

## CLINICAL PRACTICE

## Bulimia Nervosa

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

**A 20-year-old woman presents with fatigue; laboratory tests reveal a serum potassium level of 2.3 mmol per liter and a serum bicarbonate level of 36 mmol per liter. She is 163 cm (64 in.) tall and weighs 54 kg (119 lb). The findings on physical examination are normal. On questioning, she admits to binge eating and vomiting as frequently as five times per day. How should she be treated?**

## THE CLINICAL PROBLEM

Bulimia nervosa, a disorder characterized by binge eating and purging, generally begins during adolescence, with the peak period of onset around 18 years of age.<sup>1</sup> The lifetime prevalence is 3 percent,<sup>2</sup> and the ratio of female patients to male patients ranges from 10:1 to 20:1.<sup>3</sup> Most patients with bulimia have a coexisting psychiatric condition, such as an anxiety disorder or depression.<sup>4</sup> There is also an association with substance abuse and promiscuity.<sup>5</sup>

Almost half of patients with bulimia have residual features of the eating disorder after six years of follow-up.<sup>6</sup> Certain personality disorders (borderline, narcissistic, and antisocial disorders), impulsivity, and depression predict a worse prognosis.<sup>7</sup>

Bulimia nervosa is characterized by recurrent episodes of binge eating followed by inappropriate compensatory purging behavior to prevent weight gain (Table 1).<sup>8</sup> Although the formal criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV), require that both the binge eating and the compensatory behavior occur, on average, at least twice a week for a period of three months, there is wide variability in these types of behavior, and some patients purge 5 to 10 times or more per day. In contrast to anorexia nervosa, which is characterized by a weight that is less than 85 percent of the normal value, most persons with bulimia are of normal weight. The risk of death is much lower among patients with bulimia nervosa than among those with anorexia nervosa<sup>9</sup> but nevertheless appears to be greater than that among women of similar age in the general population.<sup>10</sup>

Bulimia is a disorder of uncertain cause; there is mounting evidence that genetic factors have an important role.<sup>11</sup> Disturbances in the serotonergic systems, which are implicated in the regulation of food intake, and cultural attitudes toward standards of physical attractiveness are also believed to contribute. Routine screening for bulimia is not currently the standard of care<sup>12</sup> but may be prudent in college-age populations.

There are three main modes of purging: self-induced vomiting, abuse of laxatives, and misuse of diuretics. Most patients with bulimia induce vomiting with a finger, but some use ipecac. As the illness progresses, many can vomit reflexively without mechanical stimulation. The laxatives abused are the stimulant type containing bisacodyl, cascara, or senna. Diuretic preparations and diet pills such as those containing ephedrine are less frequently used.<sup>13</sup> The medical complications of bulimia nervosa are related to the mode and frequency of purging, whereas in anorexia nervosa, they arise as a result of starvation (restricting) and weight loss.

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**Table 1. DSM-IV Criteria for Bulimia Nervosa.\***

Binge eating ( $\geq 2$ times/wk for 3 mo)
Purging or other compensatory weight-loss measures ( $\geq 2$ times/wk for 3 mo): regular self-induced vomiting or misuse of laxatives or diuretics in the purging type; other inappropriate compensatory behavior, such as fasting or excessive exercise, in the nonpurging type
Self-image unduly influenced by body weight or shape
Absence of anorexia nervosa

\* DSM-IV denotes *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition.

### MEDICAL COMPLICATIONS

#### Oral Complications

Pharyngeal soreness and loss of enamel on the lingual surface of the anterior teeth (perimyolysis) are thought to result from repeated exposure to acidic gastric contents in the vomitus. Dental caries may be more prevalent,<sup>14</sup> and dentists are in a good position to refer patients for treatment.<sup>15</sup> Another complication associated with excessive vomiting is sialadenosis, a painless swelling of the salivary glands that develops after an intense cycle of purging.

#### Gastrointestinal Complications

Frequent vomiting may lead to gastroesophageal reflux or Mallory–Weiss tears. Dyspepsia is common,<sup>16</sup> but esophageal motility is normal.<sup>17</sup> Some patients with bulimia ingest up to 50 laxative pills per day. Severe constipation with a laxative-dependence syndrome, due to damage to the myenteric plexus, may result from the abuse of stimulant laxatives.<sup>18</sup>

#### Electrolyte Complications

Recurrent purging can result in serious fluid and electrolyte disturbances (Table 2). The most severe

cases of metabolic alkalosis are almost always due to vomiting. Abuse of diuretics also causes hypochloremic metabolic alkalosis. Acute diarrhea associated with laxative use results in hyperchloremic metabolic acidosis.

Hypokalemia occurs in approximately 5 percent of bulimic patients<sup>19,20</sup> and may predispose them to cardiac arrhythmias. Given its low sensitivity, screening for hypokalemia cannot be recommended as a means of detecting bulimia. However, the finding of hypokalemia in an otherwise healthy young woman is highly specific for bulimia nervosa. Measurement of urinary potassium levels may be useful; a value of less than 10 mmol per liter in a “spot” urine specimen usually suggests a gastrointestinal cause of potassium loss. The patient with purely restricting anorexia nervosa is not at risk for any metabolic abnormality, acid–base disturbance, or hypokalemia.<sup>21</sup>

Pseudo-Bartter’s syndrome, defined as normotensive, hypokalemic alkalosis, is common among patients who vomit or use diuretics excessively.<sup>22</sup> Volume depletion induces hyperaldosteronism.<sup>23</sup> Troublesome edema in the legs, caused by persistently high levels of aldosterone, may occur in patients who purge excessively and then stop abruptly. Idiopathic edema, a condition characterized by irregular episodes of fluid retention in the absence of a recognizable cause, may also be a manifestation of bulimia in women who use diuretics to control cyclical fluid retention.<sup>24</sup>

#### Endocrine Complications

In contrast to patients with anorexia nervosa, patients with bulimia rarely have endocrine abnormalities. Generally, bone density is normal unless there is a history of anorexia nervosa, in which case, bone densitometry is warranted.<sup>25</sup> Although irregular

**Table 2. Electrolyte Levels Usually Associated with Purging.**

Method of Purging	Serum Levels					Urine Levels		
	Sodium	Potassium	Chloride	Bicarbonate	pH	Sodium	Potassium	Chloride
Vomiting	Increased, decreased, or normal	Decreased	Decreased	Increased	Increased	Decreased	Decreased	Decreased
Laxatives	Increased or normal	Decreased	Increased or decreased	Decreased or increased	Decreased or increased	Decreased	Decreased	Normal or decreased
Diuretics	Decreased or normal	Decreased	Decreased	Increased	Increased	Increased	Increased	Increased

menses, which affect fertility, are common during episodes of active bulimia, the future ability to conceive is not impaired in patients who recover from bulimia.<sup>26</sup> The majority of women with bulimia have improvement in symptoms during pregnancy, but an exacerbation of symptoms after delivery is common.<sup>27</sup>

The prevalence of bulimia nervosa may be increased among patients with type 1 diabetes; some patients deliberately avoid taking insulin in order to induce weight loss.<sup>28</sup> An earlier onset of microvascular complications has been reported among these patients.<sup>29</sup>

#### *Other Complications*

Repeated abuse of ipecac can cause serious, although usually reversible, toxic effects in the form of cardiomyopathy and muscle weakness.<sup>30</sup> Erosions covering the dorsum of the hands (Russell's sign) result from self-induced vomiting.

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### STRATEGIES AND EVIDENCE

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#### **TREATMENT OF MEDICAL COMPLICATIONS**

Most of the medical complications of bulimia nervosa are treatable. In the absence of clinical trials, suggested therapies for these complications are largely based on clinical experience.

Gentle brushing and use of a fluoride mouth rinse immediately after purging may prevent caries.<sup>31</sup> Sialadenosis responds to a combination of abstinence from vomiting, the application of heat, and sucking of tart candies. If the sialadenosis has not begun to recede after a few weeks, oral pilocarpine (5 mg three times per day) may decompress the glands.<sup>32</sup>

Reflux symptoms respond to proton-pump inhibitors. The prokinetic agent metoclopramide may occasionally be worth considering as a means of decreasing the frequency of vomiting; presumably, it acts on the central "emetic center" and by increasing the tone of the lower esophageal sphincter.

It is difficult to treat laxative dependence. Patients must be counseled about the ineffectiveness of stimulant laxatives for weight loss. The restoration of bowel function is the norm after laxative use has been discontinued, but it may take several weeks.<sup>33</sup> Ample hydration, a high-fiber diet, and moderate amounts of exercise should be encouraged, as long as the patient does not have a history of excessive exercise as a means of controlling weight. If constipation persists for more than a few days, a gly-

erin suppository or a nonstimulating osmotic laxative such as lactulose may be useful; stool softeners are of little value.<sup>34</sup> Leg edema caused by pseudo-Bartter's syndrome is treated with salt restriction (less than 3 g per day), elevation of the legs, and patience; loop diuretics will only exacerbate the problem. An aldosterone antagonist, such as spironolactone (25 to 50 mg per day), may be given for one to two weeks, at which point the symptoms will probably have resolved. Such treatment is particularly worth considering if the distress of having edema is thought likely to precipitate a relapse of bulimia.

Calcium (1200 to 1500 mg per day) with vitamin D (400 to 800 IU per day) should be recommended routinely, particularly in patients with a history of anorexia nervosa, among whom bone loss is likely. For these patients, treatment with an oral contraceptive is also reasonable, although it may not be sufficient to restore bone density.<sup>35</sup>

#### *Hypokalemia*

The treatment of marked hypokalemic metabolic alkalosis requires volume repletion (with intravenous normal saline), in order to turn off the renin-angiotensin system. Normalization of volume status is needed for effective potassium repletion. A general principle is that every decrease of 1 mmol per liter in the serum potassium level represents a loss of 150 mmol in the total body potassium level. Oral potassium chloride is generally preferred for potassium repletion. Typically, potassium is administered in a split dose of 40 to 80 mEq per day for a few days. The potassium level should initially be measured daily during replacement therapy, because the required amount cannot be calculated reliably.<sup>36</sup> Once euvolemia has been restored, if there is ongoing frequent purging, the electrolytes should be monitored; long-term potassium supplementation may be needed.

#### **PSYCHIATRIC TREATMENT**

##### *Psychotherapy*

The efficacy of cognitive-behavioral therapy in patients with bulimia nervosa has been convincingly demonstrated in randomized, controlled trials.<sup>37</sup> This therapy is designed to educate patients about other ways to cope with the feelings that precipitate a desire to purge and to try to correct maladaptive beliefs regarding body image (e.g., that physical appearance dictates one's value as a person). In a five-month study involving 220 patients who were randomly assigned to either individual cognitive-

behavioral therapy or interpersonal psychotherapy, 30 percent of the patients receiving cognitive-behavioral therapy were in remission (defined by a frequency of purging of less than twice per week) at the end of treatment, as compared with only 6 percent in the psychotherapy group.<sup>38</sup> This improvement has been corroborated in a four-month study of individual and group cognitive-behavioral therapy involving 60 bulimic patients; the rate of binge eating and purging behavior declined by 80 percent with either of these approaches.<sup>39</sup> A reduction in the frequency of purging of 70 percent or more by the sixth session of cognitive-behavioral therapy is predictive of a good longer-term response to this therapy.<sup>40</sup>

Although short-term studies of cognitive-behavioral therapy have demonstrated benefits, there are sparse data demonstrating that the benefits are maintained over the longer term. A recent study evaluated 101 women (80 percent of the original study cohort) long after they had participated in a placebo-controlled trial of cognitive-behavioral therapy, pharmacotherapy (imipramine), or both; at 10 years, women who had been treated with cognitive-behavioral therapy, imipramine, or both performed better than women in the placebo group on measures of social adjustment at work and in family activities.<sup>41</sup>

Rates of abstinence from binge eating and purging after cognitive-behavioral therapy are less impressive, averaging less than 40 percent.<sup>42</sup> Other forms of psychotherapy, such as interpersonal psychotherapy, which focuses on current interpersonal problems rather than the eating disorder, have also been used, but there is less evidence to support their use.

#### *Pharmacotherapy*

Irrespective of the presence or absence of associated depressive symptoms, various classes of antidepressants (tricyclics, selective serotonin-reuptake inhibitors, monoamine oxidase inhibitors, bupropion, and trazodone) have been demonstrated, in short-term (three-month), double-blind, placebo-controlled trials, to be effective in reducing the severity of symptoms of bulimia.<sup>43</sup> The available data suggest that each of these pharmacologic treatments may decrease the frequency of bulimic behavior by 50 to 60 percent within six to eight weeks. Fluoxetine is the only medication for bulimia nervosa that has been approved by the Food and Drug

Administration (FDA) to date. It received FDA approval on the basis of its demonstrated efficacy in two 8-week double-blind trials and in one 16-week double-blind trial. The latter was a multicenter study involving 400 outpatients that demonstrated significantly greater decreases in the number of weekly binge-purge episodes among patients treated with fluoxetine (60 mg per day) than among patients in the placebo group (a 50 percent reduction vs. a 21 percent reduction).<sup>44</sup> A study involving 387 women with bulimia who were randomly assigned to receive fluoxetine, at a dose of 20 mg per day or 60 mg per day, or placebo for eight weeks showed that the 60-mg dose was significantly more effective.<sup>45</sup> Side effects included tremor, insomnia, and nausea but were not dose-related, and the rate of discontinuation of study treatment because of an adverse event among women receiving the higher dose of fluoxetine was similar to the rate in the placebo group.

Like cognitive-behavioral therapy, pharmacotherapy alone results in complete suppression of binge eating and purging in only 30 to 40 percent of patients.<sup>46</sup> Approximately one third of patients who initially have improvement with medication will have a resurgence of their bulimic behavior; the risk of resurgence is highest during the first year after recovery.<sup>10</sup> A recent study demonstrated that fluoxetine treatment reduced the risk of a relapse of bulimia over a 52-week treatment period, as compared with placebo (19 percent vs. 37 percent).<sup>47</sup>

A combination of antidepressants and cognitive-behavioral therapy appears to be more effective in reducing the frequency of bingeing and purging than either treatment alone. A review using data from seven trials involving a total of 600 patients to assess the effect of antidepressants (desipramine, imipramine, or fluoxetine) plus cognitive-behavioral therapy as compared with the effect of one of these therapies alone reported average remission rates of 42 to 49 percent with a combination of therapies and average rates of 23 to 36 percent with any single therapy.<sup>48</sup> As a single therapy, cognitive-behavioral therapy was more effective than drug therapy. Patients in whom this therapy fails may have a response to an alternative therapy, but available data suggest that the response rate is relatively low in this situation. In a study of patients in whom cognitive-behavioral therapy had failed, the rate of response to interpersonal therapy was 16 percent, and the rate of response to pharmacotherapy (fluoxetine or desipramine) was 10 percent.<sup>49</sup>

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 AREAS OF UNCERTAINTY
 

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Most patients with bulimia nervosa may reasonably be treated as outpatients. Factors that suggest a need for hospitalization include severe depression, disabling symptoms, purging that is rapidly worsening and has proved refractory to outpatient treatment, severe hypokalemia (plasma potassium level, <2.0 to 3.0 mmol per liter), and major orthostatic changes in blood pressure (>30 mm Hg) and pulse (>30 beats per minute). Data are lacking on how these factors affect the ultimate outcome.<sup>50</sup> Although some experts advocate hospitalization for any patient with a potassium level below 3.0 mmol per liter, in practice it is not uncommon for patients with lower potassium levels to be cared for on an outpatient basis.

Most studies of cognitive-behavioral therapy and medication have not included adolescent subjects (those younger than 18 years of age); thus, it is uncertain what the preferred therapy for such patients is. Other medications that are not discussed above may be effective in treating bulimia. Limited data from three short-term clinical trials, only one of which was randomized, double-blind, and placebo-controlled, suggest that the antiemetic agent ondansetron may be effective in patients with bulimia nervosa.<sup>51</sup> Anecdotal data indicate that the novel anticonvulsant agent topiramate may also be effective.<sup>52</sup> However, more data are needed.

The effects of dietary counseling on the development and course of bulimia have not been well studied. It is also uncertain which patients can be effectively treated by a generalist rather than a psychiatrist; the involvement of both is generally recommended. It remains unknown whether bulimia may be prevented by programs that teach assertiveness to young girls and help them to be critical of media claims promoting the value of thinness.

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 GUIDELINES
 

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The American Psychiatric Association has issued comprehensive guidelines for the management of bulimia ([http://www.psych.org/clin\\_res/guide.bk42301.cfm](http://www.psych.org/clin_res/guide.bk42301.cfm)).<sup>53</sup> These offer guidance regarding the site of treatment (whether it occurs in the hospital, is partially accomplished during hospitalization, is provided on an intensive outpatient basis, or is office-based) and the type of treatment, including cognitive-behavioral therapy and medications. Al-

though definitive data are lacking, the American Dietetic Association has published a position paper regarding nutritional counseling for patients with bulimia nervosa,<sup>54</sup> which recommends the involvement of a dietitian in order to develop a plan for normalizing eating patterns, minimizing restrictions on the types of food consumed, and correcting misconceptions about dieting.

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 CONCLUSIONS
 

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Bulimia nervosa should be considered in patients with unexplained hypokalemia and metabolic alkalosis and is particularly common in late adolescence. The primary objectives of treatment are to interrupt the binge-purge cycles with the use of pharmacotherapy, cognitive-behavioral therapy, or both and to treat associated medical complications. All patients should be educated about the medical complications of bulimia and about the benefits of restoring a regular pattern of eating.

On the basis of the degree of hypokalemia in the woman described in the vignette, I would recommend a short stay in the hospital to restore a normal volume status with intravenous saline at 75 ml per hour and would aim to replenish her potassium orally by providing 60 to 80 mEq per day in a split dose, with daily monitoring of electrolytes until the levels returned to normal. Subsequently, the electrolyte levels should be monitored intermittently; although there are no clear guidelines, I would do so at least every few months initially to screen for evidence of surreptitious purging and to rule out potentially dangerous potassium levels.

With the goal of reducing the frequency of bingeing and purging, if not completely eliminating this behavior, I would refer the patient for cognitive-behavioral therapy with a mental health specialist who had expertise in eating disorders, and I would also treat her with medication. Fluoxetine would be my first choice, because of its proven efficacy and tolerability. Given data showing the superiority of a 60-mg dose over a 20-mg dose, I would aim to increase the dose to 60 mg over the course of several days. Although data on the effects of nutritional counseling are lacking, seeing a dietitian may also be helpful for some patients, particularly those who have extensive lists of "forbidden" foods or whose bulimia has been active for years.

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