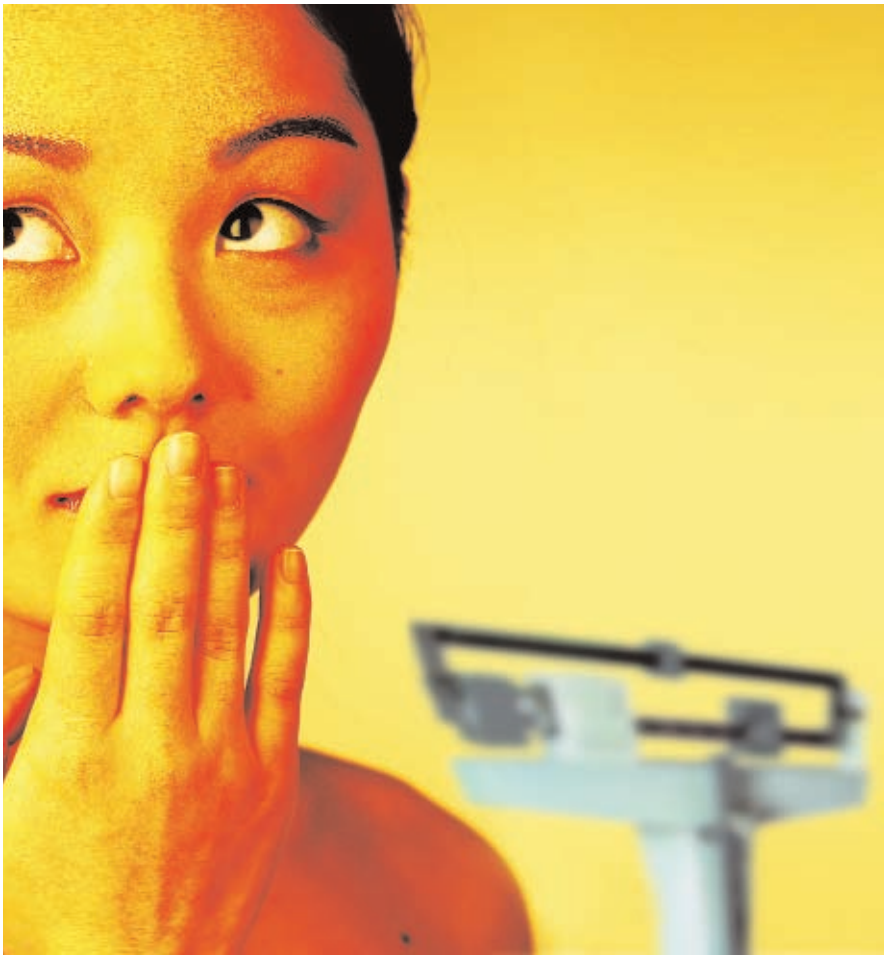
by KIRANMAI GORLA, MD, MAJU MATHEWS, MD

Dr. Gorla is Resident in Pediatrics, Metrohealth, Cleveland, Ohio; Dr. Mathews is Assistant Professor of Psychiatry, Drexel University College of Medicine, Philadelphia, Pennsylvania.

# Pharmacological Treatment of Eating Disorders

## INTRODUCTION

Eating disorders continue to be one of the most important disorders affecting a significant proportion of adolescents and young adults. The prevalence of eating disorders, especially binge eating disorders, is on the rise and has caused significant problems because of the associated comorbidities. According to the 2001 Youth Risk Behavior Survey, 35 percent of the adolescent girls thought they were overweight and as many as 62 percent of them were attempting to lose weight.[1] Eating disorder patients present not only to primary care physicians and psychiatrists, but are also commonly seen in pediatric outpatient clinics and gastroenterology clinics. These patients are a challenge, both diagnostically and from a management point of view. Although much is written about the importance of therapy in eating disorder patients, there is little, if any, literature on the pharmacological management of eating disorders. Psychotherapy continues to be the mainstay of



ADDRESS CORRESPONDENCE TO:
Maju Mathews, MD, Department of Psychiatry, 8th Floor, 1427 Vine Street, Philadelphia, PA 19102
Phone: (215) 762-6660; E-mail: maju_mathews@yahoo.com

**DIAGNOSTIC CRITERIA OF ANOREXIA NERVOSA**

1. **Refusal to maintain weight within a normal range for height and age (more than 15 percent below ideal body weight)**
2. **Fear of weight gain**
3. **Severe body image disturbance in which body image is the predominant measure of self worth with denial of the seriousness of the illness**
4. **In post-menarchal females, absence of the menstrual cycle, or amenorrhea (greater than three cycles)**

**DIAGNOSTIC CRITERIA OF BULIMIA NERVOSA**

1. **Episodes of binge eating with a sense of loss of control**
2. **Binge eating followed by compensatory behavior of the purging type (self-induced vomiting, laxative abuse, diuretic abuse) or non-purging type (excessive exercise, fasting, or strict diets)**
3. **Binges and the resulting compensatory behavior occuring for a minimum of two times per week for three months**
4. **Dissatisfaction with body shape and weight**

treatment, but unfortunately, the lack of trained therapists and unwillingness of many of these patients to see a therapist puts a huge burden on the primary care physicians and pediatricians to treat these patients to the best of their abilities. Here we have attempted to present an overview of the pharmacological management of eating disorders. This article is intended for psychiatrists whose main goal in cases like these is to initiate appropriate pharmacological treatment to address emergent conditions and to refer the patient to an appropriate facility to address the needed psychotherapy. It is beyond the scope of this article to discuss psychological treatments.

## EATING DISORDERS

According to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), eating disorders are classified into anorexia nervosa, bulimia nervosa, and a catch-all category eating disorder termed *not otherwise specified* (NOS). Binge eating disorder is a category currently used only for research purpose.

**Diagnostic criteria.**

*Anorexia nervosa.* According to DSM-IV, the diagnosis of anorexia nervosa requires four of the following criteria:

1. Refusal to maintain weight within a normal range for height and age (more than 15 percent below ideal body weight)
2. Fear of weight gain
3. Severe body image disturbance in which body image is the predominant measure of self-worth with denial of the seriousness of the illness
4. In post-menarchal females, absence of the menstrual cycle, or amenorrhea (greater than three cycles).

Adolescents with anorexia nervosa may drop 15 percent below ideal body weight without losing weight if they do not gain appropriate amounts during their pubertal growth spurts.

There are two subtypes of anorexia nervosa: restricting and binge eating/purging type. Patients with the restricting subtype use only restriction of intake to reduce their weight, while those with the binge/purge subtype may either binge or use purging (e.g., vomiting, laxatives, diuretics) to control their weight. Thus, a patient with anorexia may induce vomiting, yet can still be considered anorexic (rather than bulimic) if he or she is 15 percent below ideal body weight and meets the other physiologic and psychologic criteria.

*Bulimia nervosa.* According to DSM IV, the diagnosis of bulimia nervosa requires four of the following criteria:

1. Episodes of binge eating with a sense of loss of control
2. Binge eating followed by compensatory behavior of the purging type (self-induced vomiting, laxative abuse, diuretic abuse) or non-purging type (excessive exercise, fasting, or strict diets)
3. Binges and the resulting compensatory behavior occuring for a minimum of two times per week for three months
4. Dissatisfaction with body shape and weight.

Also, the disturbance should not occur exclusively during episodes of anorexia nervosa.

*Eating disorder not otherwise specified (ED-NOS).* This category includes all patients with disordered eating patterns and weight management problems who do not meet the criteria for anorexia nervosa or bulimia nervosa.

*Binge eating disorder (BED).* Currently, this is used only for research purposes. According to the research criteria, BED involves binge eating (eating, in a distinct period of time, an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances) two days per week for a six-month duration or longer. The binge eating is associated with a lack of control over the eating and with distress over the binge eating. The binges associated with BED must have at least three of the following five criteria:

1. Eating much more rapidly than normal
2. Eating until uncomfortably full

3. Eating large amounts of food when not feeling physically hungry
4. Eating alone because of embarrassment
5. Feeling disgusted, depressed, or very guilty after overeating.

**Epidemiology.** Eating disorders in general are more common in female patients than in male patients. According to a study published in 2004[3] that reviewed most of available literature, the prevalence rates in Western countries for anorexia nervosa range from 0.1 to 5.7 percent in female subjects. Prevalence rates for bulimia nervosa range from 0 to 2.1 percent in male subjects and from 0.3 to 7.3 percent in female subjects in Western countries. Prevalence rates in non-Western countries for bulimia nervosa range from 0.46 to 3.2 percent in female subjects. However, eating disorders are becoming more common even in developing countries and minority populations living in western countries.[5] While most studies report an increased prevalence of anorexia nervosa and bulimia nervosa over the past 50 years, some of the studies done recently have shown the opposite.[4] But it is widely agreed that more eating disorder patients are currently seen in practices than before.

**Etiology.** *Biological factors.* Evidence for the role of genetic factors is supported by the fact that first-degree relatives of patients suffering from eating disorders are at 10-fold increased risk of developing an eating disorder.[6] There is emerging evidence for the role of neurotransmitters, especially serotonin imbalance, in anorexia nervosa.[7]

*Psychological factors.* Higher rates of obsessive-compulsive personality traits, sense of lack of control, and impulsivity are noted in patients with eating disorders. Higher rates of sexual abuse were reported in women with bulimia nervosa, compared to general population.[8]

*Social factors.* The idealization and normalization of underweight females may contribute to the increasing prevalence of eating disorders.

## TREATMENT

The general principles of treatment of eating disorders are to take an interdisciplinary approach. Ideally, the treatment team should include a medical doctor, a psychiatrist, a dietitian, and a therapist. Education and involvement of the family and other support network is crucial. Consistency in the treatment plan and rewarding behavior changes has also shown to be effective. Cognitive behavioral therapy, interpersonal therapy and family therapy have all been tried and are found to be effective. However, cognitive behavior therapy has the most evidence available.[1,2]

Here, we will try to review mainly the evidence for pharmacotherapy in the treatment of eating disorders.

**Anorexia nervosa.** Despite initial promise, none of the medicines available have been shown to be very effective on their own in the treatment of anorexia nervosa. The APA guidelines state that psychotropic medications should not be used as the sole or primary treatment for anorexia nervosa, but they can be considered for the prevention of relapse in weight restored patients or to treat depression or obsessive compulsive disorder.[5]

There have been few controlled trials, and most have demonstrated efficacy only for treating comorbid disorders such as depression and obsessive compulsive disorder.[16] There is limited evidence that antidepressants may help maintain weight

### GUIDELINES FOR HOSPITALIZATION FOR EATING DISORDERS

1. Severe malnutrition (weight less than 75 percent of average body weight for age, sex, and height)
2. Dehydration
3. Electrolyte disturbances (hypokalemia, hyponatremia, hypophosphatemia)
4. Cardiac dysrhythmia
5. Physiologic instability (severe bradycardia [heart rate less than 50 beats per minute during the day or less than 45 at night], hypotension [less than 80/50 mmHg], hypothermia [less than 96° F], orthostatic changes in pulse [more than 20 beats per minute] or blood pressure [more than 10 mmHg])
6. Arrested growth and development
7. Failure of outpatient treatment
8. Acute food refusal
9. Uncontrollable binging and purging
10. Acute medical complication of malnutrition (e.g., syncope, seizures, cardiac failure, pancreatitis, etc.)
11. Acute psychiatric emergencies (e.g., suicidal ideation, acute psychosis)
12. Comorbid diagnosis that interferes with the treatment of eating disorders (e.g., severe depression, obsessive compulsive disorder, severe family dysfunction).

## ANOREXIA NERVOSA

- **Antidepressants may help maintain weight gain in successfully treated patients.**
- **Anxiolytic medications may be helpful before meals for anorexic patients who have anxiety before eating.**
- **Olanzapine may stimulate appetite and weight gain.**

gain in successfully treated patients.[17] Anxiolytic medications may be helpful before meals for the anorexic patient who is having anxiety before eating. Several reports have been published in which olanzapine (Zyprexa®, Eli Lilly) was successfully used in patients with severe anorexia nervosa for stimulating appetite and weight gain.

**Bulimia nervosa.** Bulimia nervosa has more evidence for the use of medications. A number of studies have confirmed the efficacy of various medications.

*Fluoxetine.* The evidence for the use of fluoxetine (Prozac®, Eli Lilly) in the treatment of bulimia nervosa comes in the form of various case reports, systematic studies, and double-blind, randomized placebo controlled trials. In a double-blind, placebo-controlled study by Halmi, et al., 382 patients were randomly assigned to receive fluoxetine or placebo at a dose of 20mg or 60mg daily for eight weeks.[9,10] Treatment with the lower dose of fluoxetine resulted in reductions in binge eating and vomiting compared with placebo (45 vs. 33% and 29 vs. 5%, respectively). Those receiving 60mg of fluoxetine had even greater improvement with a 67-percent reduction in binge eating and a 56-percent reduction in vomiting.

*Other classes of drugs.* Tricyclic antidepressants, such as desipramine (Norpramin®, Aventis), imipramine (Tofranil®, Ciba Geigy), and amitriptyline (Elavil®, Merck & Co.) are also found to be effective.[11–14] Monoamine oxidase inhibitors were also found to be more effective than placebo in decreasing the binging and vomiting in patients with bulimia nervosa. Similarly, buspirone (Buspar®, Bristol Myers Squibb) was also effective in decreasing binging and vomiting in patients with bulimia nervosa. However, studies with lithium did not find it to be effective in the treatment of bulimia nervosa.[15,16]

The anticonvulsant topiramate (Topomax®, Ortho-McNeil Pharmaceutical) administered at a dose of 25 to 600mg daily in a randomized study of 61outpatients (53 women, 8 men) with binge eating disorder (not bulimia nervosa) significantly reduced binge frequency and weight compared with placebo (94 vs. 46% reduction, 5.9kg versus 1.2kg weight loss, respectively). However, a large percentage of patients in both the topiramate and placebo groups did not complete the full 14 weeks of treatment.[17]

Ondansetron (Zofran®, GlaxoSmithKline) (24mg/day), an anti-emetic medication, is also reported to reduce binge eating and self-induced vomiting in a small placebo-controlled study of 29 patients with bulimia nervosa.[18]

**Binge eating disorders.** Various classes of drugs have been found to be effective in the treatment of binge eating disorders. These include SSRIs,[19]

## BULIMIA NERVOSA

**The following drugs and drug classes may help to decrease binge eating and purging episodes:**

- **Fluoxetine**
- **Tricyclic antidepressants**
- **Monoamine oxidase inhibitors**
- **Buspirone**
- **Topiramate**
- **Ondansetron**

antiepileptics,[17] and appetite suppressants.[20] Of all these medications, topiramate is most promising.

**Hospitalization for eating disorders.** The Society for Adolescent Medicine has published guidelines for hospitalization. According to their guidelines, one or more of the following criteria justify hospitalization:[21]

1. Severe malnutrition (weight less than 75 percent of average body weight for age, sex, and height)
2. Dehydration
3. Electrolyte disturbances (hypokalemia, hyponatremia, hypophosphatemia)
4. Cardiac dysrhythmia
5. Physiologic instability (severe bradycardia [heart rate less than 50 beats per minute during the day or less than 45 at night], hypotension [less than 80/50mmHg], hypothermia [less than 96° F], orthostatic changes in pulse [more than 20 beats per minute] or blood pressure [more than 10 mmHg])
6. Arrested growth and development
7. Failure of outpatient treatment
8. Acute food refusal
9. Uncontrollable binging and purging
10. Acute medical complication of malnutrition (e.g., syncope, seizures, cardiac failure, pancreatitis, etc.)
11. Acute psychiatric emergencies (e.g., suicidal ideation, acute psychosis)
12. Comorbid diagnosis that interferes with the treatment of eating disorders (e.g., severe depression, obsessive compulsive disorder, severe family dysfunction).

The guidelines published by the APA are similar but emphasize psychiatric and behavioral factors along with medical factors.[22]

**KEY POINTS**

- **The prevalence of eating disorders is high.**
- **More of these patients are seen in the outpatient clinics of psychiatrists, pediatricians, and primary care physicians.**
- **Frontline physicians should be aware of the manifestations of eating disorders and their management.**
- **Limitations of pharmacotherapy or psychotherapy, when used on their own should be realized.**
- **Patients with eating disorders generally should be cared for by a multidisciplinary team consisting of a medical doctor, psychiatrist, therapist, and a dietitian.**
- **Patients with anorexia nervosa benefit mainly from psychotherapy, and medications should only be used as adjunctive treatment.**
- **Patients with bulimia nervosa and binge eating disorder benefit significantly from pharmacotherapy.**
- **Some eating disorder patients require hospitalization.**
- **If left untreated, the morbidity and mortality rates associated with eating disorders are high.**

The choice between medical or psychiatric hospitalization is based on resources available, medical condition, and age of the patient. Whether it is a psychiatric unit or a medical unit, the hospital unit must have experience in treating this special population and should have guidelines and protocols in place. A caring and experienced team comprising a medical doctor, a psychiatrist, nurses, a dietitian, and a therapist are very important for any successful treatment of eating disorder patients. The patient should remain in the hospital until his or her physical condition stabilizes, mental status improves, and a care plan is in place. Unfortunately, the managed care health system does not always allow this. One study looked into the outcomes after hospitalization and found that those eating disordered patients who remained in the hospital until they had regained adequate weight (90–92% of ideal body weight) had a better outcome compared with those who did not regain adequate weight.[23] These findings support the argument for adequate length of stay in the hospital for the successful treatment of eating disorders.

## PROGNOSIS

Although numerous studies have been performed regarding the outcome of eating disorders, many of these studies had a very high dropout rate, and therefore the data available is debatable. A systematic review by Steinhausen of all the published studies done on anorexia nervosa found that about 50 percent of patients have good outcomes, 25 percent have intermediate outcomes, and 25 percent have poor outcomes.[24]

**Mortality.** Anorexia nervosa is a fatal illness. It is associated

with significant mortality if early intervention is not done. A meta-analysis performed by Sullivan found that the overall mortality rate was as high as 0.56 per year. Women with anorexia nervosa have a 10-fold increase in mortality compared to women who were unaffected. Causes of death include complications of the eating disorder, suicide, and other causes.

## SUMMARY

- The prevalence of eating disorders is high.
- More of these patients are seen in the outpatient clinics of psychiatrists, pediatricians, and primary care physicians.
- Frontline physicians should be aware of the manifestations of eating disorders and their management.
- Limitations of pharmacotherapy or psychotherapy, when used on their own should be realized.
- Patients with eating disorders generally should be cared for by a multidisciplinary team consisting of a medical doctor, psychiatrist, therapist, and a dietitian.
- Patients with anorexia nervosa benefit mainly from psychotherapy, and medications should only be used as adjunctive treatment.
- Patients with bulimia nervosa and binge eating disorder benefit significantly from pharmacotherapy.
- Some eating disorder patients require hospitalization.
- If left untreated, the morbidity and mortality rates associated with eating disordersr are high.

## REFERENCES


1. Grunbaum JA, Kann L, Kinchen SA, et al. Youth risk behavior surveillance—United States, 2001. *J School Health* 2002;72(8):313–28.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Arlington, VA: American Psychiatric Publishing Inc., 1994.
3. Makino M, Tsuboi K, Dennerstein L. Prevalence of eating disorders: A comparison of Western and non-Western countries. *Med Gen Med* 2004;6(3):49.
4. Heatherton TF, Nichols P, Mahamedi F, Keel P. Body weight, dieting, and eating disorder symptoms among college students, 1982 to 1992. *Am J Psychiatry* 1995;152(11):1623–9.
5. American Psychiatric Association. Practice guidelines for eating disorders. *Am J Psychiatry* 1993;150:212.
6. Woodside DB. A review of anorexia and bulimia nervosa. *Curr Probl Pediatr* 1995;25:67.
7. Kaye WH, Gwirtsman HE, George DT, Ebert MH. Altered serotonin activity in anorexia nervosa after long-term weight restoration. Does elevated cerebrospinal fluid 5-HIAA levels correlate with rigid and obsessive behavior? *Arch Gen Psychiatry* 1991;48:556.
8. Kendler KS, MacLean C, Neale M, et al. The genetic epidemiology of bulimia nervosa. *Am J Psychiatry* 1991;148(12):1627–37.
9. Fluoxetine Bulimia Nervosa Collaborative Study Group. Fluoxetine in the treatment of bulimia nervosa. A multicenter, placebo-controlled, double-blind trial. *Arch Gen Psychiatry* 1992;49:139.
10. Kaye WH, Weltzin TE, Hsu LK, et al. An open trial of fluoxetine in patients with anorexia nervosa. *J Clin Psychiatry* 1991;52:464.
11. Bacaltchuk J, Hay P. Antidepressants versus placebo for people with bulimia nervosa. *Cochrane Database Syst Rev* 2003;(4):CD003391.
12. Hughes PL, Wells LA, Cunningham CJ, Ilstrup DM. Treating bulimia with desipramine: A double-blind, placebo-controlled study. *Arch Gen Psychiatry* 1986;43:182.
13. Pope HG Jr, Hudson JI, Jonas JM, Yurgelun-Todd D. Bulimia treated with imipramine: A placebo-controlled, double-blind study. *Am J Psychiatry* 1983;140:554.
14. Mitchell JE, Groat R. A placebo-controlled, double-blind trial of amitriptyline in bulimia. *J Clin Psychopharmacol* 1984;4:186.
15. Horne RL, Ferguson JM, Pope HG Jr, et al. Treatment of bulimia with bupropion: A multicenter controlled trial. *J Clin Psychiatry* 1988;49:262.
16. Hsu LK, Clement L, Santhouse R, Ju ES. Treatment of bulimia nervosa with lithium carbonate. A controlled study. *J Nerv Ment Dis* 1991;179:351.
17. McElroy SL, Arnold LM, Shapira NA, et al. Topiramate in the treatment of binge eating disorder associated with obesity: A randomized, placebo-controlled trial. *Am J Psychiatry* 2003;160:255.
18. Faris PL, Kim SW, Meller WH, et al. Effect of decreasing afferent vagal activity with ondansetron on symptoms of bulimia nervosa: A randomized, double-blind trial. *Lancet* 2000;355:792.
19. Arnold LM, McElroy SL, Hudson JI, et al. A placebo-controlled, randomized trial of fluoxetine in the treatment of binge-eating disorder. *J Clin Psychiatry* 2002; 63:1028.
20. Appolinario JC, Bacaltchuk J, Sichieri R, et al. A randomized, double-blind, placebo-controlled study of sibutramine in the treatment of binge eating disorder. *Arch Gen Psychiatry* 2003;60:1109.
21. Golden, NH, Katzman, DK, Kreipe, RE, et al. Eating disorders in adolescents: Position paper of the Society for Adolescent Medicine. *J Adolesc Health* 2003;33:496.
22. American Psychiatric Association. Practice guidelines for the treatment of patients with eating disorders. *Am J Psychiatry* 2000;157 Suppl 1:1.
23. Baran, SA, Weltzin, TE, Kaye, WH. Low discharge weight and outcome in anorexia nervosa. *Am J Psychiatry* 1995; 152:1070.
24. Steinhausen, HC. The outcome of anorexia nervosa in the 20th century. *Am J Psychiatry* 2002; 159:1284-49.
25. Sullivan, PF. Mortality in anorexia nervosa. *Am J Psychiatry* 1995; 152:1073.