The Female Athlete Triad

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ABSTRACT
The female athlete triad is a spectrum of interrelated pathophysiologic consequences of low energy availability, menstrual dysfunction, and low bone mineral density. Components of the triad are not only counterproductive to athletic performance goals, but can lead to serious long-term negative health outcomes. Practitioners caring for female athletes play an important role detecting at-risk athletes early in their course along the disease spectrum. Importantly, women who are evaluated for one component of the triad should always be screened for the other two. Detecting the disorder early is the most important factor for preventing the potentially severe consequences, and requires heightened vigilance on the part of all those who work with this special patient population. In this article, we discuss the epidemiology, pathophysiology, diagnosis, evaluation, and management of the female athlete triad.

KEYWORDS: female athlete triad, menstrual dysfunction, disordered eating, altered bone density

INTRODUCTION
Female involvement in athletics and exercise has increased over recent decades. While exercise is encouraged for general health and disease prevention, female athletes are susceptible to negative health outcomes if energy balance is not maintained. Physicians should be familiar with the female athlete triad to enable proper evaluation, diagnosis, and management of the disorder.

DEFINITION
The female athlete triad is a spectrum of disease encompassing a broad set of disorders involving low energy availability, menstrual dysfunction, and low bone mineral density (BMD). First identified by the American College of Sports Medicine (ACSM) in 1992, the triad was initially characterized by disordered eating, amenorrhea, and osteoporosis. Since then, the nosology has been modified to reflect the disease continuum. The current definition reflects variable manifestations within each component of the triad. For example, negative energy balance can occur in athletes with average caloric intake but excessive energy expenditure, or in those with eating disorders. Menstrual dysfunction includes primary amenorrhea, secondary amenorrhea, and oligomenorrhea. Low BMD may manifest as an asymptomatic finding on dual-energy X-ray absorptiometry (DEXA) scan, stress fractures, or pathologic fractures. Fundamentally, the female athlete triad is a spectrum of three distinct pathophysiologic states with varied presentations.

EPIDEMIOLOGY
A recent review examining young women ages 17–25 years old who exercise suggested that the prevalence of all three components of the disorder ranged between 0-15.9%. The wide prevalence estimates are due to several factors, including the changing definition of the female athlete triad, variance in prevalence between types of athletes, as well as inherent diagnostic challenges. It is uncommon for all components of the triad to be diagnosed in concert. Rather, women afflicted with the female athlete triad evolve symptoms and features of the syndrome along non-congruent disease continuums for each component of the triad. Women participating in “lean sports” which assign aesthetic value to performance including gymnastics, ballet dancing, and ice skating are at higher risk for developing the female athlete triad. Studies comparing lean-sport athletes versus non-lean sport athletes demonstrated a prevalence of all three components of the female athlete triad in up to 6.7% of lean-sport athletes compared to 2.0% of non-lean sport athletes.

Epidemiological data exist for components of the female athlete triad. Negative energy balance is the primary disorder in the female athlete triad driving menstrual dysregulation and low BMD. Low energy availability can occur in the setting of both caloric restriction and excessive exercise. In the general adolescent female population, the prevalence of disordered eating is estimated between 13-20%. By contrast, between 15% and 62% of female high school and college athletes exhibit disordered eating, but it is unclear how many have clinical eating disorders or low energy availability leading to triad sequelae. Menstrual dysfunction manifesting as secondary amenorrhea is reported as high as 69% prevalence in female athletes who participate in lean sports compared with 5% of the general population. The prevalence of low BMD is difficult to define in the female athlete population as most young women are not candidates
for BMD testing. Some studies estimate the prevalence of low bone density in female athletes is as high as 13% compared to 2.3% in the general adult population. Despite lack of epidemiologic clarity, the association between these three disorders is well established, meriting evaluation of all components of the triad when one disorder is identified.

Pathophysiology: Low Energy Availability

Low energy availability, defined as insufficient energy to supply metabolic demand, is the primary disorder driving pathophysiologic changes in the female athlete triad. Negative energy balance results in insufficient metabolic supply for normal menstrual function, bone development, and bone maintenance. Factors dictating energy availability include caloric intake, baseline metabolic function, and energy expenditure.

Female athletes may maintain adequate nutrition for average caloric requirements but rigorous training demands contribute to caloric deficit. Alternatively, maladaptive dietary habits such as restriction, purging, laxative, stimulant and diuretic use may lead to insufficient energy availability. When evaluating the female athlete triad, it is important to distinguish between excessive energy expenditure for caloric intake, disordered eating, and a clinically defined eating disorder, the latter of which would necessitate psychiatric evaluation.

Pathophysiology: Menstrual Dysfunction

Menstrual dysfunction may present as primary amenorrhea, secondary amenorrhea, or oligomenorrhea. Primary amenorrhea is the absence of menses at age 15 in the presence of normal growth and secondary sexual characteristics or the absence of menses three years after development of secondary sexual characteristics. Secondary amenorrhea is the absence of menses for more than three cycles or six months in women who previously had regular menses, or the absence of menses for more than nine months in women who previously had irregular menses. Oligomenorrhea is defined as menstrual cycles >35 days apart. Because eumenorrhea may not be established until late in adolescence or early adulthood, menstrual dysfunction may be difficult to establish. When a female athlete develops negative energy balance and subsequent hypometabolic state, hypothalamic GnRH pulsatility is altered. Hypothalamic dysfunction leads to anovulation and subsequent menstrual disturbances.

Pathophysiology: Altered Bone Mineral Density

Bone health is maintained through a continuous process of balanced osteoblastic and osteoclastic activity. In females with a negative energy balance, altered GnRH pulsatility suppresses the hypothalamic-pituitary axis and results in a hypoestrogenic state. In healthy menstruating females, estrogen suppresses osteoclastic activity, promoting bone development and normal BMD. Thus, low BMD in women with the female athlete triad is secondary to the lack of adequate estrogen supply for optimal bone health. Women with menstrual dysfunction and low estrogen can lose up to 2% of BMD annually. Rigorous athletic activity alters the development and maintenance of bone health in preferential anatomic locations. In female athletes, sport activity may increase density of weight bearing bones such as the femur while other bones, including the spine may demonstrate altered BMD. Pathologic and stress fractures should prompt clinical evaluation for the female athlete triad.

Diagnostic Evaluation: The Female Athlete Triad

Primary care providers may play an integral role in the diagnosis of the triad. Identifying at-risk athletes optimally occurs during academic and sports related screenings or in the setting of office visits for menstrual dysfunction, pathologic or stress fractures or disordered eating. Ideally, parents and athletic trainers should be able to recognize components of the female athlete triad and its negative health consequences.

Assessing Low Energy Availability

Evaluation of energy state is essential in evaluating a patient for the female athlete triad. Important historical aspects include dietary habits (current and past), highest and lowest weight, and perception of ideal body weight. Patients should be assessed for disordered eating including restriction,
purging, and use of diuretics, laxatives, or stimulants. Activity level should be determined by evaluating duration and intensity of daily exercise and sports involvement. Examination should include measurement of orthostatic vital signs assessing for resting tachycardia and volume depletion, weight, and BMI. It is important to note findings suggestive of eating disorders including lanugo, parotid gland enlargement, dental enamel erosions and knuckle calluses caused by self-induced vomiting. Laboratory evaluation should include complete blood counts, complete metabolic profile, thyroid function tests and urinalysis. If electrolyte abnormalities are present or the patient presents with bradycardia, an EKG should be performed to assess for arrhythmia or prolonged QT interval.

**Menstrual Dysfunction**

The ACSM recommends screening for the triad in any female athlete with a total of six months of amenorrhea or oligomenorrhea. When evaluating a patient for menstrual dysfunction, providers should ask about age at menarche, frequency and duration of menstrual cycles, last menstrual period, and medication use including oral contraceptives. Careful examination of the patient with a focus on secondary sexual characteristics, signs of hyperandrogenism or findings suggestive of thyroid dysfunction may help distinguish other causes of menstrual dysfunction from altered GnRH pulsatility seen in the female athlete triad. The first step in laboratory evaluation is a pregnancy test. Subsequent work up may include evaluation for polycystic ovarian syndrome, thyroid or pituitary abnormalities. Drugs which affect the menstrual cycle such as contraceptives, antipsychotics or thyroid medications should be identified. Depending on the clinical scenario, evaluation of follicle stimulating hormone (FSH), leutinizing hormone (LH) and possibly MRI evaluation for a pituitary process may be indicated. Importantly, hypothalamic amenorrhea due to decreased GnRH pulsatility seen in the female athlete triad is a diagnosis of exclusion.

**Altered Bone Mineral Density**

Altered BMD may present as abnormal bone development, osteopenia, and osteoporosis. Initial evaluation should include obtaining a history of stress fractures, overuse injuries, and pathologic fractures. A careful assessment of ovulatory status should be performed. The evaluation of BMD can be difficult in the female athlete given continued bone development in adolescence. Osteoporosis can be evaluated with DEXA scanning using the T-score or the Z-score. The T-score compares BMD to a thirty year old adult control whereas the Z-score compares BMD to age and gender matched controls. The latter is a more appropriate diagnostic method for female athletes who have yet to achieve maximum bone density. Evaluation of osteoporosis in the young female athlete is further complicated by site dependent alteration in BMD as discussed previously.

**TREATMENT CONSIDERATIONS**

**Low Energy State**

Due to increased caloric requirements of female athletes, nutritional support and dietary counseling are integral to the treatment of these patients, regardless of the presence or absence of disordered eating. The ACSM recommends establishing weight goals in writing in order to continue athletic participation. Realistic training goals should be identified. Additionally, the organization recommends a nutrition education program, stress reduction, and consideration of bone densitometry screening. If there is concern for an eating disorder, referral to a mental health specialist is appropriate.

**Menstrual Dysfunction**

While a weight or energy requirement goal for the resumption of eumenorrhea has not been definitively established, one study found that restoration of eumenorrhea in anorexia nervosa patients required weight gain of 2 kilograms over the weight at which secondary amenorrhea occurred. Patients who wish to become pregnant require special consideration. While normalization of menstrual cycle and ovulation can be attained by increasing energy availability, weight gain, and subsequent normal pulsatile GnRH activity, other endocrinologic interventions are available and may be necessary but are beyond the scope of this article.

**Altered Bone Mineral Density**

The ACSM recommends consideration of DEXA screening in at risk patients. Resolving the low-energy state is the optimal treatment for altered BMD. A variety of therapies have been proposed. Bisphosphonates are used for the treatment of osteoporosis in post-menopausal women and have been considered in this disorder. Their effectiveness has yet to be demonstrated in premenopausal women. Human trials have not established bisphosphonate teratogenicity but animal trials have shown adverse effects on the fetus. A reasonable pharmacologic approach to bone health supplementation in the female athlete includes vitamin D (400-1000 IU/day) and calcium (1300 mg/day).

**FUTURE RESEARCH**

Future directions will include a focus on examining the role of hormone replacement in re-establishment of menstruation and normal BMD. Oral contraceptive pills have been used to treat adolescents with menstrual dysfunction from other causes, but their use has not been adequately studied in the female athlete population. Initial data in female athletes is mixed with respect to the effect of oral contraceptive pills on bone health. Transdermal estrogen is also an emerging area of research interest. It is thought that transdermal preparations of estrogen may be preferable to oral contraceptive pills in that they have less of an inhibitory effect on insulin-like growth factor-1, a trophic hormone that has been shown to promote bone formation. In
postmenopausal women, transdermal estrogen has reduced fracture risk, but its potential benefits and harms have not been well studied in the young female athlete population.

References

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