Impact of Anorexia, Bulimia and Obesity on the Gynecologic Health of Adolescents

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Dieting behaviors and nutrition can have an enormous impact on the gynecologic health of adolescents. Teenaged patients with anorexia nervosa can have hypothalamic suppression and amenorrhea. In addition, these adolescents are at high risk of osteoporosis and fractures. Unfortunately, data suggest that estrogen replacement, even in combination with nutritional supplementation, does not appear to correct the loss of bone density in these patients. Approximately one half of adolescents with bulimia nervosa also have hypothalamic dysfunction and oligomenorrhea or irregular menses. Generally, these abnormalities do not impact bone density and can be regulated with interval dosing of progesterone or regular use of oral contraceptives. In contrast, the obese adolescent with menstrual irregularity frequently has anovulation and hyperandrogenism, commonly referred to as polycystic ovary syndrome. Insulin resistance is thought to play a role in the pathophysiology of this condition. While current management usually involves oral contraceptives, future treatment may include insulin-lowering medications, such as metformin, to improve symptoms. Because all of these patients are potentially sexually active, discussion about contraception is important. (Am Fam Physician 2001;64:445-50.)

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Adolescence is a time of tremendous growth and development, in which nutrition plays a key role. The adolescent growth spurt accounts for approximately 25 percent of adult height and 50 percent of adult weight.[1] Moreover, girls develop reproductive capacity during this time. Adolescents with disordered eating behaviors, such as anorexia nervosa, bulimia nervosa or obesity, frequently have menstrual abnormalities that reflect their abnormal nutritional intake. In this article, we will address these three common adolescent conditions and describe the pathophysiology and management of the abnormal menstrual patterns that accompany each.

Anorexia Nervosa

Once described by Hilde Bruch as the "relentless pursuit of thinness,"[2] anorexia is a disorder that plagues approximately 0.5 to 1.0 percent of adolescents.[3] The diagnostic criteria have evolved to those described in the *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed., and are summarized in *Table 1*.[4] The intense fear of weight gain and the lack of self-esteem cannot be overstated and are factors that make this condition so painful for the young patient with anorexia. In addition, certain personality traits such as being perfectionistic, obsessive-compulsive, socially withdrawn, high-achieving (but rarely satisfied) and depressed are often noted in these patients. The patient with anorexia may exclusively restrict dietary intake (restrictive subtype) or may experience episodes of bingeing and purging (bulimic subtype).[4]

While the female adolescent with anorexia frequently experiences symptoms such as weakness, dizziness or fatigue, she often seeks help (or is brought for medical attention by a distressed parent) because her weight loss has resulted in amenorrhea. The precise mechanism of amenorrhea in the patient with anorexia is not known. However, the severe caloric restriction suppresses the hypothalamic-pituitary axis.[5] Biochemical mediators that have been implicated in this process include cortisol, leptin, growth hormone and insulin-like growth factor I[6–9]; all of these mediators play a role. The result is a dramatic suppression of the pituitary production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Without normal cycling of LH and FSH, the circulating level of estrogen is very low

TABLE 1
Diagnostic Criteria for Anorexia Nervosa

A. Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected).

B. Intense fear of gaining weight or becoming fat, even though underweight.

C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight.

D. In postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles. (A woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration.)

Specify type:

Restricting type: during the current episode of anorexia nervosa, the person has not regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics or enemas)

Binge-eating/purging type: during the current episode of anorexia nervosa, the person has regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics or enemas)

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and ovulation will not occur. Fertility is therefore compromised in these patients.

The patient with anorexia also is at high risk of developing osteopenia and frank osteoporosis.[10] Although the pathophysiology of osteoporosis is not well understood, it is known that adolescence is a critical time of bone mineralization. Estrogen appears to play a major role,[11] although nutritional factors are also crucial.[12] One study[13] compared patients who had anorexia with those who had hypothalamic amenorrhea from other etiologies and found that those with anorexia had more profound osteopenia, supporting the theory that nutrition also plays an important role. Normalization of the patient's weight appears to be the single most important factor in regaining bone density.[14] Even when this is achieved, bone may not remineralize to normal levels.

The key goals of managing patients with anorexia are overall improvement of body weight and normalization of eating patterns. For example, while oral contraceptives have successfully restored menses in such patients in clinical trials, they do not appear to substantially mitigate the osteoporosis. One study[15] that examined women with amenorrhea from various causes suggested that prolonged treatment with oral contraceptives and calcium supplementation (duration of more than 12 months) may have a beneficial effect, but other studies[16] do not support this finding.

In the adolescent with anorexia nervosa, normalization of body weight is the single most important factor in regaining bone density.

A recent, small study[17] found that the use of oral dehydroepiandrosterone had a favorable effect on bone turnover in young women with anorexia; however, additional studies are necessary. Because some physicians use the return of menses to demonstrate regained health in the patient, they may not want to mask this outcome with the use of oral contraceptives. Therefore, evidence to date does not support the routine use of oral contraceptives in the management of patients with anorexia, but newer modalities may be on the horizon.

Osteoporosis is of concern not only later in life when the patient becomes postmenopausal but also during the adolescent years. The patient with anorexia characteristically exercises frequently and strenuously, and may be prone to stress fractures even after a short duration of the disorder. These patients must be informed about the risk of osteoporosis and fractures, and must be assessed with a bone mineral density study to ascertain their individual risk of pathologic fractures. In the female athlete, this is a particular concern. Eating disorders in these athletes are prevalent, and the triad of a menstrual disorder, an eating disorder and osteoporosis, or the "female athlete triad,"[18] makes these patients quite vulnerable to fractures.

Bulimia Nervosa

Just as the diagnostic criteria for anorexia have been redefined over the years, so too have the criteria for bulimia. The current diagnostic criteria are detailed in *Table 2*.[4] Whereas the prominent features of anorexia are the caloric restriction and resulting underweight, the

prominent elements of bulimia are episodes of binge eating (large amounts of food with a lack of control) and the compensatory behaviors that follow, in a patient who is either normal weight or overweight. The compensatory behaviors include self-induced vomiting, abuse of laxatives and diuretics, over-exercise, caloric restriction and abuse of diet pills. Usually the patient suffers painful remorse after the behaviors but is unable to control the impulse to repeat them. The young woman with bulimia characteristically has low self-esteem, is depressed and/or anxious, and has poor impulse control. She typically engages in other risky behaviors, such as substance abuse, unprotected sexual activity, self-mutilation and suicide attempts.

While amenorrhea is a diagnostic criterion for anorexia, menstrual irregularity occurs in only about one half of patients with bulimia, probably because these women rarely achieve underweight when irregularity occurs. The mechanism appears to be related to hypothalamic-pituitary function. One study[19] that examined body weight as a predictive factor of abnormal menstruation in patients with bulimia concluded that when current weight was less than 85 percent of a patient's past high weight, abnormal 24-hour secretion of LH is likely. This study followed another study[20] that suggested decreased pulsatile LH secretion as a factor. Another very small study[21] showed elevated levels of free testosterone in patients with bulimia.

The oligomenorrhea in patients with bulimia does not, however, appear to impact their bone mineral density. According to one study[22] that compared patients with anorexia, patients with bulimia and matched control patients, bone mineral density in those patients with bulimia was similar to that in the control patients. Interestingly, this study also showed that weight-bearing exercise had a protective effect in patients with bulimia that did not occur in those with anorexia. Therefore, osteoporosis may not be a concern in patients with bulimia, particularly those who exercise regularly.

TABLE 2
Diagnostic Criteria for Bulimia Nervosa

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   (1) eating, in a discrete period of time (e.g., within any two-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances
   (2) a sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)

B. Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, enemas or other medications; fasting; or excessive exercise.

C. Binge eating and inappropriate compensatory behaviors both occur, on average, at least twice a week for three months.

D. Self-evaluation is unduly influenced by body shape and weight.

E. Disturbance does not occur exclusively during episodes of anorexia nervosa.

Specify type:

Purging type: during the current episode of bulimia nervosa, the person has regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics or enemas

Nonpurging type: during the current episode of bulimia nervosa, the person has used other inappropriate compensatory behaviors, such as fasting or excessive exercise, but has not regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics or enemas

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If menstrual irregularity occurs in the adolescent with bulimia, a limited evaluation is necessary. After completing a careful history and physical examination, the laboratory work-up depends on the particular pattern seen. If significant oligomenorrhea is reported, it may be helpful to obtain the patient's levels of LH and FSH, thyroid-stimulating hormone, prolactin, and total and free testosterone. If androgenization is present, obtaining a dehydroepiandrosterone sulfate level will help to evaluate adrenal function. If a patient has not menstruated in three months or more, a progesterone challenge test (administration of medroxyprogesterone acetate [Provera] in a dosage of 10 mg daily for seven days) would be indicated. A withdrawal bleed two to seven days after treatment indicates sufficient levels of estrogen. In a chronically anovulatory teenaged patient who is not underweight and who has an elevated androgen level and positive results on the progesterone challenge test, one must assume that the patient has chronically circulating unopposed estrogen. In this

A few small studies have demonstrated that metformin (Glucophage) improves menstrual function and hyperandrogenism in patients with polycystic ovary syndrome.

situation, it is necessary to induce a withdrawal bleed at least every three months to reduce the risk of endometrial cancer later in life. This is done by repeating progesterone administration every three months or by cycling with combined oral contraceptive pills.

Obesity

Obesity is a rapidly increasing, preventable cause of morbidity and mortality in the United States. Unfortunately, it frequently begins long before adulthood. Current estimates of the prevalence of obesity in youth as measured by the third National Health and Nutrition Examination Survey range from 11 to 24 percent.[23] Estimates vary because measurement techniques, instruments and the actual definitions of overweight and obesity frequently differ from study to study. The importance of defining obesity and overweight is to determine when an adolescent is at risk of negative health consequences related to their weight. For example, while some researchers rely on the body mass index (BMI = weight in kilograms divided by height in meters squared),[24] others use fat distribution, or waist-to-hip ratio.[25-27]

One large, prospective study[28] demonstrated a direct correlation between increasing BMI (i.e., higher than 25) and increasing risk of premature death. If approximately one third of obese adolescents are predicted to be obese as adults,[29] one may assume that the prevention or treatment of obesity can have a major impact on the future health of these patients.

Obesity may or may not impact the gynecologic health of an adolescent female. The effects of obesity are mediated primarily through hormonal changes. Insulin resistance is a well-established consequence of obesity.[30,31] When it occurs, it can become so profound that it lowers glucose tolerance and precipitates type 2 diabetes mellitus (formerly known as non–insulin-dependent diabetes mellitus), even during adolescence.

Insulin resistance also increases circulating levels of insulin, which elevate androgen production. A number of mechanisms for this have been found, including the lowering of sex-hormone–binding globulin, increased androgen production by direct stimulation or indirectly by the production of insulin-like growth factor I. The relationship between insulin and androgens is thought to be the underlying trigger of polycystic ovary syndrome (PCOS), which is also known as functional ovarian hyperandrogenism.[32] PCOS is a frequent cause of menstrual dysfunction in the adolescent.

PCOS is defined by elevated androgen associated with anovulation, which manifests clinically as oligomenorrhea and/or dysfunctional uterine bleeding. While it usually occurs in obese patients, it also may occur in patients with a normal weight. Hyperandrogenism can also lead to other undesirable effects such as hirsutism, acne, acanthosis nigricans and, less commonly, clitoromegaly. Because of the anovulation and the lack of progesterone production, a state of unopposed estrogen is induced. As mentioned earlier, this state increases the risk of endometrial cancer. Lowered fertility is also characteristic.

The diagnosis of PCOs is a clinical one; however, certain laboratory data, such as ele-

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vated androgen levels, can help to support the diagnosis. An elevated LH:FSH ratio may also be found but is not necessary for diagnosis. When evaluating the patient with suspected PCOS, it also is necessary to rule out other potential hormonal abnormalities such as thyroid disease, hyperprolactinemia or adrenal abnormalities. It is important to note, however, that ultrasonographic evidence of polycystic ovaries is not necessary for diagnosis and, in fact, polycystic ovaries may occur in normally menstruating patients.

Management of PCOS in the adolescent depends on each patient's clinical presentation. Most patients can be treated with combined oral contraceptives. This can reduce the potential worsening of the negative consequences of the syndrome, such as acanthosis nigricans, hirsutism, acne and glucose intolerance.[33] This allows regular shedding of the endometrial lining of the uterus and lowers the patient's risk of endometrial cancer. If a patient is adverse to starting oral contraceptives, oral progesterone (Prometrium) may be used in a dosage of 10 mg daily for seven days, given every three months, to induce a withdrawal bleed. However, this will not alter the androgenic manifestations. In the young woman with severe hirsutism, spironolactone (Aldactone) in a dosage of 50 mg twice daily may be used as an effective alternative when the patient does not feel comfortable using oral contraceptives.

When the patient is overweight, a weight loss of at least 10 percent can improve the hormonal profile and the clinical manifestations of PCOS. Unfortunately, even with the best multidisciplinary programs, weight loss is difficult to achieve and even more difficult to maintain in many patients. Because insulin is thought to play a major role in the etiology of PCOS, researchers have begun to examine the regulation of insulin as a way to control PCOS. For example, a few recent, small studies have demonstrated that metformin (Glucophage) improves menstrual function and hyperandrogenism in patients with PCOS.[34] Therefore, metformin or similar insulin-lowering medications may become the treatment of the future for PCOS.

Final Comment

An important note for the family physician caring for adolescent patients is the management of contraception in the patient who has an eating disorder or who is overweight. One must not assume, even in the morbidly obese patient, that an adolescent female is not sexually active. Therefore, it is essential to question all teenaged patients in a confidential, nonjudgmental manner about their sexual and gynecologic history and to assess their desire for contraception. Condoms alone or condoms plus spermicide are the options that have the fewest possible side effects. In the past, oral contraceptives have been associated with increased weight gain; however, the low-dose pills currently being used are much less likely to have this effect.[35] In addition, for those adolescent patients who are identified as having PCOS, low-dose oral contraceptives will accomplish contraception while also lowering androgen levels. The hormonal contraception options that are more likely to cause weight gain are those with long-acting progestin, such as medroxyprogesterone acetate (Depo-Provera) and levonorgestrel (Norplant). These may be used as a last resort in patients whose need for contraception may override the potential harm from additional weight gain.

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