

# EATING DISORDERS



BY MARTHA P. FANKHAUSER, MSPHARM., FASHP, BCPP

Reviewed by Sally K. Guthrie, Pharm.D., FCCP, BCPP; Brian A. Hemstreet, Pharm.D., BCPS; and Kristi Kelley, Pharm.D., BCPS, CDE

## LEARNING OBJECTIVES

1. Analyze different types of eating disorders on the basis of diagnostic criteria, clinical course, and prognosis.
2. Apply knowledge of the etiologies of eating disorders to the clinical findings in a patient.
3. Devise a plan for appropriate assessments and treatments of comorbid medical and psychiatric disorders encountered in patients with eating disorders.
4. Assess nonpharmacologic and pharmacologic treatment approaches for eating disorders.
5. Justify pharmacotherapy approaches for eating disorders on the basis of clinical presentation or laboratory findings in different patient populations.
6. Detect potential pharmacokinetic and pharmacodynamic drug interactions and adverse effects with drugs used in the treatment of eating disorders.

## INTRODUCTION

The spectrum of eating disorders comprises anorexia nervosa (AN), bulimia nervosa (BN), and eating disorder(s) not otherwise specified (ED-NOS); the last category includes binge-eating disorder (BED) and night-eating syndrome (NES). These eating disorders are characterized by aberrant or restricted eating; purging behaviors; excessive exercise; and a preoccupation with food, weight, and body image. Eating disorders impose a

considerable public health burden from increased use of medical services, decreased quality of life, and increased mortality.

## Epidemiology

### Prevalence Rates

Most studies report an increased prevalence of eating disorders in the past 50 years in Western countries. The recent increased comorbid rates of compulsive overeating, binge eating, and obesity may also reflect this higher prevalence. About 34% of adults 20 years and older in the United States are obese. African Americans have a 51% higher prevalence of obesity, and Hispanics have a 21% higher prevalence compared with whites.

For lifetime prevalence rates of eating disorders, 1% develop AN, 1% to 4.2% develop BN, and 0.7% to 4% of community samples have BED. About 50% of individuals with AN will later develop bulimic symptoms, and 25% of individuals with BN have a history of AN. The category of ED-NOS includes both BED and NES and is the most common eating disorder diagnosed in epidemiologic studies, being reported in almost 3% to 5% of women between the ages of 15 and 30 years in Western countries. About 0.6% of women and 2% of men have subthreshold BED, and 5% of women and 4% of men have BED. Regarding ethnic differences in these disorders, AN and BD are less common among African American women than in white and Hispanic women.

## BASELINE REVIEW RESOURCES

The goal of PSAP is to provide only the most recent (past 3–5 years) information or topics. Chapters do not provide an overall review. Suggested resources on this topic include:

- American Psychiatric Association. Practice guideline for the treatment of patients with eating disorders, 3rd ed. *Am J Psychiatry* 2006;163(suppl 7):1–128. Available at [www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=EatingDisorders3ePG\\_04-28-06](http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=EatingDisorders3ePG_04-28-06). Accessed June 4, 2010.
- Fankhauser MP, Lee KC. Eating disorders. In: Koda-Kimble MA, Young LY, Alldredge BK, Corelli RL, Guglielmo BJ, Kradjan WA, et al, eds. *Applied Therapeutics: The Clinical Use of Drugs*, 9th ed. Baltimore: Lippincott Williams & Wilkins, 2009:chapter 82.

## ABBREVIATIONS IN THIS CHAPTER

AN	Anorexia nervosa
BDD	Body dysmorphic disorder
BED	Binge-eating disorder
BMI	Body mass index
BN	Bulimia nervosa
CBT	Cognitive behavior therapy
ED-NOS	Eating disorder not otherwise specified
MAOI	Monoamine oxidase inhibitor
NES	Night-eating syndrome
OCD	Obsessive-compulsive disorder
SSRI	Selective serotonin reuptake inhibitor
TCA	Tricyclic antidepressant

Prevalence rates for NES have been reported as 1.5% to 5.7% in the general population, and rates of 6% to 16% among individuals in overweight and obese weight-loss populations. Nighttime eating has been reported in 9% of candidates for bariatric surgery, 3.8% of older adults with type 2 diabetes, and 12% of psychiatric outpatients.

### *Sex and Age Differences*

Epidemiologic studies have found that most patients with eating disorders are women between 12 and 25 years old. Young women are particularly vulnerable to eating disorders because of their desire to have an ideal body image, and they are more likely to go on strict diets by restricting food intake compared with men. Anorexia nervosa typically emerges between ages 14 and 16, and BN usually occurs around age 19 or 20. Eating disorders such as AN and BN are 10–15 times more common in women than in men. Women are more often given a diagnosis of BED, but the disorder may occur equally often in men.

### **Etiology**

#### *Genetic and Biologic Factors*

The causes of eating disorders are multifactorial and include genetic, family, environmental, biological, psychological, and sociocultural factors. Genetic predisposition is a risk factor because eating disorders appear to run in families, particularly among female relatives. Family studies of NES have found an odds ratio of 4.9 for the presence of the disorder in first-degree relatives. Twin studies have estimated a 50% to 83% genetic risk for the twin of an individual with AN, BN, and BED. Identical twins have a higher concordance rate for eating disorders than fraternal twins. Young women who have a first-degree relative with an eating disorder have a 6- to 10-fold increased risk of developing an eating disorder. First-degree relatives of the individual with an eating disorder also have a higher prevalence of alcoholism and affective

disorders. Genetic studies are attempting to determine whether chromosomes such as 1p, 4, and 10p and genes related to serotonin, endorphin, and brain-derived neurotrophic factor contribute to eating disorders.

Biochemical causes of eating disorders involve the neuroendocrine and neuropeptide systems and circadian rhythms that regulate neurotransmitters and hormonal functioning. Feedback mechanisms are involved with appetite and digestion, growth and development, energy metabolism, hormonal and autonomic systems, sleep, emotions, impulse control, and cognitive functioning. For NES, phase delays in the circadian rhythm ingestion of protein, fat, and carbohydrate may be secondary to neuroendocrine circadian delays in food regulatory hormones such as insulin and leptin, as well as thyroid-stimulating hormone, melatonin, prolactin, and cortisol.

Leptin, one of the most important adipose-derived hormones, plays a role in controlling energy intake and expenditure. Restriction of food, calories, and dietary fat reduces leptin concentrations (hypoleptinemia) and suppresses the hypothalamic-pituitary-gonadal axis, resulting in amenorrhea. Ghrelin is a hormone produced from the cells in the stomach and pancreas as well as the hypothalamus and increases food intake and fat mass. Ghrelin stimulates hunger and is the counterpart of leptin that causes satiation. Ghrelin concentrations increase before meals and decrease after eating. A phase advance of ghrelin concentrations by 5.2 hours has been observed in nighttime eaters.

Individuals with AN and depression have higher concentrations of cortisol, a neurohormone released in response to stress. People with NES report higher levels of stress before the onset of night eating; these individuals also have higher cortisol concentrations than control subjects, which may reflect a biologic stress. Concentrations of vasopressin, a peptide hormone, are elevated in people with obsessive-compulsive disorder (OCD), AN, and BN. Neuropeptide Y and peptide YY, which both stimulate eating behaviors, are increased in both AN and BN. Cholecystokinin concentrations, which are thought to be involved with satiety and ending the drive to eat, are low in some women with BN. Individuals with BN who have low cholecystokinin concentrations may not feel satisfied after eating a normal amount of food and thus continue to binge. Adding protein to the diet stimulates both cholecystokinin and glucagon release, which contribute to increased satiety and reduced food intake. Serotonin, which is important in the regulation of the brain's appetite and satiety centers, is also involved in depression, anxiety disorders, and OCD. Deficiency in L-tryptophan and serotonin represents a link between eating and psychiatric disorders. In addition, norepinephrine deficiency secondary to starvation may account for the presence of fatigue, hypotension, and bradycardia.

Individuals with AN and BN display changes in brain structure, neurochemistry, and metabolism similar to

those found in severe malnutrition. Brain atrophy, disturbances in serotonin pathways, and abnormalities in neuropeptide systems are found in both AN and BN and may persist after recovery from the disorder.

### **Psychological Factors**

One key trigger of eating disorders is the use of stringent dieting or restriction of food intake to lose weight, occurring in conjunction with low self-esteem or self-control. A traumatic event, family stress, or psychosocial problems also may precipitate the onset. There may be an association between childhood sexual abuse and BN, but such an association is not seen in AN. Mothers who are overly concerned about their child's weight and physical attractiveness may increase the risk of dieting and the development of an eating disorder. Girls may develop low self-esteem that leads to an eating disorder if their fathers, brothers, or male friends are overly critical about their weight.

### **Sociocultural Factors**

Athletes or individuals with careers that emphasize thinness (e.g., dancing, gymnastics, wrestling, modeling, long-distance running) are more susceptible to eating disorders. Images of slender celebrities and fashion models portrayed in magazines, television, and movies are probably stronger risk factors in the development of body dissatisfaction and abnormal eating behaviors for young women compared with men. Eating disorders that result in obesity increase the risk of mistreatment by peers, discrimination, stigmatization, low self-esteem, depression, and substance and alcohol abuse.

## **DIAGNOSIS**

Extremes in body weight – either severely underweight or extremely overweight – may indicate the presence of an eating disorder. Obesity is defined as a body mass index (BMI) of 30 kg/m<sup>2</sup> or greater. Adults with a BMI less than 18.5 kg/m<sup>2</sup> are considered underweight, whereas children and adolescents with an age-adjusted BMI below the 5th percentile for age are considered underweight. For children and teens, a healthy weight is between the 5th and 85th percentile for age-adjusted BMI.

### **Diagnostic Criteria**

Two eating disorders, AN and BN, are recognized as diagnostic entities in the American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, Text Revision (DSM-IV). Clinical symptoms, complications, and diagnostic criteria for AN and BN are listed in Table 1-1. A third eating disorder, BED, is a proposed new diagnostic entity in the DSM-IV. Still another category, ED-NOS, refers to eating disorders that are subclinical or that do not completely meet the diagnostic criteria for AN or BN. The differential

diagnosis for eating disorders should rule out medical conditions; drug-induced appetite and weight changes; psychiatric disorders (e.g., OCD, depression, attention deficit-hyperactivity disorder, psychotic disorders, personality disorders); and nicotine, caffeine, alcohol, or other substance use.

### **Anorexia Nervosa**

Individuals with AN may starve themselves or use excessive exercising or other purging behaviors that result in extreme weight loss, defined as 15% below ideal body weight for age, sex, and height. Despite looking emaciated, patients with AN are convinced they are overweight and become terrified of gaining additional weight. Behaviors common in AN include unusual eating habits such as avoiding specific foods, skipping meals, selecting only a few foods to eat, weighing their food, counting calories, and excessive exercising. Individuals with AN may lose weight gradually and may not receive medical or psychiatric attention until their malnourishment leads to serious medical and psychiatric changes.

### **Bulimia Nervosa**

People with BN consume large amounts of food at one time and then try to rid their bodies of the excessive calories by using one or more purging behaviors (i.e., self-induced vomiting; use of enemas, laxatives, or diuretics; or exercise). Binge eating is defined as consuming more high-calorie food than most people would eat in a similar period while feeling a lack of control over eating during the episode. Strict dieting or fasting between episodes of bingeing and purging is also common. Because individuals with BN maintain their weight in normal ranges and binge and purge in secret, family members and medical professionals may not easily detect the disorder. Individuals may be so ashamed of their eating habits that they do not seek help or treatment until they are in their 30s or 40s.

### **Binge-Eating Disorder**

Binge-eating disorder is similar to BN and is characterized by episodes of bingeing or uncontrolled consumption of food but without the purging behaviors, although dieting between bingeing episodes may occur. The restriction of food between bingeing episodes may be a biologic trigger for intense craving of food and eating excessive amounts of food at one time. Most people with BED are overweight or obese and have a history of large weight fluctuations. They often have difficulty losing weight and keeping it off because of their bingeing on excessive amounts of foods with high fat and carbohydrate content. About one-third of people participating in weight-loss programs have BED.

The research criteria for BED include experiencing at least two binge-eating episodes a week for 6 months, a lack of control over bingeing behaviors, and marked

**Table 1-1.** Sign and Symptoms, Diagnostic Criteria, and Complications of Eating Disorders

	Anorexia Nervosa	Bulimia Nervosa
Signs and symptoms	<ul style="list-style-type: none"> <li>Losing a significant amount of weight</li> <li>Continuing to diet although very thin</li> <li>Feeling fat, even after losing weight</li> <li>Fearing weight gain</li> <li>Having a preoccupation with food, calories, nutrition, and/or cooking</li> <li>Avoiding meals, not eating with others</li> <li>Exercising compulsively</li> <li>Bingeing and purging</li> <li>Missing a monthly menstrual cycle</li> <li>Experiencing fatigue or low energy</li> <li>Feeling cold all the time</li> <li>Growing fine, soft hair over the body</li> <li>Losing hair and breakage of nails</li> <li>Not attending social activities involving food</li> </ul>	<ul style="list-style-type: none"> <li>Rapid weight gain, weight fluctuation, or obesity</li> <li>Bingeing or eating uncontrollably</li> <li>Eating late at night</li> <li>Hoarding food</li> <li>Purging by strict dieting, fasting, vigorous exercise, vomiting, abusing laxatives or diuretics in an attempt to lose weight</li> <li>Using the bathroom frequently after meals</li> <li>Experiencing depression or mood swings</li> <li>Having irregular menses</li> <li>Developing dental problems, swollen cheek glands, heartburn and/or bloating</li> <li>Experiencing problems with alcohol or drugs</li> <li>Regularly buying enemas, laxatives, and diuretics</li> <li>Not attending social activities involving food</li> </ul>
Diagnostic criteria	<ul style="list-style-type: none"> <li>Two subtypes: restricting and binge eating/purging</li> <li>Weight at least 15% below normal for the same height and age</li> <li>Missing at least three consecutive menstrual cycles (if childbearing age)</li> <li>Fear of weight gain or becoming fat even though underweight</li> <li>Refusing to maintain the minimal normal body weight</li> <li>Believing themselves overweight despite being dangerously thin and malnourished</li> <li>Using food restriction, purging, and/or excessive exercise to lose weight</li> </ul>	<ul style="list-style-type: none"> <li>Two subtypes: purging or nonpurging</li> <li>Averaging at least two binge/purge episodes a week for at least 3 months</li> <li>Eating a large amount of food in a discrete period (e.g., within any 2-hour period) that is larger than most people would eat during a similar period</li> <li>Using purging (self-induced vomiting, laxatives, diuretics, enemas) or nonpurging behaviors (fasting or excessive exercise) to prevent weight gain</li> <li>Lacking control over bingeing behaviors</li> <li>Obsessing and having dissatisfaction about their body shape and weight</li> </ul>
Complications of anorexia nervosa and bulimia nervosa	<ul style="list-style-type: none"> <li>Growth delay (growth retardation and short stature)</li> <li>Osteopenia or osteoporosis (a 2- to 7-fold increased risk of fractures later in life)</li> <li>Cardiac impairment (bradycardia, orthostatic hypotension, prolonged QTc interval, arrhythmias, mitral valve prolapsed, congestive heart failure, sudden death)</li> <li>Bone marrow suppression (mild anemia, leukopenia, thrombocytopenia)</li> <li>Gastrointestinal dysfunction (nausea, bloating, slowed motility, constipation, esophagitis, Mallory-Weiss tears, Barrett esophagus, acute pancreatitis, gallstones)</li> <li>Fluid and electrolyte abnormalities from purging (hypokalemia, hyponatremia, hypochloremic alkalosis, inability to concentrate urine, elevated BUN, ketonuria)</li> <li>Endocrine abnormalities from low body weight (decreased serum LH, FSH, DHEA, IGF-I, leptin; increased serum GH, cortisol)</li> <li>Delayed puberty and infertility secondary to amenorrhea</li> <li>Psychiatric impairment (depression, anxiety, insomnia) and cognitive changes</li> <li>Neurologic impairment (peripheral neuropathy, myopathy, headaches, seizures, cortical atrophy)</li> <li>Dental erosion and enlarged salivary glands secondary to vomiting</li> <li>Dermatologic changes (hair loss, lanugo, brittle nails and hair, acrocyanosis, pitting edema, Russell sign [calluses over the knuckles])</li> </ul>	

Information from American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Washington, DC: American Psychiatric Association, 2000.

BUN = blood urea nitrogen; DHEA = dehydroepiandrosterone; FSH = follicle-stimulating hormone; GH = growth hormone; IGF-I = insulin-like growth factor-I; LH = luteinizing hormone.

distress regarding binge eating. The binge-eating episodes are associated with three or more of the following: eating rapidly; eating until feeling uncomfortable; consuming a large amount of food when not hungry; eating alone because of embarrassment; and feeling guilty, disgusted, or depressed after overeating.

### **Night-Eating Syndrome**

Nighttime or nocturnal bingeing episodes have been reported with BED. Night-eating syndrome is characterized by morning anorexia; awakenings accompanied by nocturnal food intake; and hyperphagia, defined as consuming 25% or more of daily calorie intake after the evening meal at least two times/week for 3 months. Individuals with NES have significant sleep disturbances with lower sleep efficiency and more frequent awakenings compared with control subjects. Many night eaters report being more depressed in the evening, and many have a history of mood disorders (e.g., major depression [56%], dysthymia [11%]) and anxiety disorders (e.g., generalized anxiety disorder [17.5%], posttraumatic stress disorder [18%]). Studies have reported a strong relationship between NES and overweight status: up to 50% of obese individuals report that nighttime eating preceded their obesity.

## **Eating Disorders in Special Populations**

### **Pregnancy**

Because eating disorders are common in women of childbearing age, they are at higher risk of infertility, menstrual irregularities, and unplanned pregnancies because of unprotected sex and menstrual cycle abnormalities. Women with eating disorders should receive treatment before conceiving because food restriction, nutritional deficits, binge eating, and purging can cause significant adverse effects in both the mother and fetus.

An estimated 5% of pregnant women have eating disorder behaviors and symptoms. Pregnancy complications such as preterm births, smaller gestational infants, and postpartum depression are common in women with eating disorders. During pregnancy, women with AN may require additional monitoring and nutritional counseling on healthy eating habits because of the need to gain weight. These women may restrict food or use excessive exercise to minimize weight gain; this may result in maternal malnutrition, anemias, and increased risk of miscarriage, preterm birth, cesarean delivery, hypertension, and preeclampsia. Women with BN or BED may gain excessive weight during pregnancy because of increased food intake or bingeing and decreased compensatory behaviors such as vomiting and laxative abuse.

Infants born to mothers with eating disorders are at higher risk of fetal growth restriction, lower birth weight, lower Apgar scores, malformations such as cleft lip and palate, nutritional deficiencies, and failure to thrive. Often, the children of mothers with eating disorders

have increased risks of both nutritional and emotional problems.

### **Diabetes**

Patients with type 1 and type 2 diabetes mellitus may have an underlying eating disorder such as BN, BED, or NES that should be evaluated and treated to minimize long-term health risks. Obesity is associated with an increased risk of diabetes mellitus, cardiovascular disease, hypertension, and certain cancers. Medical complications related to abnormal eating behaviors include episodes of hypoglycemia or ketoacidosis, dehydration, and elevated A1C values despite taking antidiabetic drugs.

### **Middle-aged and Older Adults**

About 5% of individuals with eating disorders are aged 30–40 years. Some individuals with a previous diagnosis of AN, BN, or BED may have a relapse later in life secondary to life stresses (e.g., after childbirth, a divorce, loss of a spouse) or because of premenstrual syndrome, perimenopause, or menopause. Significant weight gain or loss in an older person should be monitored to rule out a medical condition such as thyroid abnormalities, diabetes, or cancer. Anorexia-like adverse effects are associated with many drugs such as central nervous stimulants, theophylline, norepinephrine or dopamine augmentation, and anticancer agents. Other drugs may stimulate the appetite (e.g., serotonin, dopamine, histamine receptor antagonists). Older individuals with an eating disorder are at a higher risk of medical and psychiatric complications such as depression, anemia, obesity, diabetes, and gastrointestinal and cardiovascular disorders.

### **Comorbid Psychiatric and Medical Conditions**

Individuals with AN are characteristically excellent athletes, outstanding students, perfectionists, and obedient individuals. However, psychiatric comorbidities are often associated with eating disorders; these include depression; anxiety disorders; impulse control disorders with self-destructive behaviors; abuse of alcohol, tobacco, or drugs; personality disorders such as borderline personality disorder; somatoform disorders; and other psychological problems. The family/caregivers of individuals with eating disorders have high levels of psychological distress and increased risks of mental illness because of the long-term complications from eating disorders.

Anxiety disorders often precede the onset of AN, and both anxiety and depression persist after recovery from AN. Obsessive-compulsive traits characterized by repetitive thoughts and behaviors are also common with AN. In the more acute phases of AN, individuals have cognitive, emotional, and social dysfunctioning (e.g., impaired decision-making and executive thinking abilities, generalized and social anxiety disorder).

Body dysmorphic disorder (BDD) is serious, lifelong somatoform disorder characterized by excessive concern and preoccupation with a perceived defect in their physical features (e.g., skin, hair, nose, body shape). Although they look normal to the objective observer, individuals suffering from BDD believe that these body parts are ugly. They frequently look at themselves in the mirror, or exercise or groom excessively to try to correct the perceived problem. They may go so far as to seek cosmetic surgery, liposuction, collagen/fat injections. Even when cosmetic surgery is successful, these individuals are unhappy with the outcome and may want additional procedures. A muscle dysmorphia syndrome has been described in men who are obsessed with exercising either to lose or gain weight to become more muscular. Some men may even use anabolic steroids or other drugs to increase muscle mass.

The rates of medical complications associated with eating disorders are among the highest for any psychiatric disorder. The highest risk of irregular heart rhythms and heart failure is in individuals who use central nervous system stimulants, weight-reduction drugs, or drugs to induce vomiting, bowel movements, or urination. Starvation results in deficiencies of amino acids, vitamins, and minerals; muscle wasting; reductions in subcutaneous fat; and eventual damage to vital organs such as the heart and brain. The production of thyroid and gonadal hormones is reduced, and blood pressure and pulse rate decrease because of limited energy from calories and fat.

Significant weight loss causes growth retardation, osteoporosis, mild anemia, and reduced muscle mass; the many physical changes in the body include brittle nails and hair, dry skin, hair loss, and the growth of fine, soft hair called lanugo. Reduced body fat results in lowered body temperature, intolerance to cold, and amenorrhea. More than 90% of women with AN develop amenorrhea because of low concentrations of leptin, follicle-stimulating hormone, and luteinizing hormone. A *female athlete triad* is sometimes used to describe young women athletes who have an eating disorder, amenorrhea, and osteoporosis. Estrogen deficiency, inadequate calcium and vitamin D intake, low body weight, and decreased insulin-like growth factor are associated with bone loss in AN. Men with AN often become impotent if gonadotropin functioning is abnormal.

Repeated episodes of bingeing and purging, together with starvation or restricting food, may cause significant damage to the body. Individuals with BN often have clinical depression or dysthymia, anxiety disorders such as OCD, personality disorders, and impulsive control behaviors or disinhibition (e.g., stealing, engaging in risky behaviors, alcohol use or binge drinking, substance abuse). Because impulsive behaviors are common, they are at risk of suicidal behaviors. Laboratory and physical findings common with BN include disturbances in electrolyte and acid-base balances because of

frequent vomiting. Electrolyte imbalances such as hypokalemia and hyponatremia increase the risk of irregular heartbeats and heart failure. Tooth enamel may be damaged secondary to repeated exposure to acidic stomach contents. Chronic constipation, bowel paralysis, gastrointestinal bleeding, peptic ulcers, and pancreatitis may also occur. Enlarged parotid glands become visually prominent when the esophagus is inflamed. Scarring on the backs of the hands or fingers (Russell sign) may occur when these are used to induce vomiting.

Comorbid disorders associated with BED include obesity, type 2 diabetes, hypercholesterolemia, hypertension, sleep apnea, gallbladder disease, joint pain, arthritis, kidney disease, heart disease, strokes, pregnancy-related complications, menstrual irregularities, ovarian abnormalities, skin disorders, and upper respiratory problems. Those with severe obesity may receive bariatric surgery that can result in serious complications. Individuals with BED often have other psychiatric disorders such as depression, anxiety, other mood disorders, nicotine and alcohol dependence, and substance abuse.

### Outcomes and Prognosis

Self-induced starvation, binge eating, or purging of food can cause alterations in brain functioning, impairment in cognition, poor judgment, emotional instability, restriction in daily life activities, and role impairment. The consequences of eating disorders are severe: 1 in 10 women with AN dies of starvation, cardiac arrest, or suicide. The mortality rate in AN is estimated to be 4% to 6% and is 12 times higher than the annual death rate from all other causes in women aged 15–24 years. Longitudinal outcome studies suggest that less than 50% of individuals with AN experience full recovery (defined as weight gain and return of menses). Menses usually resume within 6 months after attaining 90% of ideal body weight. Another 20% to 25% of these individuals show improvement, but 25% are chronically ill with poor outcomes. About 33% of those who recover from AN will have a relapse.

A large-scale mortality and outcome study found mortality rates of 3.9% for BN and 5.2% for ED-NOS; these rates are similar to those for AN. Suicide mortality ratios were also elevated for both BN and ED-NOS, suggesting that suicide risk is common in all patients with eating disorders. A review of long-term outcome studies reported that 45% of individuals with BN fully recovered, 27% improved, and 23% had a chronic course. Crossing over to another eating disorder during the course of BN was also reported in 10% to 32% of individuals.

## ASSESSMENT AND TREATMENT

### Guidelines for Eating Disorders

Steps in the management of eating disorders are listed in Box 1-1. The laboratory assessment and medical monitoring of patients with eating disorders are outlined in

## Box 1-1. Steps in the Management of Eating Disorders

### 1. Implement management resources

- Develop a therapeutic alliance
- Determine the diagnosis and types of behaviors (restricting, binge eating/purging)
- Consult and collaborate with other professionals and clinicians
- Implement nutritional counseling/rehabilitation

### 2. Assess for presence of factors requiring hospitalization<sup>a</sup>

- Rapid and excessive weight loss (less than 85% of body weight for height, age, and sex)
- Serious metabolic disorders (dehydration, hypokalemia, hyponatremia, hypophosphatemia)
- Cardiac abnormalities (arrhythmias, bradycardia, hypotension, severe orthostatic changes)
- Uncontrollable and severe binge eating and purging
- Acute psychiatric conditions (psychosis, depression, suicide ideation with a plan or attempt)
- Need for intravenous fluids, nasogastric tube feedings, or several daily laboratory tests
- Supervision required during and after meals and in the bathroom
- Poor motivation for outpatient treatment
- Severe family conflicts, living alone without adequate support, unable to receive outpatient treatment
- For AN: hospitalization may be required until 90% to 92% of ideal body weight is maintained

### 3. Determine treatment goals and therapeutic end points

- For AN: restore weight gradually through refeeding and vitamin, mineral, and electrolyte supplementation (risk of heart failure is highest during the first 2 weeks of refeeding). A target weight for AN is usually a BMI of 19–21 kg/m<sup>2</sup>
- Treat coexisting psychiatric disorders with therapy, support, and pharmacotherapy if needed
- Establish a normal eating pattern without restricting or binge-eating behaviors
- Eliminate purging behaviors
- Improve social and interpersonal functioning
- Prevent suicidal behavior
- Prevent relapse
- Reduce morbidity and mortality

### 4. Provide psychiatric assessment, treatment, and monitoring

- Assess and monitor psychiatric symptoms, behaviors, and medical status
- Initiate psychosocial treatments. Psychotherapy may be needed for a long-term basis
- For BN, BED, BDD, and NES: consider an SSRI to reduce symptoms of anxiety, OCD, depression, and impulsivity and to reduce binge eating and vomiting. For relapse prevention, continue for at least 9 months
- For AN: after weight restoration, consider an SSRI for anxiety, OCD, and depression
- Monitor for suicidal thoughts or behaviors when starting or changing an antidepressant

<sup>a</sup>Information from American Psychiatric Association. Practice guideline for treatment of patients with eating disorders, 3rd ed. *Am J Psychiatry* 2006;163(suppl 7):1–128.

AN = anorexia nervosa; BDD = body dysmorphic disorder; BED = binge-eating disorder; BMI = body mass index; NES = night-eating syndrome; OCD = obsessive-compulsive disorder; SSRI = selective serotonin reuptake inhibitor.

Table 1-2. The American Psychiatric Association provides the current clinical guidelines for the assessment and treatment of eating disorders (available at [www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=EatingDisorders3ePG\\_04-28-06](http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=EatingDisorders3ePG_04-28-06)). A more recent comprehensive book that addresses the diagnosis, assessment, and treatment of patients with AN, BN, BED, and ED-NOS was published by the experts who wrote the 2006 clinical guidelines (see annotated bibliography).

### Level of Care

If a specialized eating disorder program is necessary, a comprehensive treatment plan involving a variety of

experts and approaches is recommended. Some communities have available resources such as ambulatory clinics, residential treatment facilities, partial hospitalization programs, and inpatient medical or psychiatric units. Clinics and clinicians who specialize in eating disorders (e.g., nutritionist, psychiatrist, psychotherapist) are the best resources for evaluating a person with an eating disorder. Consultation with a nutritional specialist is recommended in the restoration of body weight and in providing optimal nutritional status for patients with AN.

During pregnancy and the postpartum period, a nutritionist, obstetrician, and psychiatrist are recommended to monitor nutrition, weight gain, and psychiatric

**Table 1-2. Medical Assessment and Monitoring of Eating Disorders**

Laboratory Tests and Screening	Conditions to Monitor For
BMI <sup>a</sup> and waist circumference; adult ranges for BMI: ≤ 17.5 = severe weight loss < 18.5 = underweight 18.5–24.9 = normal weight 25.0–29.9 = overweight 30.0–34.9 = obese class I 35.0–39.9 = obese class II ≥ 40.0 = obese class III	AN – low body weight and BMI, malnutrition, weakness, lassitude, hypothermia, cachexia, low body fat BN, BED – overweight or obesity, weight fluctuations, changes in abdominal fat Obese individuals – atherogenic dyslipidemia, insulin resistance or glucose intolerance, high fibrinogen or plasminogen activator inhibitor-1, elevated C-reactive protein, elevated blood pressure
Vital signs: blood pressure, pulse, temperature	Palpitations, arrhythmias, bradycardia, weak irregular pulse, orthostatic hypotension, hypertension, weakness
Drug screening: alcohol and substance use (e.g., cannabis, cocaine, methamphetamine, benzodiazepines)	Comorbid substance or alcohol use, nicotine and caffeine dependence (provide treatment)
Comprehensive metabolic panel: glucose, calcium, albumin, total protein, sodium, potassium, bicarbonate, chloride, blood urea nitrogen, serum creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase	Low glucose, albumin, total protein, electrolytes, and renal and liver dysfunction During refeeding – hypokalemia, hypomagnesemia, and hypophosphatemia. Individuals who vomit – hypokalemia and hypochloremic alkalosis
Thyroid functioning: thyroid-stimulating hormone, triiodothyronine, thyroxine	Hyperthyroidism or hypothyroidism with symptoms of fatigue, hypothermia, and cold intolerance
Complete blood cell count with differential, vitamin and iron values: 25-hydroxy vitamin D, red blood and serum folate, vitamin B <sub>12</sub> , niacin, thiamine, ferritin, serum iron, total iron-binding capacity, transferrin saturation	Anemia, leukopenia, low erythrocyte sedimentation rate, thrombocytopenia bruising and clotting abnormalities During refeeding – thiamine deficiency
Lipid profile: total cholesterol, high- and low-density lipoproteins, triglycerides	Hyperlipidemia, hypertriglyceridemia
Additional blood chemistry: serum magnesium, phosphorus, amylase	If purging – electrolyte abnormalities and increased amylase If vomiting or abusing laxatives – hypomagnesemia, hypophosphatemia
Urinalysis: urine-specific gravity and urine osmolality	Dilute urine from increased fluid intake and electrolyte abnormalities
Skeletal disorders: DEXA bone density scan (hip and lumbar spine)	Osteopenia and osteoporosis, bone pain with exercise, arrested skeletal growth, short stature
Hormonal imbalance and pregnancy: serum estradiol and luteinizing hormone, follicle-stimulating hormone, beta-human chorionic gonadotropin and prolactin (in women); serum testosterone (in men)	Menstrual irregularities, amenorrhea, sexual dysfunction, fertility problems, prolactinoma, pregnancy
Cardiac functioning: electrocardiography and physical symptoms: faintness, dizziness, weakness, shortness of breath, chest pain, cold extremities	Bradycardia, arrhythmias, mitral valve prolapse, QTc prolongation, increased PR interval, first-degree heart block, ST-T abnormalities If using ipecac – cardiomyopathy
Brain functioning: computerized tomography, magnetic resonance imaging, and electroencephalogram	Cognitive impairment, seizures, neurologic abnormalities With severe malnutrition – neuropsychiatric changes
Stool guaiac	If purging or abusing laxatives – blood.
Gastrointestinal functioning: heartburn, reflux, abdominal pain, involuntary vomiting, constipation, dehydration, and bloating	Gastrointestinal symptoms, bowel irregularities, enlarged salivary glands If purging or abusing laxatives – gastric or esophageal rupture or perforation
Oropharyngeal: dental decay, pain in pharynx, swollen cheeks and neck	If purging – dental caries and erosion of the enamel, enlarged salivary glands

Information from American Psychiatric Association. Practice guideline for treatment of patients with eating disorders, 3rd ed. *Am J Psychiatry* 2006;163(suppl 7):1–128.

<sup>a</sup>For adults, BMI = weight (kg)/[height (m)]<sup>2</sup> or weight (lb)/[height (in)]<sup>2</sup> × 703. A BMI calculator for adults 20 years and older is available at [www.cdc.gov/healthyweight/assessing/bmi/index.html](http://www.cdc.gov/healthyweight/assessing/bmi/index.html). For children and teens 2–19 years old, the BMI age- and sex-specific percentiles are recommended. A BMI-for-age percentage calculator for children and teens is available at <http://apps.nccd.cdc.gov/dnpabmi/>.

<sup>b</sup>To determine waist circumference, locate the upper hipbone, and place a measuring tape around the abdomen. The tape measure should be horizontal and snug. Information is available at [www.cdc.gov](http://www.cdc.gov).

AN = anorexia nervosa; BED = binge-eating disorder; BN = bulimia nervosa; BMI = body mass index; DEXA = dual emission x-ray absorptiometry.



symptoms. A pediatrician should closely monitor the weight and growth of the infant after delivery because women with eating disorders are more likely to underfeed their infants compared with women who do not have eating disorders.

Access to care and reimbursement for hospitalizations or residential programs are often a challenge for individuals with eating disorders. Individuals with AN often require hospitalization, creating a significant economic burden for health services costs and health care utilization. If the individual with AN is not hospitalized or placed in a residential treatment facility, a health care provider or therapist should have at least weekly face-to-face sessions with the individual and close family members or caregivers. More intense monitoring with scheduled appointments and telephone assessments should be performed during the first few months of treatment.

### **Medical and Psychiatric Assessment**

The first step in evaluating a patient with a potential eating disorder is to do a psychiatric and medical assessment and laboratory testing to rule out any other psychiatric disorders or medical illnesses (Table 1-2). Rare but serious medical disorders that may present with weight loss include adrenal insufficiency, new onset diabetes mellitus, major depression with anorexia, gastrointestinal disorders (e.g., celiac disease), inflammatory bowel disease, and abdominal masses. Obesity may cause a metabolic syndrome that results in type 2 diabetes, coronary heart disease, and atherosclerosis; this syndrome may increase the risk of stroke and peripheral vascular disease. During pregnancy, weight gain should be closely monitored and laboratory evaluations performed such as fasting glucose, complete blood cell counts, electrolytes, serum creatinine, and blood urea nitrogen.

### **Nonpharmacologic Approaches**

#### ***Nutritional Counseling and Rehabilitation***

While other health care professionals monitor or treat any medical complications, consultation with a nutritionist is essential to recommend necessary diets, supplements, and eating regimens. Individuals with BN and BED tend to binge on foods high in fats and carbohydrates that have relatively low protein content. Adding protein to meals decreases hunger and reduces food intake and bingeing. Vitamins, minerals, calcium supplemented with vitamin D<sub>3</sub>, essential fatty acids, and other nutritional supplements may be needed during the refeeding phase and maintenance therapy.

Women who are pregnant or breastfeeding should be taking a prenatal vitamin with adequate folic acid, and additional vitamin D<sub>3</sub> supplementation if at risk of vitamin D deficiency, as well as ensuring regular intake of protein, fats, carbohydrates, and water. Pregnant women may require additional counseling about the impact of eating disorders on the health of the fetus and their other

children. Nutritional approaches for NES include having a regular daytime eating schedule to minimize the urge for nocturnal ingestion of food, keeping a sleep and food diary, and undergoing nutritional education. Treatment approaches for individuals with BN or BED who are overweight or obese include monitoring of glucose, A1C, and potassium concentrations; nutritional counseling; and weight-reduction programs.

A challenge for nutritional recommendations is the effect that eating behaviors have on metabolic rates. To gain weight or to maintain a normal weight, individuals with AN may require a higher daily intake of calories than a person without an eating disorder. The individual with BN and BED may have a slower metabolism because of intermittent food restrictions or dieting between binges; therefore, these individuals can quickly gain excess weight while consuming the same amount of calories required by an individual of a similar age and size who does not have an eating disorder.

Nutritional rehabilitation is required for all individuals with AN who are underweight. Normal rates of weight gain are about 2–3 lb (1 kg) per week for inpatients and 0.5–1 lb (0.5 kg) per week for outpatients. Intake of calories usually starts at 30–40 kcal/kg/day (about 1000–1600 kcal/day) and is increased up to 70–100 kcal/kg/day based on weight gain and fluid balance. Nasogastric feeding should only be used if the person refuses to eat normally. A refeeding syndrome may result from rapid changes in electrolytes and fluids when malnourished individuals are given excessive feedings during the first few weeks. Therefore, monitoring of electrolytes, fluid retention, cardiac functioning, and mental status changes is important. The refeeding syndrome occurs more often with parenteral than enteral feeding in malnourished individuals.

#### ***Psychosocial Interventions***

Psychological treatments have been shown in several studies to improve the outcome in eating disorders; these treatments include cognitive behavior therapy (CBT), interpersonal therapy, dialectical behavioral therapy, behavioral weight-loss programs, and self-help groups. Several different types of psychotherapeutic approaches may be needed during the course of treatment to maximize the outcomes for AN, BN, and BED. Although psychosocial approaches are the cornerstone for the management of eating disorders, individuals may continue to be symptomatic without the addition of pharmacotherapy.

In the early treatment of individuals with AN, supportive therapy with a psychotherapist who has empathy and acceptance of the individual is important for establishing a therapeutic alliance and may be more effective than CBT or interpersonal therapy. When individuals are severely malnourished, they are not cognitively or psychologically able to participate in more intensive psychotherapeutic interventions. Individual or group CBT

is usually recommended as the first-line treatment for BN and BED. In this therapy, individuals learn how to change abnormal thoughts and behaviors (e.g., distorted and rigid thoughts about eating) through rewards or modeling of the correct eating behaviors. If CBT is not effective, interpersonal or psychodynamic therapies are other options. Intensive group psychotherapy and antidepressant drugs, either alone or in combination, are effective in treating BN and preventing relapse. Combining CBT and antidepressants may also be effective for BED and NES.

Family therapy should always be considered for adolescents who live with their parents or for older individuals with significant parental interaction. Couples therapy may be beneficial for those with relationship issues or marital discord. Self-help groups, online support through other peers or national organizations, and 12-step recovery programs for eating disorders, alcohol, and/or substance abuse help patients and their families to better understand the causes and treatment of eating disorders and thereby decrease relapse. Alcohol and tobacco cessation interventions that use a bio-psychosocial approach, together with pharmacologic treatments, should be included for all individuals with dependence issues. Behavioral weight-loss programs that combine nutritional counseling, exercise regimens, and psychosocial approaches are recommended for obese individuals with BN, BED, and NES.

### **Pharmacologic Approaches**

Nutritional rehabilitation, psychological therapies, physical fitness programs, and medical/psychiatric monitoring continue to be the foundation of successful pharmacotherapy interventions. Pharmacotherapy should be based on a symptom approach for AN, BN, and BED. For the acute treatment of AN, drugs are primarily used to improve gastrointestinal motility during refeeding, to treat medical complications, and to stimulate weight gain. For BN and BED, drugs are recommended for decreasing binge eating and purging behaviors and for the treatment of comorbid depression and anxiety disorders. Adherence to treatment may be difficult because of adverse effects of drugs; therefore, regular monitoring for efficacy and adverse effects, together with patient counseling, is essential for optimal outcomes.

### **Depression, Anxiety, and OCD**

Antidepressants are helpful for treating comorbid symptoms of anxiety, obsessive-compulsive behaviors, depression, and impulse control behaviors such as binge eating. For individuals with BN, the combination of serotonin-augmenting antidepressants with psychological treatment such as CBT provides the best remission outcomes. For pregnant women with BN, antidepressant drugs may be needed for the treatment of binge eating and purging. Individuals with BED, BDD, or muscle dysmorphia syndrome have significant anxiety symptoms and

obsessive-compulsive behaviors and may respond to serotonin-augmenting antidepressants together with CBT.

### *Antidepressants*

Serotonin-augmenting antidepressants are effective in the initial treatment approach for individuals with BN, and may also assist in treating the bulimic or obsessive-compulsive symptoms of BED. Antidepressant drugs are not effective in AN until the individual has consumed adequate essential amino acids and vitamins to synthesize neurotransmitters such as serotonin and norepinephrine. Individuals with BN or BED who restrict food intake between binges may also be unable to synthesize the neurotransmitters required for antidepressant efficacy.

Not all selective serotonin reuptake inhibitors (SSRIs) are labeled for use in children and adolescents, and most have little clinical data for efficacy and adverse effects in individuals with eating disorders. The choice of a SSRI is usually based on tolerance to adverse effects and response to treatment. In most placebo-controlled studies in BN and BED, SSRIs are more effective in reducing binge-eating episodes when used at the higher dosages.

Fluoxetine is the only SSRI with a labeled indication for use in adults with BN. In children, fluoxetine dosing is 10–20 mg/day for depression and 10–60 mg/day for OCD; in adults, the recommended dosage is 20–40 mg/day for depression and 40–80 mg/day for OCD. However, higher dosages of 60–80 mg/day may be required for BN and BED. Sertraline is labeled for use in OCD with dosages of up to 25 mg/day for children ages 6–12 years, 50 mg/day for adolescents ages 13–17 years, and 50–200 mg/day for adults. Fluvoxamine is labeled for use in OCD in children and adolescents ages 8–17 years; dosage ranges are 50–200 mg/day for children 8–11 years, 50–300 mg/day for adolescents, and 100–300 mg/day for adults. Paroxetine is labeled for OCD only in adults with dosages of 20–60 mg/day. Citalopram and escitalopram do not have a labeled indication for OCD. Dosages of citalopram for depression are 10–40 mg/day for adolescents and 20–60 mg/day for adults. Escitalopram dosing for depression is 10–20 mg/day for adolescents and up to 30 mg/day for adults.

Studies in patients with BN have shown tricyclic antidepressants (TCAs) to be more effective than placebo in decreasing vomiting and bingeing; however, the adverse effect profile of these agents makes them second-line alternatives to SSRIs. Sibutramine, a norepinephrine-serotonin reuptake inhibitor, is marketed as an anorexiant for the treatment of obesity. This agent, in several placebo-controlled trials, reduced binge eating and caused weight loss in adults at dosages of 10–15 mg/day. Venlafaxine and desvenlafaxine are not labeled for OCD or depression in children and adolescents. Other dual-mechanism reuptake inhibitors (e.g., duloxetine, milnacipran) have not been studied.

Mirtazapine may increase appetite and stimulate weight gain because of antagonist effects of serotonin 2 and 3 receptors and histamine<sub>1</sub> receptors in patients with AN; however, this agent would not be recommended in BN or BED because of the risk of weight gain. Initial dosages of mirtazapine in adults range from 7.5 mg to 15 mg at bedtime, with titration up to 15–45 mg/day. Cyproheptadine, a histamine and serotonin antagonist, has been used in dosages of up to 24 mg/day in patients with AN with food restriction behaviors to promote appetite, and it may also have some antidepressant effects secondary to weight gain and restoration of neurotransmitter activity in the brain.

#### *Drug Interactions*

Antidepressants that inhibit the cytochrome P450 (CYP) enzymes may interact with other drugs and should be monitored if there is a potential for drug interactions. The SSRIs that inhibit the CYP enzymes include fluoxetine (1A2 and 2C19 moderate; 2D6 strong), fluvoxamine (1A2 and 2C19 strong), paroxetine (2B6 moderate and 2D6 strong), and sertraline (2B6, 2C19, 2D6, and 3A4 moderate). Citalopram and escitalopram are weak inhibitors of CYP enzymes and have the fewest drug interactions.

Because of drug-food and drug-drug interactions, monoamine oxidase inhibitors (MAOIs) are not recommended. Binge eating can be lethal in an individual taking an MAOI if a sympathomimetic appetite suppressant is used or if foods high in tyramine content are ingested. Pharmacodynamic interactions, such as when a serotonin antagonist (e.g., cyproheptadine, mirtazapine, trazodone, atypical antipsychotics) is combined with an SSRI, may decrease SSRI efficacy by blocking postsynaptic serotonin receptors.

#### *Adverse Effects*

All classes of antidepressants have a black box warning for increased risks of suicidal thoughts and behaviors, particularly in adolescents and young adults. The most common adverse effects of SSRIs are nausea, diarrhea, headache, insomnia, and sexual dysfunction. Most SSRIs are considered weight neutral except for paroxetine, which may increase weight. Paroxetine and fluvoxamine, if abruptly discontinued, have a higher risk of withdrawal syndrome than other SSRIs and should be avoided if nonadherence is a concern.

Because of overdose risks and cardiac effects, TCAs are seldom used. Mirtazapine may cause significant weight gain, sedation, dizziness, constipation, neutropenia, and an increase in serum cholesterol and triglyceride concentrations. Adverse effects of sibutramine include increased blood pressure and pulse rate, headache, insomnia, anorexia, and constipation. Benzodiazepines and nonbenzodiazepine sedative-hypnotic agents may cause sedation,

depression, and dependence; therefore, these should only be used short term for SSRI-induced insomnia.

#### ***Gastrointestinal Symptoms***

Constipation and bloating secondary to slowed gut motility may occur in AN and BN. Stool softeners such as docusate together with adequate hydration may be needed to treat constipation associated with the eating disorder. Anticholinergic agents such as diphenhydramine and TCAs should be avoided because of worsening of constipation. Metoclopramide, a dopamine antagonist and promotility agent, has been used to help relieve gastrointestinal symptoms but may cause extrapyramidal symptoms, sedation, and depression. Metoclopramide dosing should be at the lowest level for prokinetic activity (e.g., 5–10 mg up to four times/day, 30 minutes before meals and at bedtime) and should be tapered to avoid a discontinuation syndrome. Osmotic laxatives (e.g., polyethylene glycol 3350 products such as GoLYTELY or MiraLAX) may also be used as needed to treat occasional constipation or irregular bowel movements, along with monitoring for electrolyte abnormalities and dehydration.

#### ***Decreased Bone Density***

Recovery of bone density requires adequate weight gain, the resumption of a normal menstrual cycle, and supplementation with 1200–1500 mg/day of elemental calcium and at least 800 international units/day of vitamin D3 (cholecalciferol). Obese individuals, those with fat malabsorption, dark-skinned individuals, and people with limited sun exposure may require higher daily doses of vitamin D3 to achieve serum 25-hydroxyvitamin D concentrations greater than 30 ng/mL; optimal health ranges are 40–70 ng/mL.

Excessive weight-bearing exercise may cause estrogen deficiency and amenorrhea; therefore, this form of exercise is not recommended until there is sufficient weight gain and menstruation has resumed. Hormone therapy and combination oral contraceptives have not been successful in increasing bone mineral density in women with amenorrhea. Bisphosphonates and calcitonin are not recommended for the treatment of osteopenia or osteoporosis associated with eating disorders because of the potential for adverse effects and lack of efficacy and safety studies in women of childbearing age. Concentrations of dehydroepiandrosterone, a precursor to testosterone and estradiol, are typically reduced in women with AN. Preliminary studies suggest replacement therapy with dehydroepiandrosterone reduces bone resorption and increases bone formation.

#### ***Other Agents***

Onansetron was evaluated in a 4-week, double-blind, placebo-controlled study for reducing binge eating and self-induced vomiting in BN. Participants were instructed

to take one 4-mg dose if they felt an urge to binge and wait 30 minutes; they could take up to six capsules per day or 24 mg total. The ondansetron group had significant reductions in binge episodes compared with the placebo group. Adverse effects of ondansetron include headache, constipation, drowsiness, and dizziness. Ondansetron is a major substrate for CYP3A4, so it has the potential for drug-drug interactions with inducers or inhibitors. Ondansetron is expensive and is not approved for the prevention of binge eating and vomiting in BN or for BED.

Orlistat has shown positive weight-loss effects in obese individuals with BED. For the management of obesity, orlistat must be combined with a reduced-calorie diet, and dietary intake of fat should be distributed over three meals. Orlistat reduces the absorption of fat-soluble vitamins; therefore, additional supplements may be needed. There have been reports of orlistat misuse as a means of purging in individuals with BN because of its over-the-counter availability.

Topiramate in dosages of 25–600 mg/day has been reported to reduce binge-eating frequency and cause weight loss compared with placebo in outpatients who were obese and with BN or BED. Topiramate may be an option in patients with BN or BED and comorbid alcohol dependence because of its reported ability to decrease alcohol intake and enhance abstinence. Topiramate causes adverse effects such as memory difficulties, paresthesias, dizziness, ataxia, sedation, nausea, weight loss, and anorexia. Further studies are needed before topiramate or other antiepileptic drugs such as zonisamide are considered a treatment option for BN or BED.

There are a few case reports and controlled studies of atypical antipsychotic use (e.g., olanzapine in daily doses of 2.5–10 mg) in individuals with AN with comorbid obsessive-compulsive behaviors and agitation. Antipsychotics should not be used as a primary treatment of AN because of their risk of causing extrapyramidal symptoms, tardive dyskinesia, diabetes, and metabolic syndrome. Although atypical antipsychotics have been used as augmenting agents to SSRIs for treatment-resistant depression, these agents have not been adequately studied in patients with eating disorders. In BN and BED, atypical antipsychotics can increase appetite, binge eating, and weight gain; therefore, they are not recommended for overweight or obese individuals.

Mood stabilizers have not been adequately studied in treating eating disorders, and these agents have significant adverse effects and drug interactions. Lithium, carbamazepine, gabapentin, and valproic acid cause weight gain; this increases the risk of nonadherence in this population. Lithium may cause hypothyroidism, and bingeing/purging may result in erratic lithium serum concentrations and electrolyte fluctuations, increasing the risk of cardiotoxicity. Carbamazepine and oxcarbazepine may cause hyponatremia, hepatic and hematologic adverse

effects, and drug interactions secondary to induction of CYP enzymes. Most of these agents have potential risks to the fetus and should be avoided in women of child-bearing age.

Treatment of comorbid substance use such as alcohol and nicotine may require pharmacotherapy and supportive psychosocial approaches. Naltrexone has been used in the treatment of alcohol dependence in dosages of 50 mg/day. In dosages up to 150 mg/day, naltrexone has been studied in the treatment of BN with mixed results; it may decrease bingeing and purging in some patients but carries a risk of hepatotoxicity. Acamprosate is used for alcohol abstinence at dosages of 666 mg three times/day. Dosing should be reduced in patients with a body weight less than 132 lb (60 kg).

For nicotine replacement therapy, the use of transdermal patches provides a more gradual reduction of the nicotine dose over 10–12 weeks. Nicotine gum, lozenge, nasal spray, and inhaler are alternative treatments to the transdermal patches and can be used as needed for craving. Bupropion is contraindicated in eating disorders because of its increased seizure risk. Varenicline is effective in dosages up to 1 mg/day for smoking cessation but carries a risk of behavioral and psychiatric changes such as depression, suicidal ideation and behavior, agitation.

## ROLE OF THE PHARMACIST

Pharmacists have a role in providing counseling about drugs, as well as in assessing, treating, and monitoring therapy in both inpatient and outpatient settings. Pharmacists should screen adolescents, young adults, and women receiving prenatal and postpartum care for eating disorders. Screening evaluations include assessment of food intake and regimens, binge-eating episodes, fluctuations in weight, concerns about body weight or fear of gaining weight, purging and compensatory behaviors, exercise and fasting behaviors, and presence of menstrual cycle abnormalities. Many prescription and over-the-counter products can cause weight loss. These agents include diuretics, laxatives, ipecac, topiramate, zonisamide, amphetamines, methylphenidate, bupropion, metformin, thyroid drugs, and orlistat; individuals may misuse these agents to lose weight. Because individuals with eating disorders may not want to take drugs, they should be provided with counseling and support.

Individuals suffering from eating disorders are at increased risk of comorbid anxiety, mood, and substance use disorders; therefore, assessment and monitoring are required. Pregnant women should be counseled about use of drugs with the potential for fetal harm, such as nicotine, alcohol, appetite suppressants, diuretics, and laxatives. Antidepressants may increase the risk of suicidal behavior and thinking; therefore, it is important to assess for this risk before treatment and to closely monitor for clinical worsening and suicidal thinking or behaviors

during therapy initiation. Because of higher mortality rates and suicidal risk in individuals with eating disorders, health professionals should regularly monitor patients throughout their lifetime. Referral sources for patients with eating disorders include the National Association of Anorexia Nervosa and Associated Disorders ([www.anad.org](http://www.anad.org)); National Eating Disorders Association ([www.nationaleatingdisorders.org](http://www.nationaleatingdisorders.org)); and Eating Disorder Referral and Information ([www.edreferral.com](http://www.edreferral.com)).

## CONCLUSION

The earlier the recognition, diagnosis, and treatment of an eating disorder, the better the chances for a successful outcome. The prognosis for eating disorders is better if the individual is treated during adolescence. The longer the abnormal eating behaviors persist, the more difficult it is to overcome them and to prevent medical complications. Eating disorders may result in obesity that has significant comorbidities and increased mortality rates. Without long-term treatment, individuals with eating disorders have a poor quality of life, impaired social functioning, and a lower vocational or educational level because of absences from school and work. Further studies are needed to better identify and diagnose eating disorders, understand the pathogenesis, and improve treatment outcomes.

## ANNOTATED BIBLIOGRAPHY

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Washington, DC: American Psychiatric Association, 2000.

These diagnostic guidelines provide the accepted criteria for eating disorders in the United States. The diagnostic criteria for AN and BN and their associated features, including differential diagnosis, common laboratory findings, physical signs and symptoms, and comorbid medical conditions are reviewed. Information on the prevalence, clinical course, age- and sex-related differences, and genetics of the disorders is discussed. In addition, the criteria for ED-NOS and the proposed research criteria for BED are included. The DSM-IV does not include information on assessment and treatment approaches for eating disorders.

2. Berkman ND, Lohr KN, Bulik CM. Outcomes of eating disorders: a systematic review of the literature. *Int J Eat Disord* 2007;40:293–309.

A systematic review of the literature from 1980 through September 2005 was conducted to determine what factors were associated with outcomes for AN, BN, and BED and if the outcomes differed by sociodemographic variables. For AN, BN, and BED, articles and studies were reviewed for factors predicting eating-related outcomes. Individuals with AN were more likely to have anxiety disorders (primarily OCD), depression, an autism spectrum disorder

such as Asperger syndrome, cluster C personality disorder, a lower BMI, amenorrhea, and higher mortality rates compared with controls. Predictors of poor outcomes with chronic AN included compulsive exercising, poor social relationships before the onset of the illness, higher scores on paranoia and hypochondriasis, and a hostile attitude toward their family. Predictors of recovery included less purging behavior, a higher body weight at intake, and a shorter duration of AN. Predictors for continued BN included parental obesity; a higher lifetime psychiatric comorbidity, particularly depression; substance use; and impulse control disorders. For BED, individuals were more likely to have gastric banding and increased bingeing if they had cluster B personality disorders.

3. Brownley KA, Berkman ND, Sedway JA, Lohr KN, Bulik CM. Binge eating disorder treatment: a systematic review of randomized controlled trials. *Int J Eat Disord* 2007;40:337–48.

In a search of six databases from 1980 to September 2005, 26 randomized controlled studies using drug and behavioral interventions for the treatment of BED were reviewed. Many of the studies had insufficient sample sizes and high attrition rates. Four drug-only trials were rated as good and included fluoxetine, fluvoxamine, sertraline, and sibutramine. These controlled studies showed that drug treatment resulted in improvement of depression, less bingeing, and less weight gain. Three trials included drugs alone, CBT, or combination therapy for BED (e.g., fluoxetine, desipramine, orlistat). Eight behavioral-only trials, three self-help trials, and one exercise and virtual reality trial were reviewed for the treatment of BED. Individual or group CBT was helpful in reducing binge-eating behaviors. Compared with placebo, the SSRIs resulted in less binge eating, lower depression scores, and weight loss. Combination therapies of drugs plus CBT help decrease binge eating and weight gain, but more long-term studies are needed to compare different pharmacologic and behavioral treatments in larger BED populations.

4. Bulik CM, Berkman ND, Brownley KA, Sedway JA, Lohr KN. Anorexia nervosa treatment: a systematic review of randomized controlled trials. *Int J Eat Disord* 2007;40:310–20.

Six major databases from 1980 to September 2005 were searched to find 32 treatment studies in AN for drugs, behavioral interventions, and drug plus behavioral interventions. Only two drug trials with fluoxetine (up to 60 mg/day) versus a placebo were rated as good, and neither study found a significant benefit in the treatment for AN. No drug has been found to significantly affect weight gain or the psychological symptoms of AN. Several drug trials had high dropout rates (e.g., amitriptyline, cyproheptadine) that could be related to weight gain or adverse effects. For behavioral interventions, CBT may have efficacy in reducing relapse in adults with AN after weight restoration but may not be as effective in low-weight individuals. Studies of AN are weakened by small sample sizes, the reluctance of patients to take drugs, and high attrition rates. For low-weight individuals with AN (defined as less than

75% of ideal body weight), the primary treatment should be weight restoration or refeeding. No guidelines are available for nutritional approaches for inpatient or outpatient settings or for when to use behavioral or drug interventions based on underweight or weight-restored states.

5. Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Echert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. *Am J Psychiatry* 2009;166:1342–6.

A computerized record linkage to the National Death Index was used to determine mortality rates in individuals with AN (n=177), BN (n=906), and ED-NOS (n=802) who were assessed at an academic medical center eating disorder clinic for 8–25 years. Mortality rates were 4.0% for AN, 3.9% for BN, and 5.2% for ED-NOS. Elevated rates for suicide were found in individuals with BN and ED-NOS as well as in those with AN. The finding of high all-cause and suicide mortality rates supports the need to recognize and treat all types of eating disorders as serious mental and physical illnesses.

6. Field AE, Javaras KM, Aneja P, Kitos N, Camargo CA, Taylor B, et al. Family, peer, and media predictors of becoming eating disordered. *Arch Pediatr Adolesc Med* 2008;162:574–9.

This prospective cohort study used a self-report questionnaire to determine predictors of developing an eating disorder in adolescents aged 9–15 years at baseline who were evaluated over 7 years. The main purpose of the study was to determine if parents, peers, and the media were influential in the development of binge-eating and purging behaviors such as vomiting or using laxatives to control weight in adolescents. Girls (n=6916) and boys (n=5618) received a questionnaire every 12–18 months to collect self-reported data about weight and height to calculate BMI. For girls, age at menarche was also collected, and weight concerns and influences on the perception of weight were assessed. The main outcome measure was the time of initiation of bingeing and/or purging at least once weekly. During the 7-year follow-up, 10.3% of girls and 3.0% of boys started to binge eat or purge at least once weekly to control their weight. For girls, binge-eating and purging behaviors were associated with dieting, a high level of concern about weight, trying to look like a same-sex person in the media, negative comments about their weight from boys, and the importance of weight expressed by their fathers and peers. Purging behaviors in girls younger than 14 years were 3 times more likely if their mother had a history of an eating disorder. For boys, a predictor for binge eating and purging was a high level of concern about their weight, and a predictor of binge eating was negative comments from their fathers about their weight.

7. Franko DL, Spurrell EB. Detection and management of eating disorders during pregnancy. *Obstet Gynecol* 2000;95:942–6.

The purpose of this review was to provide guidelines for the recognition, assessment, and treatment of eating

disorders during pregnancy. Because AN and BN have significant consequences in both the woman and the fetus, health care providers such as obstetricians should perform a thorough assessment of women who are considering pregnancy or who do not gain weight during pregnancy, as well as those who have miscarriages or excessive vomiting during pregnancy. An assessment tool, the Eating Disorder Examination, may be used to evaluate dieting behaviors, body image, food avoidance, and other eating disorder behaviors. Birth complications in women with eating disorders include low Apgar scores, low birth weight, preterm delivery, and cesarean delivery. Mothers with eating disorders have a high risk of postpartum depression. The authors suggest three warning signs for the presence of eating disorders during pregnancy: (1) a history of an eating disorder, (2) no weight gain in two consecutive visits during the second trimester, and (3) hyperemesis gravidarum.

8. Grilo CM, White MA, Masheb RM. DSM-IV psychiatric disorder comorbidity and its correlates in binge eating disorder. *Int J Eat Disord* 2009;42:228–34.

This prospective outpatient study used a structured diagnostic clinical interview to determine whether 404 individuals with BED (310 women, 94 men) had current or lifetime DSM-IV psychiatric disorders. The mean age of the study sample was 44.9 years; 82% were white, and 84% attended or graduated from college. Of this sample, 74% had at least one lifetime psychiatric disorder, and 43% had at least one current psychiatric disorder. The most common lifetime disorders were mood (54%), anxiety (37%), and substance abuse (25%). The most common current disorders were mood (26%) and anxiety (25%). Men had higher lifetime rates of substance use disorders and higher current rates of OCD than women. Individuals with BED and current comorbid psychiatric disorders reported dieting at an earlier age, having a higher lifetime BMI, higher depression scores, and lower self-esteem than those without comorbid disorders or those with only a past lifetime psychiatric disorder. Current comorbidity with other psychiatric disorders may predict a more severe psychopathology of BED that requires treatment for underlying mood, anxiety, and substance abuse disorders.

9. Hebebrand J. Diagnostic issues in eating disorders and obesity. *Child Adolesc Psychiatric Clin N Am* 2008;18:1–16.

This review addresses the biologic and genetic differences, as well as the diagnostic issues overlapping both obesity and eating disorders. Aberrant eating behaviors such as binge eating are associated with both BN and BED, but weight is not considered in the diagnosis. Weight fluctuations can occur in BN and BED from changes in eating behaviors and regulation of weight by purging, as well as the use of laxatives, fasting, and physical activity. Dieting or weight loss can trigger binge eating and behaviors associated with BN. Childhood and parental obesity is more common in BN than in healthy controls. For AN, the diagnosis may reflect weight loss from excessive physical activity while maintaining normal eating behaviors

and caloric intake. Obesity can occur from physical inactivity, with normal eating behaviors resulting in a gradual increase of weight over time. Therefore, excessive or very low energy expenditure over time will affect body weight, lean body mass, and fat mass. Intra-abdominal or visceral fat is associated with obesity-related medical conditions. Body fat distribution can be assessed by measuring the waist and hip circumferences and skinfolds (U.S. reference data and percentiles are available at [www.cdc.gov](http://www.cdc.gov)). Ethnic differences may affect sex-specific body fat distribution in obese adolescents and obesity rates. Low socioeconomic status is associated with being overweight and obese in some Westernized societies. In developing countries, being underweight is usually not associated with an eating disorder but rather secondary to lower food availability and caloric intake.

10. Herpertz-Dahlmann B. Adolescent eating disorders: definitions, symptomatology, epidemiology, and comorbidity. *Child Adolesc Psychiatric Clin N Am* 2008;18:31–47.

This review of adolescent eating disorders addresses the symptoms, diagnostic criteria, and epidemiology of AN, BN, and ED-NOS. The medical comorbidity risks, annual costs of treating the disorders, and medical complications with abnormal eating behaviors, poor nutrition, and starvation are discussed. Psychiatric comorbidities are often associated with AN and BN during both the acute and the long-term course of the disorders. Both affective and anxiety disorders may occur secondary to malnutrition, and the incidence of suicide and suicidal attempts are also high in patients with eating disorders. About 25% to 35% of patients with BN and 10% to 20% of patients with AN have attempted suicide. Other disorders such as OCD, attention-deficit/hyperactivity disorder, and substance abuse co-exist with eating disorders. Personality traits such as being a perfectionist, obsessive, or rigid are common with AN. Individuals with bulimia often display impulsive or attention-seeking behaviors, as well as cluster-B and cluster-C personality disorders. Information on eating disorder assessment rating scales, clinical interviews, and self-report questionnaires are provided, as are recommendations for medical and psychological assessments.

11. Hudson JI, Hiripi E, Pope HG, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry* 2007;61:348–58.

A national population-based face-to-face survey of American households between 2001 and 2003 reported that of the 2982 respondents, at least one other lifetime DSM-IV disorder was present in about 56% with AN, 95% with BN, 79% with BED, 64% with subthreshold BED, and 77% with any binge eating. These comorbid conditions included anxiety, mood, impulse control, and substance abuse disorders. Lifetime prevalence rates in this sample were 0.6% for AN, 1.0% for BN, 2.8% for BED, 1.2% for subthreshold BED, and 4.5% for any binge eating. The median age of onset for eating disorders was 18–21 years. Estimated lifetime prevalence rates

of eating disorders for women versus men in the United States were, respectively, 0.9% and 0.3% for AN, 1.5% and 0.5% for BN, and 3.5% and 2.0% for BED. Lifetime average weights for AN were significantly associated with a low current body weight (BMI less than 18.5 kg/m<sup>2</sup>), whereas lifetime weights for BED were associated with current severe obesity (BMI 40 kg/m<sup>2</sup> or greater). Eating disorders were associated with significant comorbid psychopathology and role impairment, yet many individuals either did not seek treatment or were undertreated.

12. Klump KL, Bulik CM, Kaye WH, Treasure J, Tyson E. Academy for eating disorders position paper: eating disorders are serious mental illnesses. *Int J Eat Disord* 2009;42:97–103.

The Academy for Eating Disorders is the largest international organization for eating disorder professionals. This paper explains why eating disorders should be considered a serious mental illness with biologic and genetic underpinnings. The position paper reviews genetic and neurobiologic findings, changes in cognitive and emotional functioning, the impact on quality of life, and medical complications associated with AN, BN, and ED-NOS. Similar to schizophrenia, bipolar disorder, OCD, and depression, eating disorders have a strong genetic predisposition. Molecular genetic studies are under way to identify genes and chromosomal regions associated with increased risks of eating disorders and comorbid psychiatric conditions. Brain imaging studies in patients with AN have found changes in the neurochemistry and brain structure that may be associated with long-term impact on the modulation of appetite, regulation of neurotransmitters, peptides, hormone feedback, obsessive and impulse control behaviors, cognitive functioning, and mood stability. Early dieting and increased exercise, combined with stress, may be primary risk factors for the onset of AN. Individuals with severe eating disorders undergo neurobiologic changes that impair their judgment, cognition, and psychiatric stability and interfere with their functioning and quality of life. Medical complications cause significant disability, and mortality rates for AN are among the highest for any psychiatric disorder. The authors also stress that individuals with eating disorders should receive health care coverage for treatment through private and state insurance plans, and research should be funded at a rate commensurate with other serious mental illnesses.

13. Kouba S, Hällström T, Lindholm C, Hirschbert AL. Pregnancy and neonatal outcomes in women with eating disorders. *Obstet Gynecol* 2005;105:255–60.

The pregnancy and neonatal outcomes of 49 nulliparous and nonsmoking women with a previous diagnosis of an eating disorder (24 with AN, 20 with BN, and 5 with ED-NOS) were compared with a control group to determine antenatal complications, type of delivery, and effect on the infant. The mean duration of the eating disorders ranged from 3 to 15 years with a mean of 9 years. Delivery events were similar between the groups, but the infants in the maternal eating disorder group had a significantly lower mean birth weight, a significantly smaller head

circumference, and a higher incidence of microcephaly compared with the control group. Small head circumference has also been reported in women with significant stress and may be related to higher concentrations of cortisol in the mother, although this was not evaluated in the study. The pregnant women with AN had significantly lower weight gain and a higher rate of anemia and hyperemesis compared with the control group. There were no significant differences in weeks of gestation, gestational hypertension or preeclampsia, delivery events, malformations, neonatal care, or Apgar scores between the patient and control groups.

14. Latner JD, Wilson GT. Binge eating and satiety in bulimia nervosa and binge eating disorder: effects of macronutrient intake. *Int J Eat Disord* 2004;36:402–15.

In this small study of 18 women with BN or BED, a comparison of a high-protein liquid supplement (280 kcal) three times/day over 2 weeks was compared with a high-carbohydrate liquid supplement (280 kcal) 3 hours before each meal for 2 weeks. The incidence of binge-eating episodes was lower with the protein supplement (1.12 episodes per week) than with the carbohydrate supplement (2.94 episodes per week). The findings suggest that adding protein to the diet reduces binge eating and food intake in both BN and BED. Protein stimulates cholecystokinin and glucagon release, which increases satiety and reduces food intake in humans. Because low-protein diets may increase feelings of hunger and binge-eating behavior, individuals need to be educated about the importance of eating regular high-protein meals and snacks such as dairy products, turkey, eggs, tuna, and beans rather than high-carbohydrate foods and drinks.

15. Mazzeo SE, Bulik CM. Environmental and genetic risk factors for eating disorders: what the clinician needs to know. *Child Adolesc Psychiatric Clin N Am* 2008;18:67–82.

The authors provide an in-depth review of the genetic-environmental risk factors that may influence the etiology of eating disorders. For both AN and BN, there is a higher genetic risk and a higher lifetime prevalence of eating disorders in relatives of eating disorder probands than in controls. Advances in genetic research may help identify single or several alleles that confer risks of eating disorders. Positive or negative environmental conditions may influence genetic expression and predisposition to a specific disorder. Negative environmental factors include the role of parents in modeling eating behaviors, how parents may overemphasize the importance of a child's weight and shape, how distress or stress and negative life events may affect eating behaviors, how teasing and critical remarks affect weight and disordered eating behaviors, and the influence of the media and peer groups on the drive to be thin. Potential environmental factors that decrease the risk of eating disorders include the importance of having family meals, eating breakfast regularly, stress-reduction techniques, learning how to regulate emotions, and cognitive-behavioral techniques. Interventions for treatment and education of the parents, peers, and patient are suggested to help break the cycle of eating disorders.

16. Mehler PS, MacKenzie TD. Treatment of osteopenia and osteoporosis in anorexia nervosa: a systematic review of the literature. *Int J Eat Disord* 2009;42:195–201.

A systematic review of six randomized controlled studies and two cohort studies identified treatments for osteopenia and osteoporosis in patients with AN. About 92% of women with AN may have osteopenia, and 40% have osteoporosis. The increased long-term risk of non-traumatic fractures is associated with low bone mineral density secondary to low body weight and amenorrhea. Therapies to improve bone density include the use of hormonal therapy, bisphosphonates, calcium, weight restoration, and weight-bearing exercises. Oral contraceptives and estrogen therapy have not increased bone density in women with AN. Oral dehydroepiandrosterone and transdermal testosterone have been used in small clinical trials to stimulate bone formation, but they cannot be recommended. Bisphosphonates have been studied with some positive results but are not recommended because there are no long-term efficacy and safety data in women of childbearing age. The most important factor for preventing osteoporosis is early weight restoration, together with 1200–1500 mg/day of supplemental calcium and at least 800 international units/day of vitamin D. Weight-bearing exercise may help once there is sufficient weight gain and restoration of menstrual cycles. If significant bone loss has occurred, the effect of weight restoration may not be as positive.

17. Powers PS, Bruty H. Pharmacotherapy for eating disorders and obesity. *Child Adolesc Psychiatric Clin N Am* 2008;18:175–87.

This comprehensive review of pharmacotherapy outlines clinical issues in the treatment of AN, BN, BED, and obesity. Pharmacotherapy for AN is primarily used to treat medical complications, increase gastrointestinal motility, and increase appetite. For AN, SSRIs are not effective until there is sufficient weight restoration. Pharmacotherapy studies for treating BN include SSRIs, TCAs, serotonin receptor antagonists, and anticonvulsants. Most efficacy studies for the treatment of BN have documented the role of SSRIs rather than TCAs or other agents. Topiramate in dosages up to 400 mg/day may decrease binge-purging episodes and reduce body weight, but this agent can cause poorly tolerated adverse effects such as word-finding difficulties and paresthesias. Lithium and mood-stabilizing anticonvulsants may cause weight gain and are associated with significant adverse effects or toxicity issues in patients with AN or BN. Weight-loss drugs are reviewed for the treatment of obesity (e.g., sibutramine, orlistat, metformin) and for weight effects of commonly prescribed drugs.

18. Shapiro JR, Berkman ND, Brownley KA, Sedway JA, Lohr KN, Bulik CM. Bulimia nervosa treatment: a systematic review of randomized controlled trials. *Int J Eat Disord* 2007;40:321–36.

Six databases were searched from 1980 to September 2005 and included 47 controlled efficacy studies of drugs only, behavioral interventions only, or combination



therapy in adults and adolescents with BN. The primary outcome was a reduction or abstinence of binge eating or purging. Secondary outcomes were reductions in depression and anxiety, other psychological features of BN, and changes in BMI. Only two drug trials were rated good and 10 as fair. These included SSRIs, TCAs, MAOIs, serotonin-3 receptor antagonists, and anticonvulsants. Higher dosages of fluoxetine (60 mg/day) were more effective than lower dosages (20 mg/day) in decreasing binge-purging behaviors, decreasing relapse after 1 year, and improving eating-related attitudes. Mixed findings were reported for changes in depression and anxiety ratings with SSRIs, and some studies had high dropout rates, which may have been related to adverse effects of the drug (e.g., up to 83% for fluoxetine and 51% for fluvoxamine). Positive results were found with CBT in both short- and long-term BN studies. Interpersonal therapy, stress management, self-help approaches, and nutritional support provided some benefit in decreasing BN symptoms. Long-term efficacy studies are needed in adolescent and adult patients with BN to compare drug and/or behavioral interventions in larger controlled trials.

19. Stunkard AJ, Allison KC, Geliebter A, Lundgren JD, Gluck ME, O'Reardon JP. Development of criteria for a diagnosis: lessons from the night eating syndrome. *Compr Psychiatry* 2009;50:391–9.

The review includes information about the proposed diagnostic criteria for NES and how it differs from BED and sleep-related eating syndrome. During an episode of sleep-related eating syndrome there is no consciousness or memory of the nocturnal binge-eating episodes, whereas individuals with NES are aware and have a memory of the nocturnal bingeing. The diagnosis of sleep-related eating syndrome is associated with the inappropriate eating of unappetizing foods or substances and comorbid parasomnias, and it is triggered by the use of hypnotic agents. Information about the prevalence of NES, its association with obesity and other psychiatric disorders, and its possible biologic features are reviewed. The biologic features of NES include a genetic predisposition, delays in circadian rhythms, and a stress-induced syndrome preceding the nocturnal eating episodes. Serotonin-augmenting antidepressants appear to be beneficial in NES and may promote weight loss in obese individuals. Topiramate has been evaluated in both NES and sleep-related eating syndrome and may have some possible benefits.

20. Yager J, Powers PS, eds. *Clinical Manual of Eating Disorders*. Washington, DC: American Psychiatric Association, 2007.

This comprehensive clinical manual was written by experts and contributors for the work group who wrote the association's 2006 "Practice Guideline for the Treatment of Patients with Eating Disorders." The purpose of the manual was to provide additional clinical information and case examples of patients with a variety of eating disorders, such as patients who have undergone bariatric surgery, patients with diabetes, pregnant patients, athletes, and older patients. The manual contains an excellent review of the diagnosis, epidemiology,

clinical course, initial treatment approaches, comorbidity issues, and management of AN, BN, BED, and ED-NOS. The review of the relationship between psychotropic drugs and their impact on weight changes is important because weight-altering drugs such as bupropion, topiramate, amphetamines, methylphenidate, and metformin may be misused to lose weight. Nonadherence secondary to weight gain is common with TCAs, mirtazapine, valproate, lithium, carbamazepine, gabapentin, cyproheptadine, metoclopramide, and most antipsychotics. This manual is highly recommended as a reference for learning about treatment goals, psychosocial and pharmacologic approaches, acute management of AN in a residential program or inpatient hospital, and the long-term monitoring and follow-up care required for chronic eating disorders.

# SELF-ASSESSMENT QUESTIONS

## Questions 1–12 pertain to the following case.

B.R. is a 16.5-year-old girl who intentionally lost 9 kg (20 lb) within 3 months after a breakup with a boyfriend. She was a little overweight and felt that her boyfriend broke up with her because she was fat. B.R. read a book recommended on the Internet about how to lose weight quickly and started an extreme diet that restricted intake of fats, carbohydrates, and proteins. At times, she would binge after food intake and then restrict food for several days in a row. She now has an intense fear of gaining the weight back. B.R. just missed her last menstrual period, which was due 2 weeks ago. Her current height is 5'3.5", and her weight is 46.6 kg (103.5 lb), giving her a body mass index (BMI) of 18 kg/m<sup>2</sup>. The BMI-for-age percentage calculator for children and teens (<http://apps.nccd.cdc.gov/dnpabmi/>) places her at the 14th percentile (range is from 5th percentile to less than the 85th percentile for a healthy weight).

- Which one of the following is the best assessment of B.R.'s status at this time?**
  - The loss of about 16% of her original weight means she is underweight.
  - The BMI based on her height, weight, sex, and age is considered a healthy weight.
  - The BMI of 18 kg/m<sup>2</sup> reflects she is significantly underweight.
  - The BMI decreased from the 61th percentile to the 14th percentile so she is underweight.
- According to the diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision*, which one of the following diagnoses best describes B.R.'s condition?**
  - Anorexia nervosa (AN).
  - Bulimia nervosa (BN).
  - Eating disorder not otherwise specified.
  - Binge-eating disorder.
- Which one of the following biologic changes is most likely to occur because of the reduction in B.R.'s dietary fat?**
  - Decreased thyroid hormone concentrations.
  - Increased cortisol concentrations.
  - Increased ghrelin concentrations.
  - Decreased leptin concentrations.
- If B.R. continues to have amenorrhea for more than 6 months, which one of the following approaches is best to promote bone revitalization together with weight restoration?**
  - Alendronate.
  - Calcium and vitamin D<sub>3</sub>.
  - Oral contraceptives.
  - Calcitonin.
- Within the past 2 weeks, B.R. has lost an additional 2 kg (5 lb) because of dieting and laxative use. When she started dieting, she was exercising for up to 2 hours/day at a health club; now, she cannot work out for more than 30 minutes before having shortness of breath and fatigue. She has started having panic attacks, headaches, and difficulty falling and staying asleep, and she has a depressed mood with crying episodes. She wishes to weigh 43 kg (95 lb) so that she will no longer be fat. Although B.R. does not think she has a problem, her family has brought her to the urgent care center because of her symptoms and loss of weight. Her pulse rate is 40 beats/minute, and her blood pressure is less than 80/50 mm Hg. **Which one of the following is best to assess B.R.'s current condition?**
  - Order electrocardiography to assess cardiac status.
  - Admit her to a mental health hospital because of her psychiatric symptoms.
  - Order a glucose concentration and give a high-calorie nutritional supplement.
  - Consult with a dietician about nutritional counseling.
- B.R. is given a diagnosis of AN and agrees to receive treatment for her eating disorder. **Because of her strict dieting, excessive exercising, and use of laxatives, which laboratory values are best to obtain as part of the initial assessment?**
  - Thyroid-stimulating hormone.
  - Serum amylase.
  - Serum sodium, potassium, chloride, and calcium.
  - Lipoprotein profile.
- Which one of the following nonpharmacologic approaches is most likely to have the best outcome in B.R.?**
  - Group cognitive behavior therapy (CBT).
  - Interpersonal psychotherapy.
  - Conjoint family therapy.
  - Supportive individual psychotherapy.

8. Several weeks after starting outpatient therapy, B.R. has maintained her weight at 45 kg (100 lb) but has had difficulty gaining additional weight. Her health care provider wants to attempt another approach to facilitate weight gain. **Which one of the following is the best drug choice for B.R.?**
- Amitriptyline 25 mg at bedtime.
  - Fluoxetine 10 mg in the morning.
  - Mirtazapine 7.5 mg at bedtime.
  - Olanzapine 10 mg two times/day.
9. Several months later, B.R. has gained sufficient weight to have a BMI of 19 kg/m<sup>2</sup>. She continues to be obsessed about what she eats and weighs herself several times a day. She has started to use over-the-counter laxatives two times/week, and every day after eating, she self-induces vomiting. **Which one of the following laboratory tests is best to rule out potential medical complications from B.R.'s purging behaviors?**
- Serum potassium.
  - Blood urea nitrogen.
  - Serum amylase.
  - Fasting glucose.
10. During the past 6 months, B.R. has continued weekly psychotherapy and has gradually regained her weight. She does not meet the diagnostic criteria for depression but continues to have obsessive-compulsive symptoms about gaining weight. Her urine drug screens have been negative during treatment, but she continues to smoke one-half pack of cigarettes and drink up to 2 L of diet cola each day. Her provider has decided to change the pharmacologic treatment approach to help reduce the obsessive-compulsive and purging behaviors. **Which one of the following is the best drug treatment for B.R.'s symptoms with the lowest risk of a discontinuation syndrome if abruptly discontinued?**
- Paroxetine.
  - Sertraline.
  - Clomipramine.
  - Fluvoxamine.
11. B.R. begins to respond to the antidepressant with less obsessive thoughts and a decreased drive to purge to lose weight. The only adverse effect she has noticed is mild constipation and difficulty falling asleep. She asks whether she can have a sleeping aid to use as needed for insomnia. **Which one of the following is the best agent for the short-term treatment of insomnia in B.R.?**
- Temazepam 15 mg.
  - Trazodone 100 mg.
  - Mirtazapine 15 mg.
  - Diphenhydramine 50 mg.
12. B.R. is now 18 years old; she dropped out of treatment more than 1 year ago. She is not currently taking any medications. She has a dysfunctional family with high parental criticism for her eating disorder. In the past few months, she has refused to eat, and her BMI is below the 3rd percentile. Her pulse, blood pressure, and temperature are low. She has become depressed and extremely obsessive-compulsive about gaining weight. **Which one of the following is the best treatment approach for B.R.?**
- Outpatient treatment with individual psychotherapy and nutritional counseling.
  - Partial hospitalization with CBT.
  - Residential treatment with group psychotherapy and pharmacotherapy.
  - Inpatient hospitalization with nutritional rehabilitation.

**Questions 13–17 pertain to the following case.**

M.S. is a 25-year-old, overweight woman (BMI 29 kg/m<sup>2</sup>) admitted to a psychiatric hospital for suicidal ideation with a plan to drive her car off a mountain road. She was initiated on paroxetine 20 mg at bedtime 3 weeks ago by her primary care physician for symptoms of depression. During the past week, M.S. has become more depressed, started to have headaches, and gained 2.25 kg (5 lb) because of binge-eating episodes. When M.S. was 15 years old, she was treated for AN in an outpatient eating disorder program. She received nutritional counseling because her weight was less than 85% of the expected weight range for her height. After gradually gaining her weight back, she responded successfully to fluoxetine 20 mg/day for about 3 years for symptoms of anxiety, obsessive-compulsive traits, and depressive episodes that occurred premenstrually. In college at age 20, M.S. began to have binge-eating episodes every 1–2 weeks when she was feeling stressed. By age 22, her binge-eating episodes were regularly occurring once or twice a week. When she started to gain weight, she began to induce self-vomiting after each binge-eating episode and occasionally used laxatives to lose additional weight.

13. **Which one of the following is the best recommendation for M.S.?**
- Change paroxetine 20 mg to fluoxetine 20 mg per day.
  - Increase paroxetine from 20 mg to 40 mg per day.
  - Decrease paroxetine dose by 50% and start fluoxetine 10 mg/day.
  - Continue paroxetine 20 mg/day and start psychotherapy.

14. Two years later, M.S. has continued on antidepressant therapy, and her binge-eating and purging behaviors are infrequent except during premenstrual episodes. She was recently married and wants to become pregnant in the upcoming year. Her BMI is 25 kg/m<sup>2</sup>, and she is concerned about gaining excessive weight during pregnancy. **Which one of the following is the best treatment option for M.S. before she becomes pregnant?**
- Discontinue the antidepressant and start a prenatal vitamin.
  - Lower the antidepressant dosage by 50% and add a prenatal vitamin.
  - Continue the antidepressant dosage and add a prenatal vitamin.
  - Continue the antidepressant, lose weight to achieve a BMI of 20 kg/m<sup>2</sup>, and add a prenatal vitamin.
15. M.S. delivers a healthy baby girl and now has a postpartum BMI of 32 kg/m<sup>2</sup>. She has decided not to breastfeed and eats only one meal a day in the evening. She also avoids fatty and animal-based foods, limiting her intake to 1200 calories/day. After several weeks, she begins to have strong urges to binge despite taking the antidepressant. **Which one of the following is the best recommendation to help M.S. reduce potential binge-eating behaviors?**
- Increase the antidepressant dosage to the highest recommended dose per day.
  - Augment the antidepressant with topiramate to reduce binge eating and body weight.
  - Continue the antidepressant and change food intake to every 4 hours with a complete protein plus a complex carbohydrate.
  - Augment the antidepressant with sibutramine to promote additional weight loss.
16. M.S. is now 30 years old and has two children, ages 1 and 3 years. Her weight is 99 kg (220 lb), and her height is 5'4" (BMI 37.8 kg/m<sup>2</sup>). She continues to struggle with nighttime-eating binges but has stopped purging behaviors. Six months ago, she started smoking cigarettes to curb her appetite and is now using 1 pack/day. **Which one of the following is best to recommend for M.S.?**
- A very low-calorie diet, emphasizing intensive exercise program, and a course in problem-solving skills.
  - A structured exercise program, orlistat for weight loss, and zolpidem for insomnia.
  - Bariatric surgery using adjustable gastric banding together with antidepressant therapy.
  - An evaluation for physical and psychiatric disorders and a program emphasizing healthy lifestyles.
17. M.S. comes to an outpatient pharmacy to fill her prescriptions for lisinopril and pravastatin. During the prescription counseling, the pharmacist does a stage-based brief tobacco cessation intervention using the five A model. M.S. is willing to set a quit date within the next 30 days and is interested in trying a drug for the treatment of tobacco dependence. **Which one of the following is the best drug to recommend for M.S.?**
- Stop smoking and start using a daily nicotine transdermal patch.
  - Stop smoking and start using nicotine gum every 1–2 hours.
  - Two weeks before the quit date, start bupropion.
  - One week before the quit date, start varenicline.
- Questions 18–20 pertain to the following case.**
- T.M. is a 21-year-old man seeking help at an outpatient psychiatric clinic for panic attacks and severe insomnia that has resulted in his buying drugs off the street for self-treatment. He binges on alcohol three or four times/week, smokes 1–1.5 packs of cigarettes daily, and drinks about 12 caffeinated coffees or diet sodas per day. T.M. has had several sex partners because of compulsive sexual behaviors that started at age 16. He started gambling while in college and has lost large amounts of money by betting on professional sports. During the psychiatric assessment, he reports that he seldom eats during the day but that, at night, will “eat tons of food” such as pasta, pizza, cakes, cookies, and pies. T.M. feels he cannot stop eating. Because he gained weight, he started sticking his fingers down his throat to throw up the food. He feels embarrassed about his abnormal eating and is dissatisfied with his body because he weighs more than 90 kg (200 lb).
18. **Aside from his binge-eating and purging behaviors, which one of the following is the best assessment of T.M.'s primary diagnosis?**
- Panic disorder.
  - Impulse control disorder.
  - Major depressive disorder.
  - Obsessive-compulsive disorder.
19. T.M. agrees to participate in outpatient psychotherapy and begins pharmacologic treatment for his behaviors. His insurance covers only generic products, and he is worried about the cost of the drug. **Based on his clinical presentation, which one of**

**the following is the best therapy to initiate for T.M.?**

- A. Bupropion.
- B. Duloxetine.
- C. Escitalopram.
- D. Fluoxetine.

20. Six months later, T.M. has started working out at a gym and spends 2–3 hours a day doing weight training and running on a treadmill. He compulsively looks in a mirror, and performs grooming behaviors for an hour before leaving the house. He feels that his nose is excessively large for his face and perceives that people regularly make fun of him. Although T.M. has lost more than 13.5 kg (30 lb), he still feels he is overweight and is very self-conscious. He has started using over-the-counter laxatives and is thinking about buying diet pills from a mail order company. T.M. feels he may need liposuction to remove fat from his stomach and plastic surgery to make his nose smaller. He has low self-esteem and is withdrawing from his family and friends. **Based on his behavior, which one of the following is the best assessment of T.M.'s current disorder?**

- A. Obsessive-compulsive disorder.
- B. Bulimia nervosa.
- C. Body dysmorphic disorder.
- D. Muscle dysmorphia syndrome.

