Eating Disorders

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LEARNING OBJECTIVES

1. Evaluate methods of screening for eating disorders throughout childhood and the general approach to determining an appropriate level of care.
2. Analyze the role of psychotropic medications in the treatment of anorexia nervosa (AN).
3. Develop a monitoring plan and appropriate recommendations for nutritional and electrolyte supplementation for a pediatric patient with AN.
4. Analyze the role of psychotropic medications in the treatment of bulimia nervosa (BN).
5. Develop a monitoring plan and appropriate recommendations for nutritional and electrolyte supplementation for a pediatric patient with BN.
6. Distinguish between diagnostic and hallmark features of AN, BN, binge-eating disorder, and avoidant/restrictive food intake disorder.

ABBREVIATIONS IN THIS CHAPTER

APA	American Psychiatric Association
AN	Anorexia nervosa
AN-R	Anorexia nervosa restricting type
AN-BP	Anorexia nervosa binge-eating/purging type
ARFID	Avoidant/restrictive food intake disorder
BED	Binge-eating disorder
BMD	Bone mineral density
BN	Bulimia nervosa
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*
FBT	Family-based treatment
HEADSS	Home, education, activities/employment, drugs, suicidality, sex
MDD	Major depressive disorder
OCD	Obsessive-compulsive disorder
SSRI	Selective serotonin reuptake inhibitor
TCA	Tricyclic antidepressant

Table of other common abbreviations.

INTRODUCTION

Clinical Significance

Eating disorders are complex psychiatric disorders characterized by a persistent disturbance in eating or eating-related behaviors that result in impaired physical and psychosocial functioning (Hornberger 2021; Couturier 2020; Hay 2020; National Guideline Alliance 2017; Harrington 2015). Restriction of dietary intake, overeating with a sense of loss of control, and compensatory behaviors (e.g., over-exercise, laxative misuse) are often accompanied by cognitive disturbances, cognitive rigidity, and thought distortions (Hornberger 2021; Couturier 2020; Hay 2020; Frank 2017; National Guideline Alliance 2017; Harrington 2015). Although eating disorders have previously been characterized as conditions primarily occurring in non-Hispanic white, adolescent girls with a high socioeconomic status, these disorders are now well-recognized across all racial, ethnic, and socioeconomic groups (Hornberger 2021). It is important to recognize that eating disorders also impact affect boys and men as well as individuals with various body habitus. Increased rates of disordered eating have also been found in sexual minority youth, with transgender youth at high risk (Connolly 2016; McClain 2016; Hadland 2014; Austin 2013).

Serious medical complications are often associated with eating disorders and can include malnutrition, weight fluctuations, self-induced vomiting, or laxative misuse. The estimated mortality rates are 1.5 times for all-cause mortality and 4–6 times for suicide in those with eating disorders compared with the general population (Hornberger 2021; Hay 2020, 2014; Frank 2017). With an estimated

mortality rate of 2% among adolescents, AN has one of the highest mortality rates among psychiatric conditions, most often related to the physiologic impact of malnutrition and suicide (Lock 2019; National Guideline Alliance 2017; Hay 2014). Neurobiologic, psychiatric, sociocultural, genetic, and environmental factors play critical roles in the subsequent development of an eating disorder. Considered together, identification and treatment require a tailored, pediatric-specific, multidisciplinary approach (Hornberger 2021; Hay 2020; Frank 2017; National Guideline Alliance 2017; Harrington 2015; Lock 2015; Hay 2014).

Screening for Eating Disorders

Early intervention in childhood is critical given the long-term physical complications of malnutrition at this age, including delayed growth and puberty, an impact on BMD, and dental issues, among others (Hornberger 2021; National Guideline Alliance 2017; Hay 2014). Almost 95% of individuals with an eating disorder are age 12–25 years, highlighting the importance of screening by pediatric providers (Harrington 2015). All children and adolescents should be routinely asked about eating patterns and body satisfaction together with routine plotting of height and weight on age- and sex-specific growth curves (Lock 2015). In the presence of eating disorders, a formal evaluation should be pursued and include a full psychosocial evaluation, HEADSS assessment, collateral history from a caregiver, and comprehensive interview with the child or adolescent (Hornberger 2021). Assessment typically involves a multidisciplinary approach and requires thorough review of medical, psychiatric, nutritional, and physical assessments (Hornberger 2021; Mitchell 2020; Lock 2015; Hay 2014).

American Academy of Child and Adolescent Psychiatry guidelines recommend validated assessments to screen for eating disorders. Among adolescents, validated, short, self-report measures that may be used in clinical practice are the Eating Disorder Examination Questionnaire (EDE-Q), Eating Disorder Inventory (EDI), and Eating Attitudes Test (EAT). For children 8 years and older, the Kids' Eating Disorder Survey (KEDS), Child Eating Disorder Examination-Questionnaire (ChEDE-Q), Eating Disorder Inventory for Children (EDI-C), and Child-Eating Attitudes Test (CHEAT) may be considered (Kliem 2017; Lock 2015; Hilbert 2013; Childress 1993). Given the denial and symptom minimization among preteen children, report by caregivers may be necessary for more accurate scoring. In addition to screening, laboratory studies are necessary to evaluate and monitor medical stability (Table 1) as well as eating disorder severity to determine the appropriate level of care (Table 2).

General Approach to Determining the Level of Care

Treatment of pediatric eating disorders consists of outpatient, partial hospitalization (PHP), residential treatment center, inpatient psychiatry/specialized eating disorder, or inpatient medical therapy (Dalle Grave 2021; Hornberger 2021; Couturier 2020; National Guideline Alliance 2017; Lock 2015; Hay 2014). As shown in Table 2, level of care is primarily determined by the presence of acute medical complications, psychiatric comorbidities, chronicity of symptoms, support needed to complete meals, ability to manage compensatory behaviors (e.g., excessive exercise, laxative misuse), and previous treatment response (Hornberger 2021; Mitchell 2020; Lock 2015). Inpatient medical treatment is essential in preventing mortality, particularly associated with AN. Once medical acuity is resolved, lower levels of care should be considered (Dalle Grave 2021; Hay 2014). Most individuals with eating disorders will be managed as outpatients but more severe cases require PHP or inpatient medical treatment (Dalle Grave 2021; Hay 2014). Overall, higher levels of care are associated with higher costs compared with PHP and outpatient treatment but are without clear evidence of improved outcomes (Frank 2017; Hay 2014). Treatment guidelines recommend a multidisciplinary approach that includes medical, psychiatric, and nutrition providers with expertise in eating disorders to maximize the chance of recovery (Hornberger 2021; Couturier 2020; Lock 2015; Hay 2014).

Treatment Goals and Considerations for a Pediatric Pharmacist

Goals of treatment include restoring weight, normalizing eating patterns and associated behaviors, establishing healthy relationships with food, and achieving realistic views of body

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- General knowledge of electrolyte disturbances and their treatment
- General knowledge of the HEADSS examination and screening for mental health conditions
- Drug knowledge of antidepressants and antipsychotics, particularly dosing and monitoring considerations in pediatric patients

Table of common pediatric laboratory reference values.

ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- American Academy of Pediatrics. Identification and Management of Eating Disorders in Children and Adolescents. Pediatrics 2021;147:e2020040279.
- CDC. BMI Percentile Calculator for Child and Teen.

Table 1. Initial Assessment for Pediatric Patients with a Suspected Eating Disorder

Patient Characteristics	Assessments
All patients at baseline	Weight, height, BMI, vital signs, orthostatic vital signs, CMP, TSH, CBC with differential, UA
Additional monitoring considerations, in presence of:	
Malnourishment, severely symptomatic	Serum calcium, magnesium, phosphorous, ferritin, ECG, 24-hour urine collection for CrCl
Self-induced vomiting	Referral for dental evaluation
Persistent amenorrhea (>6 mo)	Serum estradiol, dual-energy x-ray absorptiometry

CMP = comprehensive metabolic panel; TSH = thyroid stimulating hormone; UA = urinalysis.

Information from: Couturier J, Isserlin L, Norris M, et al. Canadian practice guidelines for the treatment of children and adolescents with eating disorders. J Eat Disord 2020;8:4; Lock J, La Via MC; American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with eating disorders. J Am Acad Child Adolesc Psychiatry 2015;54:412-25; Hay P, Chinn D, Forbes D, et al.; Royal Australian and New Zealand College of Psychiatrists. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of eating disorders. Aust N Z J Psychiatry 2014;48:977-1008.

image (Hornberger 2021; Couturier 2020; Lock 2015; Hay 2014). Broadly, the treatment of eating disorders is focused on nutritional repletion, weight restoration, and psychological therapy. Psychotropic medications may be used to target comorbid psychiatric conditions once acute medical concerns are resolved (Hornberger 2021; Couturier 2020). Pediatric pharmacists play an important role in the management of this patient population. Medical treatment of acute complications may include electrolyte, micronutrient, and vitamin supplementation; avoidance or minimization of high-risk

Table 2. Clinical Evaluation Considerations to Determine Level of Care

Level of Care	Clinical Evaluations
Inpatient Medical	Weight: <75% of expected body weight or rapid weight loss HR: <50 beats/minute in the day, <45 beats/minute at night BP: systolic <80 mm Hg Orthostatic: increase HR >20 beats/minute; decrease in systolic BP >20 mm Hg or diastolic BP >10 mm Hg Cardiac: prolonged QTc >460 ms, arrhythmia Electrolytes: hypokalemia, hypophosphatemia, hypomagnesemia Other: dehydration, renal, hepatic, cardiovascular compromise
Inpatient Psychiatry/Specialized Eating Disorder	Weight: <85% of expected body weight or rapid weight loss Severe purging behaviors (supervision needed during/after all meals and in bathroom) Severe food avoidant behaviors that may require nasogastric feeding

Information from: Bargiacchi A, Clarke J, Paulsen A, et al. Refeeding in anorexia nervosa. Eur J Pediatr 2019;178:413-22; Couturier J, Isserlin L, Norris M, et al. Canadian practice guidelines for the treatment of children and adolescents with eating disorders. J Eat Disord 2020;8:4; Hay P, Chinn D, Forbes D, et al.; Royal Australian and New Zealand College of Psychiatrists. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of eating disorders. Aust N Z J Psychiatry 2014;48:977-1008; Hornberger LL, Lane MA; Committee on Adolescence. Identification and management of eating disorders in children and adolescents. Pediatrics 2021;147:e2020040279; Lock J, La Via MC; American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with eating disorders. J Am Acad Child Adolesc Psychiatry 2015;54:412-25; National Guideline Alliance (UK). Eating disorders: recognition and treatment. London: National Institute for Health and Care Excellence (UK); 2017. Available at: https://pubmed.ncbi.nlm.nih.gov/28654225/.

medications, such as QTc-prolonging medications; and constipation management. Long-term medication management may also include the use of psychotropic medications.

ANOREXIA NERVOSA

Diagnostic Criteria and Hallmark Characteristics

Food restriction, fear of gaining weight, distorted body image, and obsessive preoccupation with food, weight, and exercise are essential features of AN (Table 3). Although weight loss is clearly defined in the adult diagnostic criteria by change in BMI, observations in children and adolescents may instead be the lack of achieving expected weight gain or maintenance of a normal developmental trajectory while growing in height. For this reason, BMI-for-age percentiles should be used to determine symptom severity with consideration for body build, weight history, and physiologic disturbance (Mitchell 2020; Lock 2019, 2015; APA 2013; CDC 2021). Based on the notable update to the *DSM-5* diagnostic criteria, amenorrhea is no longer a requirement for the diagnosis of AN (APA 2013).

The two subtypes of AN are *restricting type* (AN-R) and *binge-eating/purging type* (AN-BP) as defined in Table 3. Weight loss is achieved through excessive exercise, dieting, and fasting in AN-R, whereas weight loss is achieved through recurrent episodes of binge-eating or purging behaviors in AN-BP. Purging behaviors may include self-induced vomiting or the misuse of laxatives, diuretics, or enemas (APA 2013). Although subtypes are used to describe current symptoms, individuals may exhibit features of both subtypes over time.

Food avoidant behaviors and mealtime rituals are hallmark features of AN. Examples include cutting food into small pieces, picking/smearing/crumbling/hiding food, patting liquid off with a napkin, unusual food combinations with the goal of making food inedible, prolonged meal time, and chewing slowly/excessively (Harrington 2015).

Preteen presentation is associated with denial of body image and weight concerns, lack of insight regarding symptom severity, overall symptom minimization, nonspecific somatic concerns, low body weight, and more rapid weight loss compared with adults (Hornberger 2021; National Guideline Alliance 2017; Lock 2015; Hay 2014). Children and adolescents are less likely than adults to engage in binge-eating/purging behaviors and laxative misuse; however, these symptoms can occur later in clinical presentation (Mitchell 2020; Lock 2015). Overall, AN-R is associated with an earlier age of onset and better prognosis, although it may lead to a greater likelihood of crossover to AN-BP (Mitchell 2020).

Typical Presentation and Course

Anorexia nervosa is one of the most common chronic illnesses among girls and women, with the peak age of onset between 15–19 years (Lock 2019; Frank 2017; Hay 2014). Risk factors include a history of trauma, societal value on thinness, perfectionistic traits, cognitive rigidity, presence of childhood anxiety or OCD, and participation in activities for which weight may impact performance or assessment, such as gymnastics, ballet, and wrestling (Himmerich 2021; Mitchell 2020; Lock 2019). Initially, pediatricians may suspect an eating disorder based on unexpected weight loss or inability to gain expected weight, coupled with notable changes in behavior that promote weight loss. Medical evaluation is pursued when the rate of weight loss escalates (Hornberger 2021; Couturier 2020; Lock 2015; Hay 2014).

The course of AN among pediatric patients is variable, with about 50% achieving full recovery, 30% experiencing partial recovery, and 20% remaining chronically ill. A longer duration of illness is associated with a more chronic course and poorer

Table 3. *DSM-5* Diagnostic Criteria for AN

Core Symptoms[a]	Subtypes[b]	Severity
(A) Significantly low body weight based on age, sex, development trajectory, physical health, **and** (B) Intense fear of gaining weight or becoming fat, **and** (C) Disturbance in the experience of body weight or shape Symptom duration: ≥3 mo	(1) AN-R: weight loss primarily through dieting, fasting, and/or excessive exercise (2) AN-BP: weight loss primarily through self-induced vomiting or misuse of laxatives, diuretics, or enemas	Based on BMI percentile for children and adolescents (determine BMI-for-age percentile) Based on BMI for adults: Mild: BMI ≥17 kg/m^2 Moderate: BMI 16–16.99 kg/m^2 Severe: BMI 15–15.99 kg/m^2 Extreme: BMI <15 kg/m^2

[a]Must have all core symptoms to meet diagnostic criteria.

[b]Choose one subtype based on current symptoms.

AN = anorexia nervosa; AN-R = anorexia nervosa restricting type; AN-BP = anorexia nervosa binge-eating/purging type; *DSM-5* = *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.

Information from: American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: APA, 2013.

Table 4. Initial Review of Systems for Anorexia Nervosa

System	Considerations for Monitoring/Complications
General physical	Underweight, emaciation, loss of muscle mass Cold intolerance, hypothermia Lethargy Peripheral edema[a] Russell sign[a] (thickening of skin over dorsal surface of knuckles) Salivary gland hypertrophy[a]
Cardiac	Bradycardia, hypotension (particularly orthostatic) ECG changes including prolongation of QTc interval, arrhythmia Decreased cardiac output (reduced ventricular mass), increased vagal sensitivity
Dermatologic	Lanugo (fine hair covering face and body), brittle nails, dry skin
Endocrine	Thyroid dysfunction, osteopenia, osteoporosis
GI, liver	Delayed gastric emptying, post-prandial fullness, bloating, constipation, abdominal pain/distention, nausea Hepatic enzyme elevation
Hematology	Leukopenia (more common), macrocytic anemia, thrombocytopenia (less common)
Serum chemistry	Hypomagnesemia, hypophosphatemia, hypokalemia, hyponatremia, elevated BUN (in setting of dehydration), fluctuating SCr Metabolic alkalosis, increased amylase[a] Non-anion gap metabolic acidosis[b]
Reproductive	Amenorrhea, low serum estrogen/testosterone, reduced secretion of luteinizing hormone/follicle stimulating hormone, infertility (although unlikely after weight is restored), risk of miscarriage and preterm birth

[a]Binge-eating/purging subtype.

[b]Laxative misuse.

Information from: Bang L, Tamnes CK, Norbom LB, et al. Associations of age, body mass index and biochemical parameters with brain morphology in patients with anorexia nervosa. Eur Eat Disord Rev 2021;29:74-85; Cass K, McGuire C, Bjork I, et al. Medical complications of anorexia nervosa. Psychosomatics 2020;61:625-31; Himmerich H, Kan C, Au K, et al. Pharmacological treatment of eating disorders, comorbid mental health problems, malnutrition and physical health consequences. Pharmacol Ther 2021;217:107667; Hornberger LL, Lane MA; Committee on Adolescence. Identification and management of eating disorders in children and adolescents. Pediatrics 2021;147:e2020040279; Lock J, Derenne J. Treating eating disorders in children and adolescents: an update. Child Adolesc Psychiatr Clin N Am 2019;28:xiii-iv; Mitchell JE, Peterson CB. Anorexia nervosa. N Engl J Med 2020;382:1343-51; Mysliwiec R. Neuroscience of adolescent anorexia nervosa: implications for family-based treatment (FBT). Front Psychiatry 2020;11:418; National Guideline Alliance (UK). Eating disorders: recognition and treatment. London: National Institute for Health and Care Excellence (UK); 2017. Available at: https://pubmed.ncbi.nlm.nih.gov/28654225/.

prognosis (Mysliwiec 2020; Harrington 2015). Compared with adults, a gradual recovery and more favorable prognosis in adolescents are expected. Physiologic disturbances associated with nutritional compromise can impact most major organ systems (Table 4), which may result in life-threatening medical conditions (Lock 2015; Hay 2014; APA 2013). Complicating treatment planning are a high incidence of comorbid psychiatric conditions, including depression, anxiety, obsessive-compulsive, trauma-related, and substance use disorders; treatment resistance; mortality from medical complications; and suicide (Mitchell 2020; National Guideline Alliance 2017; Lock 2015; Hay 2014; APA 2013). Physiologic, psychological, and cognitive impairments may be greatest in early adolescence given the interruption of critical periods of physical, psychological, and social development (Hay 2014).

Treatment

Treatment Guidelines

Management of acute medical instability is essential in preventing mortality associated with AN (Hornberger 2021; Lock 2019; National Guideline Alliance 2017; Hay 2014; Ressel 2003; Golden 2003). As shown in Table 2, the decision to pursue inpatient medical or inpatient psychiatry/specialized eating disorder treatment is primarily influenced by the patient's acute medical and psychiatric condition (Dalle Grave 2021; Hornberger 2021; Couturier 2020; Mitchell 2020;

Frank 2017; National Guideline Alliance 2017; Lock 2015; Hay 2014). Once stabilized, weight restoration should be continued in a lower level of care (Dalle Grave 2021; Mitchell 2020; Hay 2014; AAP 2003; Golden 2003).

Family-based treatment is considered a first-line psychotherapy approach among children and adolescents, with evidence demonstrating greater long-term weight gain and higher remission rates compared with individual treatment (Hornberger 2021; Couturier 2020; Mitchell 2020; Lock 2019; Hay 2014). Initial phases of FBT emphasize the role of caregivers in meal planning and preparation, promoting healthy eating behaviors and nutritional support. Gradually, autonomy is reintroduced to the child or adolescent. Family communication is fundamental to FBT, with a clear focus on recovery rather than on the possible causes of the eating disorder (Hornberger 2021; Mitchell 2020; Frank 2017). Other evidence-based family therapies include parent-focused FBT, multi-family therapy, and emotion focused-family therapy (Hornberger 2021; Couturier 2020). The choice of psychotherapy intervention is case-specific and may evolve with ongoing treatment. Individual psychotherapy, cognitive behavioral therapy may be considered particularly in older adolescents.

In addition to psychotherapy, treatment guidelines provide recommendations regarding nutritional and medical treatment, rate of weight restoration, and the role of psychotropic medications among children and adolescents (Hornberger 2021; Couturier 2020; Lock 2015; Hay 2014). These recommendations are discussed in the following sections in this chapter.

Determination of Target Weight

Body mass index alone is not an appropriate tool to assess malnutrition and weight goals in children and adolescents (Marikar 2016). Instead, BMI percentile charts for children and adolescents must be used because the target weight changes with age, height, and weight-for-height changes (Hay 2014). Calculators and charts are freely available from the CDC (CDC 2021). Although there is no international consensus identifying the most meaningful target weight for children and adolescents, premorbid weight history, growth trajectory, pubertal stage, and menstrual history should be used to determine a target weight (Hornberger 2021; Bargiacchi 2019; Harrington 2015). For example, for an adolescent previously growing at the 40th BMI percentile, this percentile would likely be considered an appropriate target. Target weight should be routinely reassessed over time (Hornberger 2021).

Nutritional Support and Weight Restoration

Refeeding and Weight Gain

Oral refeeding with solid food, termed *meal-based refeeding*, is considered first-line treatment, whereas nasogastric feeding is considered second-line in cases of food refusal or in situations for which timely administration of nutrition is needed (Cass 2020; Bargiacchi 2019; Marikar 2016; Hay 2014). If nasogastric feeding is used, a daytime bolus regimen should be considered to better mimic physiologic eating (Marikar 2016). Although gastrostomy feeding and parenteral nutrition have been used, they should not be part of routine treatment because of the potential for complications (Bargiacchi 2019; Marikar 2016; Hay 2014).

Refeeding protocols should be individualized and involve a multidisciplinary team that includes a dietitian with experience in treating eating disorders. Traditional approaches of "starting low" and "going slow" have been criticized given concerns for delayed weight gain, development of underfeeding syndrome, and prolonged hospitalizations (Hornberger 2021; Mitchell 2020; Bargiacchi 2019; Lock 2019; Matthews 2018; Marikar 2016; Hay 2014). Recent evidence suggests that early weight restoration with more aggressive refeeding is associated with lower risk for underfeeding syndrome, faster weight gain, higher weight on hospital discharge, increased likelihood of long-term weight recovery, and lower levels of AN-associated psychological symptoms (da Silva 2020; Mitchell 2020; Bargiacchi 2019; Lock 2019; O'Connor 2016).

In severely malnourished patients, higher-calorie refeeding seems to be well-tolerated with close medical monitoring and electrolyte replacement if deficient (Mitchell 2020; Bargiacchi 2019; Lock 2019; O'Connor 2016). In most cases, higher-calorie meal-based approaches should be considered, starting at 1500–2600 kcal/day or 20 kcal/kg/day, with an increase of about 200 kcal/day until full nutritional requirements for weight gain are achieved. Typically, this goal should be achieved within 5–7 days (Hornberger 2021; Cass 2020; Bargiacchi 2019; Marikar 2016; O'Connor 2016). Overall, guidelines including the Junior MARSIPAN (Management of Really Sick Patients with Anorexia Nervosa) recommend aiming for a rate of weight gain of 0.5–2 kg/week with a standard macronutrient approach of 25%–35% from fat, 15%–20% from protein, and 50%–60% from carbohydrates (Hornberger 2021; Cass 2020; Bargiacchi 2019; Marikar 2016).

Refeeding Syndrome

Refeeding syndrome is a rare, potentially life-threatening condition caused by the metabolic and electrolyte alterations that occur as a result of newly introduced nutrition after a period of decreased calorie intake (Table 5) (da Silva 2020; Bargiacchi 2019; Hay 2014). Low BMI and hypophosphatemia are among the most sensitive markers for refeeding syndrome risk with persistence of malnutrition, abnormal electrolytes before refeeding, and rapid weight loss also implicated (Cass 2020; Bargiacchi 2019; Hay 2014).

Several physiologic mechanisms have been proposed to explain refeeding syndrome. A transition from fasting gluconeogenesis to carbohydrate-induced insulin release may trigger rapid intracellular uptake of potassium by insulin stimulation of the Na+/K+ ATPase enzyme, of phosphorous by phosphorylation of glucose on initiation of glycolysis,

Table 5. ASPEN Diagnostic Criteria for Refeeding Syndrome

Diagnostic Criteria	Severity[a]
(A) Decrease in serum phosphorus, potassium and/or magnesium values, **and** (B) Occurring within 5 days of reinitiating or substantially increasing energy provision/feeding	Mild: 10%–20% decrease Moderate: 20%–30% decrease Severe: >30% decrease **and/or** severe organ dysfunction associated with electrolyte and/or thiamine deficiency[b]

[a]Severity is based on decrease in serum phosphorous, potassium, and/or magnesium level

[b]Routine thiamine levels are unlikely to be of clinical value. Signs of thiamine deficiency include encephalopathy, lactic acidosis, nystagmus, neuropathy, Wernicke syndrome, Korsakoff psychosis, and wet and dry beriberi.

ASPEN = American Society for Parenteral and Enteral Nutrition.

Information from: da Silva JSV, Seres DS, Sabino K, et al.; Parenteral Nutrition Safety and Clinical Practice Committees, American Society for Parenteral and Enteral Nutrition. ASPEN consensus recommendations for refeeding syndrome. Nutr Clin Pract 2020;35:178-95.

and of magnesium by an unclear mechanism. Low baseline stores, secondary to starvation, may also explain rapid onset of hypophosphatemia, hypomagnesemia, and hypokalemia. Anabolic metabolism of adenosine triphosphate may also contribute to hypophosphatemia. Finally, insulin-triggered rebound hypoglycemia may develop secondary to depleted glycogen stores (Himmerich 2021; Cass 2020; da Silva 2020; Hay 2014).

Electrolyte/Micronutrient Monitoring and Supplementation

Proposed monitoring strategies include daily to twice daily weight assessments, electrolytes, serum creatinine, and BUN testing, cardiac monitoring, and documenting input/output for the first 3–5 days. As refeeding continues, monitoring frequency can be decreased to daily or three times per week (Cass 2020; da Silva 2020; Bargiacchi 2019; Hay 2014). Notably, increased monitoring frequency and electrolyte/micronutrient supplementation should be considered if values decrease to less than the normal range (Table 6) (Hay 2014). Hypophosphatemia is observed in about 50% of patients with AN early in the refeeding process. Mild cases can be treated with oral potassium supplementation, with intravenous treatment reserved for severe cases (Table 6) (Cass 2020). If left untreated, hypophosphatemia can be associated with acute respiratory failure, arrhythmia, and sudden cardiac arrest (Himmerich 2021; da Silva 2020; Bargiacchi 2019). Hypokalemia may result in impaired transmission of electrical impulses and increased risk of potentially lethal cardiac arrhythmias (da Silva 2020; Bargiacchi 2019). The impact of hypomagnesemia on morbidity is unclear, although the current consensus recommends treating serious deficiencies (da Silva 2020). Although hypophosphatemia, hypokalemia, and hypomagnesemia are more often associated with refeeding syndrome, hyponatremia may also be observed. This phenomenon may be related to excessive water consumption, reduced renal clearance of free water/sodium, and, less often, the syndrome of inappropriate antidiuretic hormone secretion (Cass 2020).

In addition to acute electrolyte monitoring and supplementation, consideration should also be made for the use of a daily multivitamin, thiamine, and/or zinc supplementation given the high risk for deficiencies among adolescents with AN (Table 6) (da Silva 2020; Hanachi 2019; Marikar 2016). An increased demand for thiamine is anticipated during refeeding as a cofactor for glucose-dependent metabolic pathways (da Silva 2020). For this reason, supplementation before initiation of refeeding may be considered to avoid neurologic complications associated with deficiencies, including confusion, encephalopathy, Wernicke syndrome, or Korsakoff psychosis (da Silva 2020; Bargiacchi 2019). Routine thiamine values should not be measured and likely are not of significant clinical value (da Silva 2020).

Zinc supplementation has been suggested as an appetite stimulant, with studies in children and adolescents demonstrating weight gain, increases in BMI, and improved caloric intake among those receiving supplementation (Himmerich 2021; Su 2002; Birmingham 1994). Notably, dose and duration of supplementation vary considerably. Daily supplementation can be considered; however, serum concentrations should not be measured and do not have clinical use.

Other Medical Considerations

Cardiac

Mitral valve prolapse, sinus bradycardia, and pericardial effusion are among the most common cardiopulmonary complications associated with AN (Cass 2020). Whereas pericardial effusion is typically asymptomatic, mitral valve prolapse is often associated with palpitations, dizziness, and dyspnea. Sinus bradycardia, likely the result of increased vagal tone from malnutrition, may be associated with light-headedness, syncope, cognitive slowing, chest pain, or

Table 6. Electrolyte/Micronutrient Dosing Considerations

Electrolyte/ Micronutrient	Role or Rationale	Monitoring	Dosing Considerations
Phosphate	Hypophosphatemia; early in refeeding process, many mechanisms, including starvation	Daily to BID for initial 3–5 days	Mild to moderate: PO 2–3 mMol/kg/day divided in 3–4 doses Duration: until resolution of deficiency Other: separate from oral calcium supplements by 2 hr Severe: IV replacement
Potassium	Hypokalemia; many mechanisms, including starvation		Mild to moderate: PO 2–5 mEq/kg/day in 2–4 divided doses; max single dose 20–25 mEq Duration: until resolution of deficiency Other: liquid formulations should be diluted to minimize GI irritation Severe: IV replacement
Magnesium	Hypomagnesemia; many mechanisms, including starvation		Mild to moderate: PO 10–20 mg/kg/dose elemental magnesium BID-QID Duration: until resolution of deficiency Other: separate from phosphate supplementation by 1–2 hr Severe: IV replacement
Thiamine	Risk for depletion during early stages of refeeding as a cofactor for glucose-dependent metabolic pathways	Level should not be measured	Dose: 2 mg/kg to max 100–200 mg/day PO or IV Duration: 5–7 days; consider extended duration if severe starvation, other risk factors, or symptoms of deficiency
Zinc	Potential appetite stimulant	Level should not be measured	Dose: 25–125 mg/day PO Duration: 4–12 wk
Calcium and vitamin D	Reduced bone mineral density, long-term fracture risk	Consider measuring 25(OH) vitamin D level	Dose: daily PO multivitamin (containing calcium and cholecalciferol) Consider higher dose of cholecalciferol (total of 25–50 mcg/day PO) in presence of vitamin D deficiency, insufficiency Duration: until weight restored; consider indefinitely

BID = twice daily; PO = oral; IV = intravenous; max = maximum; QID = four times daily.

Information from: Bargiacchi A, Clarke J, Paulsen A, et al. Refeeding in anorexia nervosa. Eur J Pediatr 2019;178:413-22; da Silva JSV, Seres DS, Sabino K, et al.; Parenteral Nutrition Safety and Clinical Practice Committees, American Society for Parenteral and Enteral Nutrition. ASPEN consensus recommendations for refeeding syndrome. Nutr Clin Pract 2020;35:178-95; Cass K, McGuire C, Bjork I, et al. Medical complications of anorexia nervosa. Psychosomatics 2020;61:625-31.

exercise intolerance (Cass 2020). Often cited as a risk associated with AN, QTc prolongation has long been considered the mechanism for increased risk of sudden cardiac death (Cass 2020; Krantz 2020). Recent evidence suggests that QTc prolongation alone is unlikely to explain cardiac mortality associated with AN; extrinsic factors should be considered including hypokalemia, concurrent medications, and family/personal history (Cass 2020; Krantz 2020; Treasure 2020).

Gastrointestinal

Most individuals with AN report GI issues, including postprandial fullness, early satiety, abdominal distension/pain, and nausea (Himmerich 2021; Cass 2020; Treasure 2020). Gastroparesis may help explain early satiety, nausea, and bloating particularly in patients presenting with low BMI. Patients with AN are at high risk for constipation, likely because of delayed colonic transit and pelvic floor dysfunction. A daily osmotic laxative is recommended to manage constipation. High doses may be needed especially in individuals with significant delays in colonic transit (Cass 2020; Bargiacchi 2019). Stimulant laxatives should be avoided given risks of electrolyte derangement and cathartic colon syndrome (Hornberger 2021). Additional interventions include scheduling several meals and snacks each day (e.g., 3 meals, 3 snacks) to minimize feeding volume. A low-fiber

diet and soft, easily digestible foods may also be considered (Cass 2020).

Gastroesophageal reflux disease symptoms, including heartburn, regurgitation, and dyspepsia may be present (Himmerich 2021; Cass 2020; Treasure 2020). Although traditional pharmacologic approaches are often used in clinical practice (e.g., calcium carbonate, proton pump inhibitors), no standard recommendation exists for patients with AN (Himmerich 2021). If pharmacologic treatment is considered, the duration should be closely evaluated to minimize prolonged treatment and associated adverse effects/risks (Himmerich 2021).

Lastly, changes in liver function test (LFT) values are common, especially with prolonged starvation. About 50% of patients present with an abnormal increase in values on LFTs before initiation of refeeding (Cass 2020; Bargiacchi 2019). These changes are referred to as *starvation-induced autophagy*, and result in a moderate hepatocyte injury, typically less than 10 times the upper limit of normal range. With the continuation of refeeding and weight gain, LFT values are expected to gradually normalize (Bargiacchi 2019). Routine monitoring for secondary causes of liver dysfunction in patients with AN is not recommended, unless clinical suspicion remains high for other underlying causes.

Endocrine

Anorexia nervosa is associated with broad endocrine dysregulation in response to a chronic low energy state. Disruption in the hypothalamic–pituitary–adrenal axis results in functional hypogonadotropic hypogonadism and associated amenorrhea in up to 66%–85% of patients (Cass 2020; Castellini 2020). Disruption of menstruation is typically seen with weight loss to less than 10%–15% of ideal body weight. Although weight restoration is thought to directly contribute to resumption of menstruation in most patients, it is important to note amenorrhea can precede weight loss and may persist after weight restoration in some individuals, which suggests other contributing mechanisms (Castellini 2020). In most cases, fertility is preserved with successful weight restoration (Cass 2020).

Endocrine dysregulation extends to skeletal health, including reductions in BMD and increased life-long risk for fracture (Cass 2020). Impact on skeletal health in children and adolescents is significant because peak bone mass is not reached until late adolescence. Bone loss may be irreversible especially if it occurs during critical periods of post-pubertal bone accretion (Hay 2020; Bargiacchi 2019). Decreased sex hormone production, elevated cortisol, and growth hormone resistance are thought to contribute to reductions in BMD (Cass 2020; Bargiacchi 2019). Changes in BMD occur rapidly and are usually evident within 1 year of AN onset (Cass 2020). Notably, osteopenia and osteoporosis are most likely to develop in girls and women who were malnourished early in puberty, develop amenorrhea, and/or have prolonged malnutrition (Hay 2014). Current American Academy of Pediatrics recommendations include weight restoration and supplementation with oral calcium and vitamin D (Hornberger 2021) (Table 6). Bisphosphonates and combined estrogen-progesterone oral contraceptives are not currently recommended by American Academy of Pediatrics for osteoporosis/osteopenia because of the lack of benefit to promote BMD in adolescents (Hornberger 2021; Bargiacchi 2019). Transdermal estrogen among adolescent girls has demonstrated benefit on BMD in small trials but is not considered standard of care at this time (Hornberger 2021; Bargiacchi 2019; Misra 2011).

Thyroid abnormalities, most commonly sick euthyroid syndrome, may also be observed as an adaptive response to malnutrition (Hornberger 2021; Cass 2020). On review of laboratory data, total triiodothyronine and free thyroxine are low, whereas thyroid-stimulating hormone (TSH) is normal (Hornberger 2021; Cass 2020). Thyroid supplementation is not indicated, and abnormalities should resolve with resolution of malnutrition (Hornberger 2021).

Role of Psychotropic Medications

It is estimated that more than 50% of adolescents with AN are prescribed psychotropic medications, with SSRIs and atypical antipsychotics among those prescribed most often (Hornberger 2021; Couturier 2020, 2019). Despite the frequency of prescribing, limited evidence is available to support the role of psychotropic medications in children and adolescents with AN (Bargiacchi 2019; Couturier 2019). Treatment guidelines address insufficient evidence to recommend psychotropic medications in adolescents with AN; American Academy of Child and Adolescent Psychiatry (AACAP) guidelines specifically suggest that psychotropic medications should be reserved for comorbid psychiatric conditions and refractory cases (Lock 2015; AACAP 2011).

Antidepressants

It has been proposed that SSRIs, and other serotonergic antidepressants, are unlikely to have significant effect in malnourished patients (Frank 2019; Lock 2015; Walsh 2006; Kaye 2001). Tryptophan, an essential amino acid obtained from food intake, serves as a critical precursor to serotonin production. Among individuals who restrict food intake, serotonin synthesis may be reduced given decreased availability of tryptophan. In addition, reductions in estrogen may contribute to reduced serotonin synthesis (Kaye 2001). Serotonin activity is likely restored with weight restoration.

Overall, evidence describing the use of SSRIs in pediatric populations is limited to one case-control study and several case reports (Table 7) (Couturier 2020, 2019). Treatment guidelines identify that antidepressants are not effective in acute phases of illness, although they may be considered for comorbid mental health conditions once weight has been restored (Hornberger 2021; Couturier 2020; Lock 2015; Hay

Table 7. Psychotropic Medications in AN

Author	Study Characteristics	Intervention	Results and Conclusions
ANTIDEPRESSANTS			
Holtkamp (2005)	Retrospective 32 female patients with AN; mean age 14.5 yr Psychiatric comorbidities: MDD, OCD	Mean duration of inpatient tx: 15 wk Patient groups: • 7: fluoxetine 20-60 mg/day • 8: fluvoxamine 100-150 mg/day • 4: sertraline 50-150 mg/day • 13: non-medication SSRI initiated after 10-wk inpatient tx targeting ongoing OCD or MDD symptoms Other inpatient tx regimens: refeeding, nutrition support, individual and family therapy Total duration: 6 mo	Readmission rates at 6 mo similar among SSRI and non-SSRI users (36% vs. 31% p=0.72) No differences among tx groups for core eating disorder symptoms: ANIS (p=0.79), depression (DIKJ; p=0.75), obsessive-compulsive (CY-BOCS; p=0.4) No efficacy of SSRIs among partially weight-restored adolescent females Drugs well-tolerated overall
Hrdlicka (2008)	Retrospective, case-control 18 female patients with AN; mean age 15 yr Psychiatric comorbidities: MDD, GAD	Mirtazapine 21.7 mg/day (mean dose) Concurrent tx interventions: nutritional rehabilitation, psychotherapy Duration: 4 wk	No difference between cases and controls in weight (p=0.981) or BMI (p=0.576)
ANTIPSYCHOTICS			
Hagman (2011)	Double-blind, placebo-controlled 40 female patients with AN; mean age 16 yr (12–21 yr) Psychiatric comorbidities: MDD, OCD	Risperidone: initial dose 0.5 mg/day, max dose 4 mg/day; titrated weekly to mean dose 2.5 mg/day (max 4 mg/day) Concurrent tx: nutritional rehabilitation, FBT; 16 patients concurrently prescribed antidepressants Duration: 9 wk (mean)	No significant differences in drive for thinness at 11 wk; body dissatisfaction at 7 wk; and body image distortion (EDI-2) at 7 wk; no difference in time to reach 90% of IBW Risperidone associated with significant elevations in serum prolactin at wk 7 (p=0.001)
Leggero (2010)	Prospective 13 female patients with AN-R; mean age 13.7 yr (9–16 yr) Psychiatric comorbidities: MDD, GAD	Olanzapine initial dose 1.25–2.5 mg/day; titrated to effect; mean dose 4.1 mg/day Concurrent tx: psychotherapy, psychoeducation, assisted feeding Duration: 6 mo	Significant improvement from baseline to 6-mo follow-up in BMI, global functioning (CGAS), eating attitudes (EAT-26), anxious-depressive symptoms (CBCL), and hyperactivity (SIAB) 54% (7 patients) considered overall responders at 6 mo (EAT-26) Well tolerated overall
Kafantaris (2011)	Double-blind, placebo-controlled 20 female patients with AN-R; mean age 17 yr (12–22 yr) Psychiatric comorbidities: unknown	Olanzapine initial dose 2.5 mg/day; titrated to mean dose 8.5 mg/day (goal 10 mg/day) Duration: 10 wk	No difference in median body weight between groups No change in eating attitudes and behaviors (EDE), psychological functioning, resting energy expenditure Trend in increased fasting glucose and insulin in olanzapine group (wk 10)

(*continued*)

Table 7. Psychotropic Medications in AN (*continued*)

ANTIPSYCHOTICS			
Author	**Study Characteristics**	**Intervention**	**Results and Conclusions**
Norris (2011)	Retrospective, matched-groups comparison 86 patients with AN or EDNOS; age 10–17 yr Psychiatric comorbidities: MDD, anxiety, OCD	Median olanzapine max dose 5 mg/day (3.75-7.5 mg/day) 50% of patients on concurrent SSRI or SNRI Duration: total tx duration unclear	No difference in weight gain Effect of olanzapine on eating disorder cognitions could not be assessed because of confounders Sedation and dyslipidemia in 56% of patients
Spettigue (2018)	Open-label, prospective 32 patients with AN; age 11–17 yr Psychiatric comorbidities: unknown	Olanzapine dosing schedule: a priori Concurrent tx: nutritional rehabilitation, psychotherapy, FBT Duration: 12 wk	Olanzapine associated with significant increase in weight (p=0.012) Mood, anxiety, ED cognitions/behaviors all improved over the study period; no difference observed with olanzapine 32% experienced asymptomatic increased serum prolactin with olanzapine (as early as wk 2); almost 32% discontinued as recommended by the treating physician because of adverse events
Marzola (2015)	Retrospective chart review 75 female patients; mean age 25 yr Psychiatric comorbidities: anxiety, MDD	Olanzapine mean dose 6.11 mg/day Aripiprazole mean dose 9.13 mg/day Concurrent tx: SSRIs, multimodal inpatient interventions Duration: 5 wk (mean)	All groups had improved food obsessions, compulsions, preoccupations, and rituals (YBC-EDS); significant among aripiprazole group (p=0.005) Aripiprazole seemed most effective in reducing eating-related preoccupations and rituals (YBC-EDS), p=0.017 No difference in BMI among tx groups
Frank (2017)	Retrospective chart review 106 female patients with AN Psychiatric comorbidities: anxiety, MDD	Aripiprazole for 22 patients (21%); mean dose 3.59 mg/day (1–5 mg/day) Of aripiprazole users, 16 (73%) concurrently prescribed an SSRI at hospital discharge Concurrent tx: nutritional rehabilitation, psychotherapy, FBT Duration: 40 days (mean)	Aripiprazole associated with greater weight gain vs. control group

AN = anorexia nervosa; ANIS = Anorexia Nervosa Self-Inventory; AN-R = anorexia nervosa restricting type; CBCL = Child Behavior Checklist; CGAS = Children's Global Assessment Scale; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DIKJ = Child Depression Inventory, German version; EAT-26 = Eating Attitudes Test-26; ED = eating disorder; EDE = Eating Disorder Examination; EDI-2 = Eating Disorder Inventory 2; EDNOS = Eating Disorder Not Otherwise Specified; FBT = family-based therapy; GAD = generalized anxiety disorder; IBW = ideal body weight; max = maximum; MDD = major depressive disorder; OCD = obsessive-compulsive disorder; SIAB = Structured Interview for Anorexia and Bulimia Nervosa; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; tx = therapy; YBC-EDS = Yale-Brown-Cornell Eating Disorders Scale.

Information from: Frank GK, Shott ME, Hagman JO, et al. The partial dopamine D2 receptor agonist aripiprazole is associated with weight gain in adolescent anorexia nervosa. Int J Eat Disord 2017;50:447-50; Hagman J, Gralla J, Sigel E, et al. A double-blind, placebo-controlled study of risperidone for the treatment of adolescents and young adults with anorexia nervosa: a pilot study. J Am Acad Child Adolesc Psychiatry 2011;50:915-24; Holtkamp K, Konrad K, Kaiser N, et al. A retrospective study of SSRI treatment in adolescent anorexia nervosa: insufficient evidence for efficacy. J Psychiatr Res 2005;39:303-10; Hrdlicka M, Beranova I, Zamecnikova R, et al. Mirtazapine in the treatment of adolescent anorexia nervosa. Case-control study. Eur Child Adolesc Psychiatry 2008;17:187-9. Kafantaris V, Leigh E, Hertz S, et al. A placebo-controlled pilot study of adjunctive olanzapine for adolescents with anorexia nervosa. J Child Adolesc Psychopharmacol 2011;21:207-12; Leggero C, Masi G, Brunori E, et al. Low-dose olanzapine monotherapy in girls with anorexia nervosa, restricting subtype: focus on hyperactivity. J Child Adolesc Psychopharmacol 2010;20:127-33; Marzola E, Desedime N, Giovannone C, et al. Atypical antipsychotics as augmentation therapy in anorexia nervosa. PLoS One 2015;10:e0125569; Norris ML, Spettigue W, Buchholz A, et al. Olanzapine use for the adjunctive treatment of adolescents with anorexia nervosa. J Child Adolesc Psychopharmacol 2011;21:213-20; Spettigue W, Norris ML, Maras D, et al. Evaluation of the effectiveness and safety of olanzapine as an adjunctive treatment for anorexia nervosa in adolescents: an open-label trial. J Can Acad Child Adolesc Psychiatry 2018;27:197-208.

2014). Antidepressants may be used to target depression, anxiety, and/or obsessive compulsive symptoms (Harrington 2015; Lock 2015). When an antidepressant is prescribed, guidelines for the specific condition (e.g., MDD) should be followed (Lock 2015). Among antidepressants, SSRIs are considered first-line therapies. Although serotonin norepinephrine reuptake inhibitors have not been evaluated in children and adolescents with AN, they could be considered second-line medications to SSRIs targeting comorbid depression and anxiety.

The role of atypical antidepressants such as mirtazapine has been evaluated in a small case-control study, which demonstrated no differences in weight or BMI (Table 7) (Naguy 2018; Hrdlicka 2008; Jaafar 2007). The specific mechanism of mirtazapine, including antagonism of H_1 and serotonin 2C receptors, has created interest in its role in restrictive-based eating disorders; however, ongoing evaluations are warranted to better define its role in treatment (Naguy 2018; Jaafar 2007). Mirtazapine should not be considered a first-line therapy, but it may be considered among adolescents with ongoing depression, anxiety, and sleep difficulties who have not responded to adequate trials of SSRIs. For prescription of mirtazapine, doses of 7.5–30 mg every night at bedtime can be considered.

Bupropion is contraindicated in children and adolescents with AN because of the concern for seizure. Additional considerations include the risk for weight loss and reduced appetite. Because of concerns for cardiotoxicity, QTc prolongation, and overdose risk, TCAs should be avoided.

Antipsychotics

Olanzapine is the most commonly studied psychotropic medication in children and adolescents with AN (Couturier 2020, 2019). Olanzapine may improve mood and anxiety, delusional ideation about body image/body weight, hyperactivity/impulsivity, and cognitive distortions regarding food and caloric intake (Leggero 2010). Typical dosing ranges include 2.5–10 mg/day. Although it is the most widely studied psychotropic medication in AN, controlled data are limited to one double-blind placebo-controlled trial (Kafantaris 2011) (Table 7). Notably, olanzapine is associated with high rates of adverse effects in pediatric patients with AN, including sedation, dyslipidemia, and hyperprolactinemia. This safety concern suggests the importance of routine monitoring for adverse effects, including metabolic monitoring with all antipsychotics (AACAP 2011; American Diabetes Association 2004) and limiting total duration of treatment.

Interest in aripiprazole, as a partial D_2 agonist, has grown based on hypotheses that adjunct treatment with an SSRI may be associated with a reduction in eating disorder preoccupations and rituals, cognitive rigidity, eating disorder cognitions, and behavioral changes among individuals with AN (Frank 2017, 2016b, 2014; Marzola 2015; Trunko 2011). Partial D_2 agonists could be helpful in learning and behavioral

Patient Care Scenario

A.B., a 16-year-old female adolescent (weight 43 kg [94.7 lb], height 62.9 inches), is evaluated with concern for weight loss, food restriction, and excessive exercise that has progressively worsened the past year. She reports that she started exercising and restricting her diet in attempts to improve her mood, with a gradual increase in exercise to about 2 hours/day and restricting her intake to about 300–700 kcal/day (primarily grain-based smoothies). She endorses significant fear of weight gain and denies self-induced vomiting and laxative/diuretic use. Her last menstrual period was 4 months ago.

Notable findings include the following: thinning hair, fatigue, weakness, lightheadedness, dizziness (particularly when standing), cold intolerance, 13-kg (28.6-lb) weight loss over 1 year, and heart rate (43 beats/minute day, 33 beats/minute night).

What is her most likely eating disorder diagnosis?

What symptoms or clinical presentation indicate the need for hospitalization?

What laboratory monitoring is necessary to evaluate on hospital admission, particularly considering the risk for refeeding syndrome?

What supplementation should be considered on admission?

ANSWER

A.B. meets diagnostic criteria for AN-R with, moderate severity. Her calculated BMI is 16.3, which is at the third BMI percentile for female adolescents her age (CDC 2021). Based on her weight and heart rate, inpatient medical hospitalization should be considered. Given her pronounced malnutrition and low body weight, close monitoring for refeeding syndrome is critical. Electrolytes should be measured daily, particularly the first 5 days of refeeding. If values decrease to less than the normal range, supplementation can be considered. Other acute monitoring should include renal function, cardiac function, and liver function. An ECG should be considered. Thiamine, zinc, and/or a multivitamin could be considered.

1. American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: APA, 2013.
2. Bargiacchi A, Clarke J, Paulsen A, et al. Refeeding in anorexia nervosa. Eur J Pediatr 2019;178:413-22.

changes, particularly in girls and women who are underweight and in a low estrogen state (Frank 2017, 2016a, 2014). Ongoing evaluations are warranted to better understand its role in treatment, although current studies are promising. Aripiprazole may be considered in an adolescent with comorbid MDD that is suboptimally treated with an SSRI. Doses less than 10 mg/day should be considered. Total daily doses can be split into twice-daily dosing to minimize risk of GI upset (Findling 2008).

The use of risperidone is not recommended in the weight restoration phase of AN based on negative results of a double-blind, placebo-controlled trial in pediatric patients with AN (Hagman 2011) (Table 7). Other atypical antipsychotics have not been systematically evaluated in pediatric patients with AN.

BULIMIA NERVOSA

Diagnostic Criteria and Hallmark Characteristics

Bulimia nervosa is characterized by episodes of binge-eating, compensatory/purging behaviors to prevent or minimize weight gain and preoccupations with body shape or weight (Table 8) (Treasure 2020; Harrington 2015; Lock 2015; APA 2013). Individuals with BN arrange complex schedules to accommodate episodes of binges and purges in an effort to perform them in secrecy (Castillo 2017; Harrington 2015; Lock 2015). For example, adolescents may binge after school before caregivers return home or binge at night in their bedroom. Caregivers may report that their adolescent disappears quickly after meals, makes frequent trips to the bathroom, spends an atypical amount of time in the shower after meals, and hides several food containers in their bedroom (Castillo 2017).

Adolescents often report a sense of lack of control during the binge episode, with reports of feeling "numb" or "nothing" (Castillo 2017; APA 2013). Binges may temporarily be associated with relief, although dysphoria, guilt, shame, and stress predominate after the binge episode. Relief, followed by overwhelming guilt/shame further drives the impulse to purge, which reinforces this binge/purge cycle (Castillo 2017; Lock 2015). The types of food eaten during a binge varies and may include foods that are easy to ingest or are otherwise avoided given concern for weight gain.

Self-induced vomiting is the most common compensatory/purging behavior, followed by misuse of stimulant laxatives (Treasure 2020; Castillo 2017; Mehler 2015). Male patients with BN are more likely to excessively exercise and use steroids compared with female patients (Lock 2015). Between binge-eating episodes, individuals may restrict total caloric consumption and avoid foods that are fattening or will trigger a binge (Castillo 2017; Harrington 2015; APA 2013). To meet diagnostic criteria for BN, binge/purge cycles on average must occur at least weekly over the course of 3 months. Severity is based on the number of inappropriate compensatory behaviors per week in which an individual engages (APA 2013) (Table 8).

Typical Presentation and Course

Bulimia nervosa typically presents in late adolescence or young adulthood with a mean onset at age 19 years; presentation before puberty is uncommon (Wade 2019; Castillo 2017; APA 2013). Low self-esteem, depressive symptoms, social anxiety, abuse in childhood, and a family history of an eating disorder are thought to significantly increase the risk for developing BN (Castillo 2017). Similar to AN, participation in sports (e.g., gymnastics, wrestling, long-distance running) in which

Table 8. Bulimia Nervosa *DSM-5* Diagnostic Criteria

Core Symptoms	Severity[b]
(A) Recurrent episodes of binge-eating[a], characterized by: 1) eating an amount of food larger than what most individuals would eat in a discrete period of time (usually <2 hr); 2) sense of lack of control over eating during the episode **and** (B) Recurrent inappropriate compensatory/purging behaviors to prevent weight gain, which may include self-induced vomiting; misuse of laxatives, diuretics, other medications; fasting; or excessive exercise **and** (C) Binges/purges occur at least once a week for 3 mo (on average) **and** (D) Self-evaluation is significantly influenced by body shape and weight	Mild: 1–3 Moderate: 4–7 Severe: 8-13 Extreme: ≥14

[a]One episode of binge eating does not need to occur in a single setting; for example, the binge can start in one setting and finish in another.

[b]Episodes of inappropriate compensatory behaviors/week.

DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

Information from: American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: APA, 2013.

weight is thought to impact performance may also increase the risk (Lock 2015). This disorder is difficult to identify. Individuals with BN are typically normal weight to overweight and may effectively conceal their eating disorder behaviors.

The course of BN is variable, with earlier age of onset, shorter duration of symptoms, positive parent–child relationships, and absence of laxative use associated with improved outcomes (Castillo 2017). About 50%–80% achieve full remission, with about 20% experiencing a chronic course (Castillo 2017; Harrington 2015). In addition to mood, anxiety, and substance use disorders in individuals with BN, significant impulsivity, sensation-seeking, and the tendency to pursue novel or exciting stimuli are commonly associated with BN among adolescents and young adults (Wade 2019; Castillo 2017; Lock 2015; Hay 2014; APA 2013).

It can be difficult to diagnose BN in childhood because binge-eating may occur less often. For example, children do not have independent control over food or access to food (Lock 2015). The pediatrician may initially suspect BN after concerns or suspicions of binging/purging and preoccupation with weight/shape are reported by caregivers (Castillo 2017; Lock 2015). Collateral information from caregivers is critical because children and adolescents are likely to minimize symptoms (Castillo 2017; Lock 2015). Once BN is suspected, referral to a multidisciplinary team with eating disorder experience should be considered, in addition to a full medical evaluation (Table 9).

Treatment

Treatment Guidelines

The level of care for BN is typically an outpatient or day treatment setting, although hospitalization may be required in the setting of uncontrollable binging and purging, dehydration,

Table 9. Initial Review of Systems for Bulimia Nervosa

System	Considerations for Monitoring/Complications
General physical	Normal to overweight, history of weight fluctuations Russell sign[a] (thickening of skin over the dorsal surface of the knuckles) Salivary gland hypertrophy[a] Loss of dental enamel, chipped teeth, increased frequency of dental caries, oral mucositis, dental sensitivity, xerostomia[a] Hoarse voice, difficulty swallowing, chronic cough[a] Peripheral edema Subconjunctival hemorrhage, epistaxis[a]
Serum chemistry	Hypokalemia, hypo/hyperchloremia, hyponatremia; elevated BUN, fluctuating SCr Pseudo-Bartter syndrome Metabolic alkalosis, increased amylase[a] Non-anion gap metabolic acidosis[b]
Cardiac	Bradycardia, tachycardia, hypotension (particularly orthostatic), arrhythmia, ECG changes including prolongation of QTc interval
Endocrine	Osteopenia, osteoporosis Hypothalamic–pituitary–adrenal axis dysregulation
GI, liver	Esophageal mucosal damage, dysphagia, dyspepsia, GERD-related, Mallory-Weiss tear[a] Diarrhea, hemorrhoids, rectal prolapse Cathartic colon syndrome[b]
Neurologic	Seizure
Reproductive	Amenorrhea, reduced estrogens and androgens, as a result of decreased and dysregulated gonadotropin-releasing hormone

[a]Primarily associated with self-induced vomiting.

[b]Primarily associated with laxative misuse.

GERD = gastroesophageal reflux disease.

Gibson D, Workman C, Mehler PS. Medical complications of anorexia nervosa and bulimia nervosa. Psychiatr Clin North Am 2019;42:263-74; Himmerich H, Kan C, Au K, et al. Pharmacological treatment of eating disorders, comorbid mental health problems, malnutrition and physical health consequences. Pharmacol Ther 2021;217:107667; Hornberger LL, Lane MA; Committee on Adolescence. Identification and management of eating disorders in children and adolescents. Pediatrics 2021;147:e2020040279; Mehler PS, Rylander M. Bulimia nervosa—medical complications. J Eat Disord 2015;3:12; Westmoreland P, Krantz MJ, Mehler PS. Medical complications of anorexia nervosa and bulimia. Am J Med 2016;129:30-7.

significant electrolyte imbalances, unstable vital signs, cardiac disturbances, or suicidality (Table 2) (Hornberger 2021; Castillo 2017; Hay 2014). Formal treatment is often pursued when a caregiver discovers evidence of their adolescent vomiting in the bathroom or shares other suspicions of binge/purge behaviors (Castillo 2017).

Family-based treatment is considered first-line psychotherapy intervention for children and adolescents with BN (Hornberger 2021; Castillo 2017; Frank 2017; Lock 2015). Although FBT for BN is not as well studied as FBT for AN, small studies have demonstrated superior outcomes, including abstinence from binge-eating and purging, expedited behavior change, and sustained abstinence rates up to 12 months post-treatment (Gorrell 2019; Wade 2019). Cognitive behavioral therapy has demonstrated modest outcomes for BN in adolescents and is considered an appropriate alternative or adjunct to FBT, particularly for adolescents who prefer individual treatment (Hornberger 2021; Gorrell 2019; Wade 2019; Lock 2015).

Monitoring

Complications of Self-Induced Vomiting

Electrolytes

The most dangerous features of persistent self-induced vomiting are electrolyte and acid-base alterations (Westmoreland 2016). With persistent self-induced vomiting, dehydration leads to up-regulation of the renin–angiotensin–aldosterone steroid hormone system. Aldosterone, secreted by the adrenal glands, increases renal absorption of sodium and bicarbonate, which results in water retention as a protective attempt to minimize risk for dehydration, hypotension, and volume depletion (Gibson 2019; Westmoreland 2016; Mehler 2015). Overall, this results in metabolic alkalosis and hypokalemia. This phenomenon is referred to as pseudo-Bartter syndrome (Gibson 2019; Westmoreland 2016; Mehler 2015). After self-induced vomiting ceases, aldosterone continues to be up-regulated. Ongoing retention of sodium and bicarbonate by the kidneys in the absence of vomiting may result in peripheral edema. Treatment includes slow fluid resuscitation to minimize the risk for edema. Short-term use of an aldosterone antagonist (i.e., spironolactone 25–50 mg/day, less than 14 days) has been described in literature, with improvement in peripheral edema reported (Gibson 2019). Of note, serum aldosterone concentrations should self-normalize within a few weeks of self-induced vomiting cessation (Westmoreland 2016; Mehler 2015).

Gastrointestinal

Adolescents with BN present with a variety of GI conditions. Individuals with BN or AN-BP often report gastroesophageal reflux disease-related symptoms as a result of esophageal erosion, ulcer, and/or a weakened lower esophageal sphincter (Gibson 2019; Mehler 2015). Persistent gastric acid reflux can lead to a variety of GI conditions including dysphagia, dyspepsia, hoarseness, and chronic cough (Westmoreland 2016; Mehler 2015). Less commonly, Mallory-Weiss tears, a mucosal tear at the joining of the stomach and esophagus, and/or esophageal rupture with associated hematemesis, may result from recurrent/persistent vomiting. Overall, treatment involves cessation of self-induced vomiting and standard pharmacologic treatment with a proton pump inhibitor or H_2-receptor antagonist. Upper endoscopy may be considered in some cases, but this assessment is not considered routine practice. At this time, it is unclear whether patients with BN need to be screened for Barrett esophagus (Gibson 2019; Westmoreland 2016; Mehler 2015).

Orofacial/Dental

Tooth hypersensitivity, periodontal disease, and xerostomia are among dental complications that may be reported in BN (Hornberger 2021; Gibson 2019; Westmoreland 2016; Harrington 2015; Mehler 2015). Enamel erosion, particularly on the lingual surface of teeth, may also be observed. Routine oral hygiene and fluoride mouthwash are considered routine standard treatment (Hornberger 2021; Westmoreland 2016). A patient's dentist may be the first to notice signs of self-induced vomiting (Mehler 2015).

Sialadenosis, swelling of the major salivary glands (including parotid glands), develops a few days after the cessation of chronic, excessive, self-induced vomiting. Swelling is typically bilateral with minimal tenderness and is associated with elevations in serum amylase and normal lipase (Hornberger 2021; Gibson 2019; Harrington 2015; Mehler 2015). Normally, sialadenosis resolves within 1–2 weeks without treatment, although tart candies and application of hot packs can be considered for comfort (Gibson 2019; Westmoreland 2016; Mehler 2015). Pilocarpine drops administered orally (5–15 mg/day) may be used for refractory cases, although the reported efficacy shows mixed results (Gibson 2019).

Dermatologic

Frequent self-induced vomiting may result in thickening of the skin over the dorsal surface of the knuckles, referred to as *Russell sign* (Gibson 2019; Westmoreland 2016; Mehler 2015). This symptom is not only present in BN but also AN-BP and typically resolves with resolution of self-induced vomiting (Table 9).

Complications of Laxative Misuse

All patients with BN should be screened for stimulant laxative misuse. Those who misuse laxatives are also at risk of cathartic colon syndrome, although the chronicity of laxative use, dose, and specific agent most often implicated is unclear. Impairments in peristalsis results from damage to the myenteric and Auerbach nerve plexus, resulting in constipation and associated risk for hemorrhoids, hematochezia, and rectal prolapse (Gibson 2019; Westmoreland 2016; Mehler 2015). With prolonged use of misuse of stimulant laxatives,

cathartic colon syndrome is potentially irreversible (Mehler 2015). Melanosis coli can also be seen on colonoscopy, although it is a benign finding (Gibson 2019; Mehler 2015). Stimulant laxatives should be discontinued and avoided as part of the treatment plan.

Systemic effects of acute/chronic laxative misuse and resultant diarrhea include electrolyte disturbances, fluid imbalance, and dehydration-induced secretion of aldosterone by up-regulation of the renin–angiotensin–aldosterone steroid system. Acute diarrhea results in a hyperchloremic metabolic acidosis without an increased anion gap. Chronic diarrhea, similar to persistent self-induced vomiting, results in a hypochloremic, hypokalemic metabolic alkalosis attributable to hypovolemia-induced hyperaldosteronism (Gibson 2019; Westmoreland 2016; Mehler 2015). Peripheral edema may be associated with abrupt cessation of the laxative, given persistent effects of aldosterone. Treatment includes slow fluid resuscitation in the case of chronic diarrhea, and management of associated electrolyte imbalances (Table 6).

General Complications

Cardiac

Dehydration associated with persistent episodes of self-induced vomiting and laxative misuse can result in resting and exertional sinus tachycardia, hypotension, and orthostasis (Gibson 2019; Mehler 2015). Hypokalemia, as previously described, may result in a prolonged QTc interval increasing acute risk for arrhythmia, syncope, and palpitations (Gibson 2019; Mehler 2015). For adolescents presenting with hypokalemia, close QT monitoring is warranted in addition to potassium supplementation (Table 6).

Among individuals with BN who use ipecac as a means of inducing vomiting, risk for cardiac toxicity should be considered (Gibson 2019; Mehler 2015). Emetine, the active ingredient of ipecac, has a long half-life and can accumulate with chronic use. Toxicity may result in damage to cardiac myocytes resulting in cardiomyopathy, congestive heart failure, ventricular arrhythmias, and sudden cardiac death in some cases (Gibson 2019; Mehler 2015).

Much less is known about the long-term cardiac risks of BN. A recent study has suggested that BN may be associated with long-term risk for cardiovascular disease, particularly among women previously hospitalized with BN-associated complications (Tith 2020). Several cardiovascular problems were observed, including myocardial infarction, atherosclerosis, other ischemic heart disease, and conduction disorders. Risk appeared highest within 2 years of hospital discharge, and remained elevated through 10 years of follow-up (Tith 2020). Reductions in serum estrogen, hypercholesterolemia, and nicotine use were hypothesized risk factors (Tith 2020). Although ongoing evaluations are needed, routine cardiac screening should be considered, particularly in adolescents who have a history of medical hospitalizations.

Endocrine

Dysfunction of the hypothalamic-pituitary-adrenal axis is present in both underweight and normal weight individuals with BN (Gibson 2019). Reduced estrogens and androgens, resulting from dysregulated gonadotropin-releasing hormone, contributes to hypothalamic amenorrhea. Low BMD is a common complication among both male and female patients. As described for individuals with AN, the impact on skeletal health in this age group is significant because peak bone mass is not reached until late adolescence. Bone loss may be irreversible especially if it occurs during critical periods of post-pubertal bone accretion (Hay 2020; Bargiacchi 2019; Gibson 2019). Decreased sex hormone production, elevated cortisol, and growth hormone resistance are thought to contribute to reductions in BMD (Cass 2020; Bargiacchi 2019). Current American Academy of Pediatrics include weight restoration and supplementation with oral calcium and vitamin D (Hornberger 2021) (Table 6).

Role of Psychotropic Medications

Antidepressants

Although SSRIs have demonstrated efficacy in BN, available data predominately include adult populations (Hornberger 2021; Gorrell 2019; Lock 2015). Given limited pediatric data (Table 10), guidelines recommend antidepressants as second-line treatment to psychotherapy for comorbid conditions. Adult studies suggest that SSRIs are beneficial in reducing the frequency of binge-eating/purging in combination with psychotherapy, particularly among patients with comorbid depression or anxiety (Hornberger 2021; Harrington 2015; Hay 2014). Among SSRIs, fluoxetine, sertraline, and citalopram are the most studied (Hornberger 2021; Harrington 2015). Fluoxetine has FDA approval for BN in adults and decreases urges to binge and purge, particularly at high doses (e.g., 60 mg/day) (Hornberger 2021; Castillo 2017; Lock 2015; Hay 2014). Although fluoxetine does not have FDA approval in pediatric patients for BN, it is widely used in clinical practice for pediatric patients with comorbid depressive, anxiety, and obsessive-compulsive disorders. Doses up to 60 mg/day should be considered. As in adults, sertraline and citalopram may also be considered for pediatric patients. Although not specifically studied in adolescents with BN, fluvoxamine may be a favorable option given high rates of comorbid OCD in adolescent patients with BN and the efficacy of fluvoxamine for core symptoms of OCD.

Other antidepressants, including monoamine oxidase inhibitors (MAOIs), TCAs, and bupropion are not recommended. In the case of TCAs, adverse effects and concern for lethality in overdose limit their clinical utility (Hornberger 2021; Harrington 2015; Hay 2014). The MAOIs have not demonstrated good efficacy or tolerability in pediatric patients and have a risk for drug and dietary interactions. Bupropion should be avoided in children and adolescents with BN

Table 10. Psychotropic Medications in BN: Antidepressants

Author	Study Characteristics	Intervention	Results and Conclusions
Kotler (2003)	Open-label 10 patients, age 12–18 yr Psychiatric comorbidities: MDD, anxiety	Fluoxetine 60 mg/day Concurrent treatment interventions: supportive psychotherapy Duration: 8 weeks	Significant reduction average weekly binges ($p<0.01$) and purges ($p<0.005$), overall eating disorder symptoms (EDI) ($p<0.01$) Fluoxetine associated with overall symptom improvement; 20% much improved, 50% improved, 30% slightly improved (CGI-I) Significant reduction in anxiety (SCARED, $p<0.05$) Fluoxetine was well tolerated

CGI-I = Clinical Global Impression Improvement Scale; EDI = Eating Disorder Inventory; MDD = major depressive disorder; SCARED = Self-Report for Childhood Anxiety Related Disorders.

Information from: Kotler LA, Devlin MJ, Davies M, et al. An open trial of fluoxetine for adolescents with bulimia nervosa. J Child Adolesc Psychopharmacol 2003;13:329-35.

because of concerns for seizure, weight loss, and reduced appetite. Given the risk for seizure, bupropion in all formulations in contraindicated in patients with BN.

Other Medications

Although topiramate has demonstrated short-term efficacy in adults who do not respond to SSRIs, ongoing evaluations are needed in pediatric patients as cases of topiramate worsening eating disorder symptoms have raised concerns (Hornberger 2021; Castillo 2017; Hay 2014). In addition, naltrexone and ondansetron have been evaluated in adults, although the evidence is insufficient to support their use in pediatric patients at this time (Hornberger 2021).

BINGE-EATING DISORDER

Diagnostic Criteria and Hallmark Characteristics

Binge-eating disorder is characterized by recurrent episodes of binge-eating in which large quantities of food are consumed within a short period of time, typically less than 2 hours. In addition to a sense of lack of control, marked distress, feelings of guilt, depressed mood, and physical discomfort accompany the binge-eating episode (Table 11). The type of food consumed varies significantly among individuals with BED and generally includes items that are easy to consume in large quantities. The severity of BED is determined by the number of binge-eating episodes per week. Notably, the absence of compensatory behaviors (i.e., self-induced vomiting, laxative misuse, excessive exercise) distinguishes BED from BN (APA 2013).

Diagnosing BED in children and adolescents is challenging. Defining a "large amount of food" during childhood and adolescence is difficult, given the varied caloric intake during different stages of development. In addition, articulating loss of control during a binge episode may be difficult for children and adolescents. Given these challenges, alternative diagnostic criteria have been proposed by a research group from the Western Psychiatric Institute and Clinic at the University of Pittsburgh Medical Center. These proposed criteria were not

Table 11. Binge-Eating Disorder *DSM-5* Diagnostic Criteria

Core Symptoms	Severity[a]
(A) Recurrent episodes of binge-eating, characterized by: 1) eating an amount of food that is larger than what most individuals would eat in a discrete period of time (usually < 2 hr) **and a** 2) sense of lack of control over eating during the episode (B) Binge episodes are associated with **≥3** of the following while eating: 1) rapidly 2) until uncomfortably full 3) large amounts when not feeling physically hungry 4) alone, because of embarrassment 5) feeling disgusted, depressed, or very guilty after eating (C) Binge-eating occurs at least once a week for 3 mo	Mild: 1–3 Moderate: 4–7 Severe: 8-13 Extreme: ≥14

[a]Episodes of binge-eating/week.

DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

Information from: American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: APA, 2013.

officially adopted into the *DSM-5* but continue to be evaluated (Bohon 2019; Marcus 2003). At this time, *DSM-5* diagnostic criteria for BED in adults continue to be used for children and adolescents.

Typical Presentation/Course

Binge-eating disorder typically begins in late adolescence or young adulthood and is the most common eating disorder in this age group (Bohon 2019; Guerdjikova 2019b; APA 2013). Although BED is more common in girls, BED has the highest prevalence of any eating disorder in boys (Bohon 2019). Remission rates are higher in BED that BN or AN; however, many do not seek treatment and continue to experience prolonged binge-eating and associated medical symptoms (Frank 2017). Crossover from BED to other eating disorders is uncommon. The most common psychiatric comorbidities include bipolar, depressive, substance use, and anxiety disorders (Guerdjikova 2019b; APA 2013).

Body dissatisfaction, BMI, a history of being overweight, anxiety, depression, and emotional disinhibition may be risk factors among children who develop BED (Bohon 2019). In addition, family history of BED is thought to increase risk. Adolescents with BED have higher adiposity, larger waist circumference, depressive symptoms, and disordered eating (Bohon 2019). In addition, adolescents with BED are at increased risk for developing obesity, substance use, suicidality, and other psychiatric conditions, which highlights the importance of diagnosis and treatment (Table 8) (Bohon 2019).

It is estimated that about 60% of young adults with BED are obese (Frank 2017). Binge-eating behavior is often overlooked and likely underdiagnosed, which can result in embarrassment, shame, and secrecy surrounding symptoms (Guerdjikova 2019b). When BED is suspected, it is critical to obtain collateral information from caregivers in addition to an initial review of systems (Table 12).

Table 12. Initial Review of Systems for Binge-Eating Disorder

System	Considerations for Monitoring/ Complications
General physical	Overweight and obesity, history of weight fluctuations, striae distensae
Cardiac	Hypertension, cardiovascular disease
Endocrine	Elevated BMI, hyperglycemia, hyperlipidemia, metabolic rate fluctuation type 2 diabetes, polycystic ovary syndrome
GI	Gastroesophageal reflux disease
Neurologic	Pain disorders, fibromyalgia
Reproductive	Early menarche, menstrual dysfunction

Information from: Guerdjikova AI, Mori N, Casuto LS, et al. Update on binge eating disorder. Med Clin North Am 2019;103:669-80.

Treatment

Treatment of BED primarily focuses on obesity and associated complications rather than addressing core eating disorder psychopathology and typically occurs in an outpatient level of care (Guerdjikova 2019b). Psychotherapy for BED has not been widely studied in children and adolescents. Cognitive behavioral therapy and dialectical behavioral therapy (DBT) demonstrate efficacy in adult populations and are used for children and adolescents in clinical practice. The aims of DBT in BED are to identify the emotion-related triggers of binge-eating and strategies to manage those emotions without binge-eating (Bohon 2019; Hay 2014). Although FBT has not been formally evaluated in children and adolescents with BED, it is likely beneficial given its efficacy in BN (Bohon 2019).

Monitoring

Binge-eating disorder may independently increase risk for the development of metabolic syndrome, diabetes, hypertension, and dyslipidemia. Disordered sleep, fibromyalgia, irritable bowel syndrome, and other pain conditions have also been associated with BED in adults (Guerdjikova 2019b). Comprehensive medical evaluation is critical to minimize long-term metabolic and cardiovascular risk. Primary interventions should be focused on weight loss, minimizing binge-eating episodes, and treating co-occurring psychiatric conditions.

Role of Psychotropic Medications

Stimulants

Lisdexamfetamine has FDA approval for adults with moderate to severe BED. In an 8-week randomized, double-blind, placebo-controlled trial, lisdexamfetamine 50 mg/day and 70 mg/day demonstrated efficacy for reducing the number of binge-eating episodes/day, binge-eating cessation, and global improvement among adults with moderate to severe BED (McElroy 2015). Adverse effects included hypertension, sleep disturbance, and restlessness (McElroy 2015). Lisdexamfetamine 50–70 mg/day also demonstrated efficacy in adults for global binge-eating severity, obsessive-compulsive, and impulsive features of BED in an 11–week placebo-controlled trial (McElroy 2016). Notably, doses of 30 mg/day did not demonstrate effectiveness in any controlled trials (McElroy 2015, 2016). In a long-term study, risk of binge-eating relapse over 6 months was lower in participants continuing lisdexamfetamine than those randomized to placebo (Hudson 2017). Lisdexamfetamine has not been

Table 13. Psychotropic Medications in BED: Stimulants

Author	Study Characteristics	Intervention	Results and Conclusions
Guerdjikova (2019)	Retrospective chart review 25 patients with BED, age 12–19 yr (mean 16.5 yr) Psychiatric comorbidities: ADHD, MDD	Lisdexamfetamine mean maximum dose 58 mg/day Concurrent treatment: • 68% antidepressants • 12% aripiprazole • 36% psychotherapy Duration: 19 mo (mean)	60% (n=15) reported improved in BED symptoms, as described in patient interview BMI was not significantly reduced; no significant change in BMI percentile Lisdexamfetamine was well tolerated

ADHD = attention/deficit-hyperactivity disorder; BED = binge-eating disorder; MDD = major depressive disorder.

Guerdjikova AI, Blom TJ, Mori N, et al. Lisdexamfetamine in pediatric binge eating disorder: a retrospective chart review. Clin Neuropharmacol 2019;42:214-6.

systematically evaluated in children and adolescents with BED, although one retrospective chart review suggests some positive findings (Table 13). At this time, guidelines do not provide recommendations regarding the use of stimulants in adolescents with BED given the lack of evidence. If lisdexamfetamine is considered, it should be reserved for adolescents with moderate to severe BED, without a significant cardiac history.

Antidepressants

Selective serotonin reuptake inhibitors, specifically sertraline, have demonstrated positive outcomes on impulse control and comorbid anxiety, depression, and OCD in adults. Citalopram and escitalopram have also demonstrated effectiveness in adults for similar outcomes. Higher doses (e.g., sertraline 150–200 mg/day) should be used in the setting of comorbid OCD (Himmerich 2021). Although TCAs may reduce binge frequency in adults, they are generally avoided given concerns for cardiotoxicity and risk for lethality in overdose. Antidepressants have not been evaluated in pediatric patients with BED.

Antiseizure Medications

Topiramate 100–200 mg/day has demonstrated efficacy in BED for weight loss and overall reduction of BED symptoms in adults (Himmerich 2021). Topiramate in combination with phentermine has been associated with reduction of binge-eating in adults (Safer 2020). Studies are needed to understand the role of antiseizure medications in pediatric patients.

AVOIDANT/RESTRICTIVE FOOD INTAKE DISORDER

Avoidant/restrictive food intake disorder is a new diagnosis in *DSM-5* that describes an important set of eating disorder symptomatology (APA 2013). Children and adolescents with ARFID present with avoidance of certain foods or food categories and overall food restriction (Table 14). Heightened sensitivity to certain foods, including texture, appearance, and smell, is one of the most common rationales for avoidance and restriction. Sensory-based food avoidance typically develops in early childhood and is often longstanding (Brigham 2019; Katzman 2019). Fear of aversive consequences such as choking, vomiting, or pain, may explain avoidance/restriction among individuals who have experienced food-related trauma. In addition, individuals may present with a general lack of interest in food or eating (Brigham 2019). It is important to note that restrictions in ARFID are not related to fear

Table 14. *DSM-5* Diagnostic Criteria for Avoidant/Restrictive Food Intake Disorder

(A) Eating disturbance (lack of interest in eating or food; avoidance based on sensory characteristics of food; concern about aversive consequences of eating) with failure to meet appropriate nutritional requirements **and** ≥ 1 of the following:
   1) Weight loss, failure to achieve expected weight gain, faltering growth in children
   2) Nutritional deficiency
   3) Dependence on enteral feeding or oral nutritional supplements
   4) Marked interference with psychosocial functioning

(B) Eating disturbance does not occur in the course of anorexia nervosa or bulimia nervosa, no evidence of a disturbance in body image; Not better explained by lack of available food

Information from: American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: APA, 2013.

Practice Points

Eating disorders are complex psychiatric disorders, with an onset in often adolescence, that are associated with significant medical complications, psychiatric comorbidities, and impact on physical and psychosocial functioning. New data continue to emerge regarding identification, acute medical management/monitoring, and long-term treatment of eating disorders, which includes the role of psychotropic medications. The clinical pharmacist plays a critical role in the multidisciplinary treatment of pediatric patients with an eating disorder:

- **The *DSM-5* offers updated diagnostic criteria for eating disorders, which includes important clinical updates from *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*. Notably, amenorrhea is no longer a component of AN diagnostic criteria.**
- **Eating disorders are associated with significant mortality and evaluations should be routinely performed among pediatric patients. Standardized screening tools are available, including the Eating Disorder Examination Questionnaire (EDE-Q), Eating Attitudes Test (EAT), and Kids' Eating Disorder Survey (KEDS). Screening should be approached in a nonjudgmental and open-minded manner.**
- **Guidelines provide recommendations regarding identification, treatment, and long-term planning for patients with eating disorders. Although not all guidelines include pediatric specific recommendations, evidence continues to mount for treatment of pediatric patients.**
- **A first-line psychotherapeutic approach is FBT among children and adolescents especially for AN and BN, and likely for BED.**
- **Considered alone, BMI is an inappropriate tool to assess malnutrition and weight goals. Percentiles for BMI, however, should be calculated and growth trajectory, menstrual history, and premorbid weight should also be considered.**
- **Refeeding protocols should include more aggressive refeeding (1500–2600 kcal/day) with close monitoring of electrolytes, such as phosphorous, potassium, and magnesium. This strategy is associated with improved outcomes compared with slower refeeding.**
- **Psychotropic medications can be considered. Their role is limited in acute treatment of AN with some benefit for comorbid depression/anxiety once weight is restored. High-dose fluoxetine (with FDA approval for BN in adults) has been most widely studied in BN and has shown reductions in binge-episodes in adolescents. Finally, lisdexamfetamine (with FDA approval for moderate to severe BED in adults) has not been systematically studied in adolescents and use should be considered with caution. Psychotropic medication decisions should be made primarily based on comorbid psychiatric conditions.**

of becoming overweight or efforts to control weight or body shape (Brigham 2019; Katzman 2019; APA 2013).

Compared with AN/BN, individuals with ARFID are more likely to be younger, male, and have a diagnosis of other medical conditions (Brigham 2019; Katzman 2019). Psychiatric comorbidities include anxiety, mood disorders, autism spectrum, and attention-deficit/hyperactivity disorders. Given reduced nutritional intake, patients may present with symptoms associated with acute malnutrition warranting a higher level of care (Brigham 2019). Initial evaluation and acute medical monitoring/treatment is similar to AN (Table 4). Overall, pharmacologic treatment strategies are not well described.

CONCLUSION

Eating disorders are characterized by a variety of abnormal eating behaviors with altered attitudes toward weight, body shape, eating, and interest in food. Impairments in physical health and psychosocial functioning are associated with significant morbidity and mortality in pediatric patients, which highlights the important role of pediatric pharmacists to identify the role of vitamin/mineral supplementation, necessary medication dose adjustments (e.g., altered renal clearance), and advocating for appropriate acute monitoring.

Pediatric pharmacists are critical team members to identify key medication considerations. For example, children and adolescents with restrictive eating disorders may be more sensitive to anticholinergic and cardiovascular adverse effects (e.g., orthostasis), increased risk for seizure (e.g., bupropion), and impact on BMD (e.g., antiseizure medications). In addition, hypoalbuminemia may result in more unbound drug, particularly those with high serum albumin binding, and decreased volume of distribution among fat-soluble medications/vitamins in the setting of decreased body fat. Other acute medication considerations include risk for QTc prolongation, potential for nephrotoxicity, and impact of slowed/altered GI motility.

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Self-Assessment Questions

Questions 1-4 pertain to the following case.

L.M. is a 17-year-old female adolescent (53 kg [116.8 lb], 66 inches) presenting to her pediatrician with reports of depressed mood and body image concerns. L.M. reports that she is restricting food and excessively exercises alone in her room, in addition to attending ballet practice 6 times per week. Her parents report that she has cut out all fats, peanut butter, protein, and sugary food from her diet, and that she will only eat dried fruit and asparagus. At today's visit L.M. denies recent purging and use of laxatives but endorses suicidal ideation. Previously, L.M. was growing at the 50th BMI percentile. Her last menstrual period was 6 months ago. Since her last visit to the pediatrician 1 month ago she has lost 10 kg. L.M. is admitted to the inpatient medical unit given her acute weight loss and concerns for dehydration. In addition to measuring daily weights, input/output, and laboratory tests, she is started on meal-based refeeding. A basic metabolic panel shows the following: blood urea nitrogen 46 mg/dL, phosphorus 2.6 mg/dL, potassium 3.5 mEq/L, and serum creatinine 1.2 mg/dL. Her lowest heart rate overnight was 40 beats/minute. Notable findings on physical examination include moderate salivary gland hypertrophy, skin thickening over the dorsal surface of the index finger knuckle (right hand), and peripheral edema.

1. Which one of the following options is best to recommend for L.M.?

   A. Zinc
   B. Thiamine
   C. Phosphorus
   D. Calcium/Vitamin D

2. What is the most likely rationale for deferring antidepressant initiation acutely in L.M.?

   A. AKI
   B. Hepatic dysfunction
   C. Risk for QT prolongation
   D. Malnutrition

3. Which of the following is most likely to impact bone mineral density (BMD) in L.M.?

   A. Combined oral contraceptive
   B. Prolonged malnutrition
   C. Transdermal estrogen
   D. Omeprazole

4. L.M. is now weight restored at the 44th BMI percentile. She continues to be anxious and depressed. She has previously tried fluoxetine. Which of the following is best to recommend for L.M.?

   A. Escitalopram
   B. Venlafaxine
   C. Aripiprazole
   D. Mirtazapine

5. A 13-year-old female adolescent with current diagnoses of AN restricting type (AN-R), generalized anxiety disorder, and major depressive disorder (MDD) presents to outpatient clinic. She is currently weight restored at the 50th BMI percentile. Despite achieving weight restoration, she continues to present with ongoing eating disorder rituals, significant cognitive distortions/rigidity, delusional ideations regarding body image, and depressive symptoms. These symptoms are significantly interfering with her overall level of functioning. She is currently taking fluoxetine 40 mg/day orally. Notably, she has a history of QTc prolongation and hyperprolactinemia while taking risperidone. The team is considering an adjunctive psychotropic medication to fluoxetine, what is the best recommendation. Which of the following is best to recommend for this patient?

   A. Mirtazapine 7.5 mg orally every night
   B. Bupropion SR 100 mg orally every morning
   C. Aripiprazole 1 mg orally twice daily
   D. Olanzapine 2.5 mg orally daily

6. A 17-year-old male adolescent (79 kg [174.1 lb], 74 inches) with current diagnoses of BN and obsessive-compulsive disorder (OCD), presents to the eating disorder day treatment program with ongoing preoccupation with body weight, binge-eating twice monthly on average and occasional self-induced vomiting. He is currently weight restored to the 64th BMI percentile and continues to report intrusive obsessive thoughts and compulsive behaviors. He is engaged in cognitive behavioral therapy and has been taking sertraline 200 mg/day orally for 3 months. Previous antidepressant trials include fluoxetine 60 mg/day. Which of the following is best to recommend for this patient?

   A. Clomipramine 25 mg/day orally
   B. Naltrexone 50 mg/day orally
   C. Topiramate 25 mg twice daily orally
   D. Fluvoxamine 25 mg at night orally

Questions 7-9 pertain to the following case.

R.P. is a 14-year-old male adolescent (56 kg (123.4 lb), 65 inches) presenting to the eating disorder partial hospitalization program with a preoccupation to lose weight and body image concerns. R.P. exercises twice daily most days per week to lose weight. He describes occasional binge-eating (averages one episode/week) in which he reports losing control and feeling numb. R.P. reports significant guilt and shame following the binge episodes. His parents report that

they often find empty food containers hidden in his bedroom. On admission, a basic metabolic panel shows the following: Na 135 mEq/L, K 4.4 mEq/L, serum Cl 112 mEq/L, CO_2 20 mEq/L, Scr 0.8 mg/dL. He is currently prescribed famotidine 20 mg twice daily orally. R.P. has never been prescribed psychotropic medications.

7. What is the most likely explanation for R.P.'s laboratory findings?

   A. Acute diarrhea, laxative misuse
   B. Self-induced vomiting
   C. Chronic diarrhea, laxative misuse
   D. Weight loss

8. The team is curious about acute medical management. Which of the following is best to recommend immediately for this patient?

   A. Weight restoration
   B. Laxative discontinuation
   C. Urgent fluid resuscitation
   D. Multivitamin

9. The psychiatry resident is curious about the best antidepressant choice for R.P. and consults the pharmacy team. Which of the following is best to recommend for this patient?

   A. Mirtazapine 7.5 mg every night orally
   B. Duloxetine 30 mg every morning orally
   C. Venlafaxine 75 mg every morning orally
   D. Fluoxetine 10 mg every morning orally

Questions 10-11 pertain to the following case.

G.G. is a 15-year-old male adolescent (baseline weight 57 kg [125.6 lb], height 57 inches) with OCD, who presents with concerns for malnutrition. He reports changing his diet to become a better athlete and progressively increased his rate of exercise and restricted his caloric intake in an effort to lose weight over the past 3 months. Overall, he lost 13 kg [28.6 lb] and has been bradycardic (30–40 beats/minute) for the previous two weeks. He describes significant fatigue, dizziness with standing, cold intolerance, and ongoing dissatisfaction with his current weight. He denies use of laxatives/diuretics or self-induced vomiting.

10. What is the most accurate eating disorder diagnosis for G.G.?

    A. AN-R
    B. AN binge-eating/purging type (AN-BP)
    C. BN
    D. Avoidant/restrictive food intake disorder (ARFID)

11. G.G. is admitted to the medical floor for close monitoring for refeeding. In addition to a basic metabolic panel, serum phosphate and magnesium, and complete blood count, which set of assessments/tests would be most helpful in identifying potential contributors to his clinical presentation?

    A. Hepatic function tests, echocardiogram, renal ultrasound
    B. Echocardiogram, ECG, thyroid studies
    C. Thyroid studies, vitamin D level
    D. Abdominal radiography, hepatic function tests, serum lipase

12. An 18-year-old male (74 kg [163.1 lb], 63 inches) presenting to the outpatient psychiatry clinic with reports of about six binge-eating episodes/week during which he reports a lack of control. He describes eating rapidly during the binge episodes until he is uncomfortably full and hides in his bedroom during the binge episodes. At today's visit denies self-induced vomiting, laxative misuse, and excessive exercise. Symptoms have persisted for 6 months. At this time he denies depressive and anxiety symptoms. He reports that he is also engaged in therapy.

    Which of the following is best to recommend for this patient?

    A. Fluoxetine 10 mg/day orally
    B. Sertraline 50 mg/day orally
    C. Naltrexone 50 mg/day orally
    D. Lisdexamfetamine 50 mg/day orally

13. A 15-year-old female adolescent with AN-R is currently receiving nutritional support, primarily by the nasogastric route, on the eating disorder unit. She last had a menstrual cycle 6 months ago; first cycle was at age 13 years. Her treatment team is concerned about her risk for osteopenia and osteoporosis and are curious about an evidence-based approach to preserve bone health in adolescents. Which of the following is best to recommend for this patient?

    A. Bisphosphonate
    B. Combined estrogen-progesterone oral contraceptive
    C. Transdermal estrogen
    D. Weight restoration and supplementation with oral calcium 200 mg/cholecalciferol 25 mcg daily

14. What diagnostic feature distinguishes BN from binge-eating disorder (BED) most accurately?

    A. Presence of compensatory/purging behaviors (e.g., self-induced vomiting, misuse of laxatives)
    B. Frequency of binge-eating episodes
    C. Feeling depressed, disgusted, and guilty after binge-eating
    D. Sense of lack of control overeating during the binge episode

15. A 12-year-old boy (28 kg [61.7 lb], 48 inches) presents to the eating disorder partial hospitalization program where he endorses significant anxiety, body image distortions, and preoccupation with weight. He has been in eating disorder treatment for the past two months and reports ongoing dissatisfaction with his appearance and a fear of gaining weight. Denies use of laxatives and self-induced vomiting. He is currently weight restored at the 66th BMI percentile. Laboratory tests today show the following:

ALT	22 IU/L
AST	28 IU/L
BUN	15 mEq/L
Magnesium	2.1 mEq/L
PO_4	4 mg/dL
Potassium	3.9 mEq/L
Na	140 mEq/L
SCr	0.7 mg/dL
TC	200 mg/dL
HDL	35 mg/dL
LDL-C	135 mg/dL
TG	180 mg/dL

He is currently prescribed citalopram 40 mg/day orally, polyethylene glycol 17 g twice daily orally, simethicone chewable 40 mg four times daily orally, multivitamin daily orally, and zinc sulfate elemental 50 mg daily orally. The team is curious about initiating adjunct pharmacologic treatment to citalopram. What is most appropriate to recommend for this patient?

A. Quetiapine 25 mg every night orally
B. Aripiprazole 1 mg twice daily orally
C. Olanzapine 1.25 mg every night orally
D. Risperidone 0.25 mg twice daily orally