81), may be a marker for risk for sudden death. Therefore, for patients with severe disease, electrocardiography should be used to help direct proper medication use, such as avoidance of medications that tend to prolong a borderline long QT interval.

*During the next 3 weeks, the patient gradually increases her caloric intake to 3000 kcal/d. Her weight has been steadily increasing by 1 to 2 pounds (0.45 to 0.9 kg) per week without clinical evidence of refeeding problems. Electrolytes and phosphorus levels are now being obtained every 7 to 10 days. The patient's main symptoms are early satiety and bloating.*

#### WHAT IS THE CAUSE OF THE PATIENT'S GASTROINTESTINAL SYMPTOMS?

Patients being refeed often report bloating and constipation. While these symptoms may be functional because of the underlying fear of gaining weight, gastrointestinal transit is known to be prolonged in most patients with anorexia (82–84). The prokinetic agent metoclopramide may relieve bloating. Cisapride also had some efficacy in this regard but was recently withdrawn from the market because of an associated arrhythmia risk (85–87). However, a limited-access program is available for patients who require cisapride when all other therapies have failed. Institutional review board approval and informed consent are required for participation, along with serial electrocardiography (88). The latter procedure is especially important given the prolonged QT interval found in patients with anorexia nervosa. However, pharmacologic intervention is often unnecessary because most of these symptoms abate and colonic transit normalizes in a few weeks with appropriate nutritional rehabilitation, adequate fluid intake, and patience (89, 90).

*Nine weeks after the patient's initial visit, her weight is 129 pounds (58.05 kg), her pulse is 62 beats/min, and she has no edema. She is bothered by her amenorrhea and requests oral contraceptives.*

#### WHAT IS THE VALUE OF ESTROGEN REPLACEMENT FOR PATIENTS WITH ANOREXIA NERVOSA?

Secondary amenorrhea affects more than 90% of patients with anorexia nervosa. The amenorrhea is caused by low levels of follicle-stimulating hormone and luteinizing hormone despite low estrogen levels. A prepubertal blunted response of follicle-stimulating hormone and luteinizing hormone to the pulsatile release of hypothalamic gonadotropin-releasing hormone is also present (91). Withdrawal bleeding, therefore, does not occur in more severely anorectic patients with a progesterone challenge or with oral contraceptives because they are extremely hypoestrogenic and because of the profound disturbance in release of gonadotropin-releasing hormone. Primary therapy for amenorrhea associated with anorexia nervosa must be directed toward nutritional improvement and weight gain. In men with anorexia, hypothalamic hypogonadism can present as decreased levels of serum testosterone (92).

The exact cause of amenorrhea is unknown, but loss of body weight, excessive exercise, and emotional distress are contributing factors (93). A minimal amount of body fat is necessary for normal pulsatility of gonadotropin-releasing hormone (94). However, the amenorrhea seen in patients with anorexia nervosa cannot simply be a reflection of weight loss because it often precedes weight loss and may persist despite weight gain. Serum leptin levels, which are low in patients with anorexia, may be involved (95, 96).

#### WHEN DO MENSES RESUME IN PATIENTS WITH ANOREXIA NERVOSA?

Most patients with anorexia nervosa will recover menses within 6 months of reaching 90% of their ideal body weight (97, 98). Serum estradiol levels (>110.1 pmol/L) are a good predictor of resumption of menses, as is a weight approximately 5 pounds (2.25 kg) above the weight at which menses were lost (99, 100). However, amenorrhea may persist if emotional conflicts are unresolved (101).

*After explaining to the patient when her menses are likely to resume, you decide not to prescribe oral contraceptives. The office visit concludes with a discussion regarding her concerns about fertility and other health consequences of anorexia nervosa.*

### DOES ANOREXIA NERVOSA CAUSE PERMANENT FERTILITY PROBLEMS?

Women who have recovered from anorexia do not have an increased incidence of infertility. These complications are increased only in women with an active eating disorder (102–104). It is important to note that patients with anorexia nervosa can become pregnant despite amenorrhea. Contraceptives should therefore be recommended if an unwanted pregnancy is possible. Of interest, patients with anorexia nervosa may have fewer symptoms during pregnancy (105) but may relapse after delivery because of conflicts about changes in body shape (106, 107).

### ARE PATIENTS WITH ANOREXIA NERVOSA AT RISK FOR OSTEOPOROSIS?

Although it was once thought that amenorrhea in anorectic patients had no adverse effects, this thinking has radically changed. Osteoporosis is one of the most serious clinical concerns accompanying amenorrhea and weight loss. The peak bone mass achieved as a young adult is a major determinant of bone density and fracture risk. Anorexia nervosa is associated with markedly reduced bone density, especially at the lumbar spine but also at the proximal femur and distal radius (108–112). A recent study showed that the long-term risk for any fracture is increased 2.9-fold in patients who have had anorexia nervosa (113). This could cause major widespread problems because anorexia nervosa is the third most common chronic condition in adolescence, after obesity and asthma (114).

The marked degree of osteopenia in anorexia nervosa is based on several factors other than estrogen deficiency and its resultant amenorrhea. This became increasingly clear after trials of estrogen replacement surprisingly failed to improve bone density in patients with anorexia nervosa (115–117). Further, the severity of osteopenia depends on lean body mass, not on the duration of estrogen deficiency (118). Hypercortisolemia has been reported in anorexia (115), and reduced levels of insulin-like growth factor I (119) along with excessive exercise may also be involved (120). Because osteopenia in anorexia nervosa seems to be a low-turnover condition, associated with increased bone resorption and high serum cortisol levels, and therefore differs from the osteopenia of postmenopausal women, the routine use of estrogen to attenuate bone loss must be reconsidered (121–123).

### IS TREATMENT WITH CALCIUM, VITAMIN D, OR ALENDRONATE INDICATED?

Given the unclear cause of osteopenia in anorexia nervosa, along with the at-best minimal benefit from estrogen, the primary goal of treatment must be to restore weight and avoid bone loss. Normalized weight is the best predictor of bone density (124). This must be discussed with the patient in the early phases of treatment because an increase in body weight may be insufficient to completely restore bone mineral density as anorexia nervosa becomes more chronic (125). Calcium supplementation (1500 mg/d) along with vitamin D (400 IU/d) should be prescribed, especially if cortisol excess is involved in the pathogenesis of osteoporosis (126). Currently, no definitive data support the use of bisphosphonates in patients with anorexia nervosa, although they have been found to be beneficial in preventing corticosteroid-induced osteoporosis (127). Clinicians should closely monitor levels of bone mineral density with bone densitometry in patients with moderate to severe anorexia, especially after amenorrhea has occurred. If results are abnormal, bone densitometry should be repeated every 1 to 2 years to monitor the effectiveness of therapy. When the bone density is found to be osteopenic or frankly osteoporotic despite adequate calcium and vitamin D, more aggressive therapies, such as bisphosphonates or nasal calcitonin, should be considered, given the lifelong risk for fractures (128). Bone markers, such as the resorption marker *N*-telopeptide, may also be used to assess the effectiveness of therapy because they stabilize more rapidly than bone mineral density (129, 130).

*The patient returns 2 weeks later and has gained 3 pounds (1.35 kg). She continues having difficulty with body image issues, and her psychiatrist has prescribed fluoxetine.*

### WHAT LONG-TERM THERAPIES ARE EFFECTIVE FOR ANOREXIA NERVOSA?

Anorexia nervosa is often a protracted illness. One study showed that 16% of anorectic patients continued to meet criteria for anorexia nervosa more than a decade after they initially received the diagnosis (131). A recent study found that 50% of patients had recovered, 21% had an intermediate outcome, and 26% had a poor outcome, with an overall mortality rate of 9.8% (132). Many studies have noted a less than favorable outcome

in patients with anorexia nervosa (133–135), in contrast to bulimia, which has a more favorable prognosis (136). Factors that have been found to be predictive of a poor prognosis include a longer duration of illness, older age at onset, and weight that is a larger percentage below ideal body weight (137, 138). Full recovery from anorexia nervosa is associated with the character trait of self-directedness (the ability to assume control of the direction of one's life), whereas chronic illness is linked to the temperament measure of "high harm avoidance" and to the absence of novelty seeking, which enhances a patient's ability to recover (139).

The decision to transfer a patient with anorexia nervosa to less intensive care is based on the factors described earlier in this paper (140, 141). Patients with severe anorexia who were treated in an inpatient facility and whose weight on transition to outpatient day treatment was more than 10% below ideal body weight have a substantially increased risk for relapse (142). Further, it is difficult to change behavior with psychotherapy in a patient who is experiencing the acute physiologic effects of malnutrition. Magnetic resonance imaging has revealed substantial deficits of gray matter volume in patients with anorexia that resolve with weight restoration (143, 144).

Psychopharmacologic therapy is less than optimal in treating the primary symptoms of anorexia nervosa. The decision to use psychotropics or antidepressants should be made after assessment of other psychiatric symptoms. Individual and group psychotherapy are both used. Although psychological treatment must be included in the multifaceted approach, few formal studies have evaluated its relative effectiveness. Cognitive behavioral psychotherapy is felt to be helpful (145–147), as is family counseling, especially for patients younger than 12 years of age (148, 149). Uncontrolled studies suggest that fluoxetine may be useful in preventing relapse, even in the absence of depression, in patients who have successfully restored their weight (150, 151). However, fluoxetine has not been shown to hasten weight restoration in patients with anorexia nervosa (152).

## CONCLUSION

Anorexia nervosa is associated with substantial morbidity and mortality and has become an increasingly important health concern (153). Because of the litany of medical complications associated with the disorder

(154–157), severely emaciated patients are best treated in a specialty inpatient unit for eating disorders. Patients with serious but less severe weight loss should be treated by a multidisciplinary outpatient team, which should include medical management together with behavioral and dietary therapy to prevent the inexorable decline and physiologic changes associated with weight loss. Current social norms, which mandate thinness (158, 159), emphasize the need for further study of the treatment and prevention of anorexia nervosa (160). The invaluable role of the primary care physician is to point out the reality and severity of this chronic illness while diligently monitoring and assessing the patient's physical status (161).

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