[Athletic Training]

CEU

The Female Athlete Triad

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Context: The female athlete triad (the triad) is an interrelationship of menstrual dysfunction, low energy availability (with or without an eating disorder), and decreased bone mineral density; it is relatively common among young women participating in sports. Diagnosis and treatment of this potentially serious condition is complicated and often requires an interdisciplinary team.

Evidence Acquisition: Articles from 1981 to present found on PubMed were selected for review of major components of the female athlete triad as well as strategies for diagnosis and treatment of the conditions.

Results: The main goal in treatment of young female athletes with the triad is a natural return of menses as well as enhancement of bone mineral density. While no specific drug intervention has been shown to consistently improve bone mineral density in this patient population, maximizing energy availability and optimizing vitamin D and calcium intake are recommended.

Conclusions: Treatment requires a multidisciplinary approach involving health care professionals as well as coaches and family members. Prevention of this condition is important to minimize complications of the female athlete triad.

Keywords: female athlete triad, disordered eating, amenorrhea, bone mineral density

The female athlete triad (the triad) refers to a constellation of 3 clinical entities: menstrual dysfunction, low energy availability (with or without an eating disorder), and decreased bone mineral density (BMD). This complex disorder was first coined by the American College of Sports Medicine in 1992 after many experts in the field had noticed a pattern among adolescent and young adult female athlete patients.[92,133] Even though this condition has been described for 2 decades, there is still much debate about how the components of the triad interrelate and how clinicians should manage patients with this complicated condition.

EPIDEMIOLOGY

The prevalence of menstrual irregularities, disordered eating, and low BMD varies widely in the general population and in the athletic community. In women who participate in sports that emphasize aesthetics or leanness, such as ballet or running, the prevalence of secondary amenorrhea can be as high as 69%, compared with 2% to 5% in the general population.[1,8,37,98,113]

Disordered eating—including a range of irregular eating behaviors that do not necessarily meet criteria for severe disorders, such as anorexia nervosa (AN) and bulimia nervosa (BN)—is also fairly common in the athletic community. Up to 70% of elite athletes competing in weight class sports (male and female) are dieting and have some type of disordered eating pattern with the goal to reduce weight before competition.[118] The prevalence of clinical eating disorders among female elite athletes ranges from 16% to 47%.[25,118,119,123] The differences in prevalence rates among studies are likely related to variability in the sports studied (eg, weight class or aesthetic sports versus ball games), different screening methods (eg, questionnaires versus interviews), intensity and ages of athletes, and other methodological differences.[118] However, the various prevalence rates of eating disorders in athletes are still in stark contrast to the 0.5% and 10% prevalence among nonathletic men and women in the general population.[25,119]

The prevalence of low BMD in the female athlete has been studied as well. The prevalence of osteopenia ranges from 22% to 50% in female athletes, with osteoporosis spanning 0% to 13%.[67] This compares to the 12% and 2.3% prevalence reported in the average population, respectively.[93] However, these percentages are based on *T-Score*s, a diagnostic measure previously used in research and clinical settings that is no longer applicable to premenopausal women. More recently, when assessing bone density in the adolescent population or in any premenopausal woman, *Z-Score*s are utilized to determine low bone density for age and osteoporosis.[49,59] The reason

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Table 1. Bone mineral density (BMD) definitions by various organizations.[59,62,93]

	World Health Organization		International Society for Clinical Densitometry		American College of Sports Medicine	
Population	Postmenopausal women		Premenopausal women		Premenopausal female athletes	
Terminology	Osteopenia	Osteoporosis	BMD within expected range for age	BMD below expected range for age	Low BMD	Osteoporosis
Criteria	*T-Score*: –1 to –2.5 (1 to 2.5 SD below the average value for young healthy women)	*T-Score*: ≤ –2.5 (2.5 SD or more below the average value for young healthy women)	*Z-Score*: > –2 (< 2 SD below the average value for age-, sex-, and race-matched controls)	*Z-Score*: ≤ –2 (2 SD or more below the average value for age-, sex-, and race-matched controls)	*Z-Score*: –1 to –2 with secondary clinical risk factors for fracture (eg, chronic malnutrition, eating disorders, hypogonadism, glucocorticoid exposure, previous fractures)	*Z-Score*: ≤ –2 with secondary clinical risk factors for fracture

for using *Z-Score*s (which compare DXA results among age-matched peers) instead of *T-Score*s (which compare DXA results of postmenopausal women to young adult women in their 20s) is that adolescent patients are still growing and not expected to have achieved the BMD of women outside their age group.[49] The International Society for Clinical Densitometry has defined a *Z-Score* of ≤ –2.0 SD as "below expected range for age" and a *Z-Score* > –2.0 SD as "within the expected range for age."[59] Because athletes participating in weightbearing activities typically have higher BMD than nonathletes,[121] the American College of Sports Medicine defines "low BMD" in an athlete as a *Z-Score* between –1 and –2 along with clinical risk factors for fracture (eg, decreased energy availability, amenorrhea, history of stress fractures). It considers "osteoporosis" in an athlete to be a BMD *Z-Score* ≤ –2.0 with clinical risk factors for fracture (Table 1).[93]

It is difficult to assess the pervasiveness of the triad when considered separately. One study examining female athletes found that the prevalence of all 3 components of the triad was 4.3%, not far off from the 3.4% found among healthy controls.[124] However, the prevalence of 2 components of the triad ranged from 5.4% to 26.6%.[124]

The findings in these studies indicate that while the number of athletes suffering from all 3 aspects of the triad simultaneously is fairly low, there are still many young women who are affected by some component of the spectrum of the disease. It is also important to realize that not all components of the triad need to be present concurrently for a female athlete to suffer negative health sequelae of the triad, as the 3 components may have different time sequences of presentation.

MENSTRUAL DYSFUNCTION

Menstrual dysfunction in the female athlete includes a wide spectrum of disorders. The most commonly discussed menstrual abnormality is amenorrhea, which is generally defined as the absence of menses 3 months or more, but can be subcategorized into primary and secondary types. Primary amenorrhea refers to a delay in the age of menarche (no menses by age 15 years in the presence of normal secondary sexual development or within 5 years after breast development if that occurs before the age of 10 years).[5] Secondary amenorrhea is a loss of menses after menarche. Other types of menstrual irregularity include anovulation, luteal phase deficiency, and oligomenorrhea (Table 2).[96]

Amenorrhea can be caused by a variety of diseases and genetic abnormalities, as well as energy deficiency and even stress.[126] The type of amenorrhea resulting from changes in energy availability is functional hypothalamic amenorrhea (FHA). FHA is characterized by the absence of menses due to suppression of the hypothalamic-pituitary-ovarian axis, without an identifiable anatomic or organic cause.[48,87] This type of amenorrhea, commonly associated with exercising

Table 2. Definitions of menstrual function.[93]

Menstrual Status	Definition
Eumenorrhea	Menstrual cycles at intervals near the median for young adult women (28 ± 7 days)
Amenorrhea	*Primary*: No menses by age 15 years in the presence of normal secondary sexual development or within 5 years after breast development if that occurs before the age of 10 *Secondary*: Loss of menses for ≥ 90 days after menarche
Anovulation	Absence of ovulation usually due to impaired follicular development
Luteal-phase defect	An asymptomatic condition caused by a shortened luteal phase (< 11 days) and/or a low concentration of progesterone
Oligomenorrhea	Menstrual cycles at intervals > 35 days

and stress, is most relevant to the female athlete.[86] FHA is caused by an alteration in gonadotropin-releasing hormone pulsatility,[48] which in turn causes a disruption of luteinizing hormone pulses from the pituitary and gonadal steroid release from the ovaries.[86] It reflects a state of estrogen deficiency, which may be one of the causes of decreased BMD.[85] FHA may also be associated with several physiological changes, including overactivity of the hypothalamic-pituitary-adrenal axis (causing an increase in cortisol release) and disturbances of the hypothalamic-pituitary-thyroid axis (resulting in a "sick euthyroid" pattern).[21] Leptin, a cytokine expressed by adipose tissue and strongly associated with fat mass, is lower in the amenorrheic athlete, most likely due to changes in body composition, particularly a decrease in fat mass.[28] Since leptin has a positive effect on gonadotropin-releasing hormone secretion and regulates the release of gonadotropins,[28] its deficiency contributes to the loss of menses. In amenorrheic athletes, luteinizing hormone pulsatility is disrupted while pituitary responsiveness to gonadotropin-releasing hormone is increased, causing amenorrhea of a hypothalamic origin.[80,125]

ENERGY AVAILABILITY

Energy availability is the amount of dietary energy for all physiologic functions after accounting for energy expenditure from exercise.[93] Low energy availability may be the result of an eating disorder but can also occur in the absence of a psychiatric diagnosis such as AN or BN. Athletes may have disordered eating simply by unknowingly failing to attain their energy requirements secondary to time constraints or lack of nutritional knowledge.[33] Some studies have also found that athletes often lack the appetite necessary to promote food intake as compensation for energy expenditure from intense exercise regimens.[22,78]

Female athletes are at risk of developing eating disorders due to pressure to maintain a low body weight along with poor guidance about nutrition and weight loss from the athletic community.[95] Many have placed blame on the coach, who often fails to teach athletes about healthy dieting or cultivates an environment in which weight loss is encouraged regardless of the methods employed to attain it.[33,116] Disordered eating and amenorrhea are most common among sports that emphasize leanness, aesthetics, a weight class, or endurance,[33,78,95] including gymnastics, ballet, figure skating, lightweight rowing, and running.[32,79,109,111]

There is a wide spectrum of disordered eating among athletes that ranges from simple dieting to clinically defined eating disorders such as AN, BN, and an eating disorder not otherwise specified (EDNOS) (Table 3). *Anorexia athletica* is a term used by some researchers to describe a disordered eating pattern seen in the female athlete who has an intense fear of gaining weight, even though she is underweight.[119] Women with anorexia athletica reduce their energy intake and exercise excessively. They may display features of AN and BN without meeting strict criteria for these diagnoses.[119]

Among female athletes, there also exist several different forms of dieting that fall on a continuum. Healthy dieting is considered a modest lowering of daily calories, while harmful dieting or disordered eating includes restrictive behaviors, such as fasting, skipping meals, use of diet pills or laxatives, and binging and purging.[11,108] Some athletes practice what has been called *dietary restraint*, an intent to limit food intake, regardless of how successful it is in execution.[11]

BONE HEALTH

The greatest accretion of bone mass happens during puberty.[43,44] Maximal increases in bone mass accrual occur between 11 and 14 years of age in girls.[89] Menarche is a signal of bone mass growth, and 25% of bone mass accrual occurs in the 2 years that surround menarche.[115,122] Generally, young healthy women achieve 92% of their total body bone mineral content by 18 years of age and approximately 99% by age 26 years.[56] Bone loss usually occurs later with menopause and aging.[9]

In young female athletes with the triad, a compromise in bone strength, ranging from low BMD and stress fractures

Table 3. Criteria for eating disorders.[4]

Disorder	Criteria
Anorexia nervosa	Body weight < 85% expected for age and height Intense fear of gaining weight or becoming fat Disturbed body image Amenorrhea (absence of ≥ 3 consecutive periods) *Types:* Restrictive and binge eating/purging
Bulimia nervosa	Recurrent episodes of binge eating Recurrent inappropriate attempts to compensate for overeating to prevent weight gain (eg, vomiting, laxatives, diuretics, other medications, fasting, excessive exercise) Binge eating and compensatory behaviors occurring ≥ twice a week for 3 months Perception of self-worth excessively influenced by body weight and shape *Types:* Purging and nonpurging
Eating disorder not otherwise specified	Disordered eating that does not meet the criteria for any specific eating disorder. *Examples:* All the criteria for anorexia but with regular menses All the criteria for anorexia but current weight in a normal range despite significant weight loss All the criteria for bulimia but with binge eating and inappropriate compensatory mechanisms occurring < twice weekly for 3 months Repeatedly chewing and spitting out food Recurrent binge eating without regular compensatory behavior

to osteoporosis, may occur at a much younger age.[15] Several different components contribute to bone strength, including bone mineral content, BMD, bone microarchitecture, and bone remodeling.[105] Bone remodeling, or bone turnover, is a constant process of bone formation and matrix development by osteoblasts and bone breakdown by osteoclasts. When this process is interrupted, bone is weakened and more prone to injury.[63]

Healthy athletes tend to have a higher BMD than their nonathletic counterparts as physical activity, particularly weightbearing exercise has a beneficial effect on bone accrual and architecture.[84] High-impact physical activity increases bone density in women.[84] Exercise can even cause a 4% to 5% gain in bone accrual in prepubertal children.[40] Despite similar weightbearing exercise, amenorrheic athletes have lower BMD than their eumenorrheic counterparts.[99,106] In fact, amenorrheic athletes have 10% to 20% less lumbar spine BMD than eumenorrheic athletes.[20,35] Oligomenorrhea and amenorrhea can be detrimental to bone because they are hypoestrogenic states.[34] Since estrogen normally inhibits osteoclast activity, a lack of this important hormone may cause disruption of bone remodeling and accelerated bone resorption.[102] As a result, menstrual status in these young female athletes may override the beneficial effects of physical activity on bone.

COMPLICATIONS OF THE TRIAD

Several health consequences occur in athletes with the triad. Menstrual dysfunction may lead to infertility due to lack of ovarian follicular development, anovulation, or luteal-phase defects.[93] Alternatively, in some young women recovering from the triad, while menses are being restored, premature ovulation may occur and result in unexpected pregnancy in the absence of contraception.[93] There are also negative consequences associated with hypoestrogenism. Low levels of estrogen can cause endothelial dysfunction, resulting in cardiovascular disease.[72,97] Women with hypoestrogenism have elevated low-density lipoprotein cholesterol levels.[101] Women with the triad also have decreased immune function[90,94] and impaired skeletal muscle oxidative metabolism.[55]

Many athletes with low bone density and/or menstrual irregularity suffer from stress fractures.[18,19,23,70,76,112] The most frequent site is the tibia, accounting for 25% to 63% of all stress fractures.[13,19,60,112] Menstrual irregularity increases this risk of injury.[60,76,91,112] Amenorrheic athletes have 2 to 4 times greater risk for stress fracture than their eumenorrheic counterparts.[17]

Low bone density also puts these women at risk for suboptimal peak bone mass acquisition. While the effects may not be immediate after diagnosis of the triad, a decrease

in peak skeletal BMD, along with skeletal demineralization occurring slowly over time, can lead to these conditions.[93] Similarly, the resumption of menses does not resolve BMD issues immediately but starts the necessary rebuilding of bone to decrease the risk of future osteoporosis and fracture.[93] Depending on the age of the patient, the duration of the triad, and the time to recovery, BMD may stabilize and even improve but not necessarily "catch up" to normal, age-appropriate BMD.[12,34] In adulthood, a 10% decrease in BMD is associated with a two- to threefold increase in fracture risk.[68]

Decreased energy availability may also have serious consequences. It may cause nutritional deficits; many of these athletes limit protein, carbohydrate, and fat intake and increase fiber intake.[82,129] A deficiency in macronutrients, particularly essential amino acids and fatty acids, can be detrimental to the body's ability to build bone, maintain muscle mass, repair damaged tissue, and recover from injury.[83]

Disordered eating associated with low energy availability also has serious psychological ramifications, including depression, low self-esteem, and various anxiety disorders.[73] It can be a slippery slope, leading to body image issues and severe eating disorders.[116] A 2011 meta-analysis examined outcomes in patients with AN during 166 642 person years, BN during 32 798 person years, and EDNOS during 22 644 person years.[6] There was an increased mortality rate among women with disordered eating, especially associated with AN. The standardized mortality ratios were 5.86 for AN, 1.93 for BN, and 1.92 for EDNOS; 20% of those with AN who died had committed suicide.[6]

Regardless of the severity of symptoms stemming from the components of the triad, it is important for health care professionals as well as coaches and nutritionists involved in these female athletes' care to be cognizant of the risks and potential consequences of the syndrome.

SCREENING AND DIAGNOSIS

The greatest challenge in treating young female athletes with the triad may be making the initial diagnosis of the condition. Screening for elements of the triad should take place at preparticipation physical examinations or at annual health checkups. Clinicians may also have the opportunity to make a diagnosis when athletes present with related problems, such as amenorrhea or recurrent injury, particularly multiple stress fractures. It is important to screen any athlete who presents with 1 component of the triad for the others.[93]

Screening for the triad should start with a detailed, guided history, including questions regarding physical activity, past injuries, diet and eating behaviors, and menstrual history.[83] Focused questions regarding eating habits and exercise energy expenditure can be helpful in determining energy balance in these young athletes. Patients should be asked about binging or purging behaviors and any recent psychosocial stressors.[48] Athletes with disordered eating may reveal a fear of weight gain or issues with body image and should be referred to a mental health care professional for further guidance and treatment in those cases.[93] Questions about family history and maternal age of menarche may be helpful when assessing menstrual status. When evaluating primary or secondary amenorrhea, etiologies such as thyroid disorders (hyper- or hypothyroidism), pituitary tumors (ie, a prolactinoma), polycystic ovarian syndrome, intrauterine devices, and medications (antipsychotic agents, combined oral contraceptive pills, or depot medroxyprogesterone acetate injections) should be considered.[48]

On physical examination, signs associated with the triad include bradycardia, orthostatic hypotension, and hypothermia, which are common among young women of low weight but are also common in hypothyroidism.[16] Many women with eating disorders show physical signs of persistent vomiting (Russell sign, callused knuckles), gingival abrasions, parotid enlargement, and loss of dental enamel.[48] Women with AN may also present with dry skin, hypercarotenemia, lanugo, and acrocyanosis.[16] Because hypothalamic amenorrhea is a diagnosis of exclusion, other etiologies must be ruled out.[48] For example, hyperandrogenism (hirsutism and acne) may suggest polycystic ovarian syndrome or, more rarely, an androgen-secreting tumor or late-onset adrenal hyperplasia as the cause of amenorrhea. Physical signs of hyperthyroidism include enlarged thyroid, proptosis, tremor, or increased heart rate. The musculoskeletal examination should include palpation of the spine and shins. If pain is detected, a tuning fork assessment for vibratory pain and/or radiological imaging may be warranted to rule out stress fracture.

In a young female athlete who is suspected of having disordered eating, a complete blood count, electrolytes, urea nitrogen, creatinine, glucose, calcium, phosphorus, magnesium, and albumin should be checked.[127] In athletes presenting with amenorrhea, laboratory testing should include a complete blood count and chemistry panel to rule out chronic illnesses associated with amenorrhea, beta-human chorionic gonadotropin testing to rule out pregnancy, thyroid-stimulating hormone and free thyroxine to test for primary and central thyroid dysfunction, prolactin to assess for a pituitary mass, and follicle-stimulating hormone to rule out ovarian insufficiency.[48] If hyperandrogenism is in the differential diagnosis, luteinizing hormone (to check for a luteinizing hormone:follicle-stimulating hormone ratio greater than 2:1, suggesting polycystic ovarian syndrome),[71] total testosterone and sex hormone binding globulin (to calculate the free androgen index),[132] and steroids dehydroepiandrosterone sulfate and 17-hydroxyprogesterone should also be included.[7,77] Many patients with hypothalamic amenorrhea present with a decreased estradiol level, but this is not necessary for diagnosis.[48] A progesterone challenge test may be considered in patients as part of the initial workup or after mild weight gain to assess estrogen status. The progesterone challenge test is performed by giving oral medroxyprogesterone acetate (Provera), 10 mg daily for 5 to 10 days. Withdrawal bleeding 2 to 7 days later confirms that there is some estradiol present and there is not an outflow obstruction (see Table 4).[58]

Table 4. Suggested diagnostic tests for triad.[1,48,93,127]

Component of Triad	Diagnostic Testing
Low energy availability	Complete blood count Comprehensive metabolic panel Phosphorus Magnesium
Menstrual dysfunction	Urine human chorionic gonadotropin Follicle-stimulating hormone Thyroid-stimulating hormone and free thyroxine Prolactin If suspect hyperandrogenism: Luteinizing hormone (to assess luteinizing hormone:follicle-stimulating hormone ratio) Total testosterone Sex hormone binding globulin Dehydroepiandrosterone sulfate 17-hydroxyprogesterone To confirm estrogen status: Progesterone challenge
Low bone mineral density	Dual-energy x-ray absorptiometry

BMD should be assessed in all young women with a history of hypoestrogenism (ie, amenorrhea), disordered eating, and/or a history of stress fractures or a fracture from minimal trauma.[66] There are several imaging modalities available for analysis of bone structure. Dual-energy x-ray absorptiometry (DXA) is most commonly used to assess BMD because of its speed, precision, safety, low cost, and widespread availability.[9,10,49] DXA is one of the few imaging techniques with reference to pediatric data.[10] It can measure bone mass and areal BMD for the whole body as well as specific regions such as the lumbar spine, hip, and distal radius.[10] Measurement of spine and hip are standard for young adult women.[54,65] Measurement of the spine and whole body is preferred in adolescents because of the lack of precision in the hip region in identifying anatomic landmarks.[9] If symptoms of the triad persist, low DXA BMD results should be reevaluated every 12 months, ideally with the same machine to ensure comparison with accuracy and precision.

Bone microarchitecture is an important factor to consider when assessing bone strength and fragility. Amenorrheic athletes have impaired bone microarchitecture compared with their eumenorrheic and nonathletic counterparts, which may increase fracture risk.[2] Unfortunately, DXA is unable to directly measure bone geometry and microstructure. High-resolution peripheral quantitative computed tomography is employed in research settings to determine these parameters. It assesses bone structure and distinguishes between cortical and trabecular bone elements, which further details the effects of menstrual status and exercise on bone health.[24]

TREATMENT

There is still much debate on the best method of treatment for young female athletes with the triad. A multidisciplinary approach is usually necessary for recovery. Support from a primary care and/or sports physician, as well as a nutritionist or dietitian, psychiatrist or therapist, the team coach, and family members, is extremely important throughout the rehabilitation process.

The primary goal of treatment is restoration of regular menstrual cycling and enhancement of BMD. The first step in attaining these goals is modification of the diet and exercise regimens to increase overall energy availability (ie, reduce energy expenditure and maximize energy intake). Athletes may need to increase energy availability to at least 30 kcal/kg of fat-free mass per day to resume menses.[81] LH levels were measured in 29 regularly menstruating sedentary women (18-30 years old) with controlled levels of energy expenditure and intake. Luteinizing hormone pulsatility was disrupted when caloric intake was restricted to < 30 kcal/kg fat-free mass per day in most women.[81] These exact numbers might not be applicable to all women; each patient has a different response to changes in energy balance. There may also be differences in acute versus chronic energy restriction.

The concurrent increase in body weight that occurs with alteration of diet and exercise and resumption of menses improves BMD in previously amenorrheic athletes.[36,41,74] However, this change is not immediate and does not always

fully undo the negative effects of amenorrhea on bone health. In fact, increases in BMD are small and short-lived if not achieved at a young enough age and sustained.[64]

Many athletes are resistant to reductions in training or alterations in their diet. Therefore, other methods of treatment may need to be explored while concurrently emphasizing the need to improve the energy balance. Drug intervention is often considered for these women to help restore menstruation or provide adequate hormonal supplementation. The oral contraceptive pill (OCP) contains estrogen and progestin and has few side effects.[3] It also has the added benefit of being an effective form of contraception for young women. It has been widely used in adolescents suffering from amenorrhea and low bone density, even though data are unresolved regarding its benefits in this patient population. Some studies have found hormonal replacement therapy with an OCP to improve BMD,[26,31,52,53,57,100] but other research has shown no significant effect.[42,69,110] An OCP can also have a masking effect in the amenorrheic athlete with the triad. OCPs can cause a resumption of menstrual bleeding, giving young women a false sense of improvement without any change in energy availability. It may be helpful to allow athletes time to alter their workout and dietary habits before starting an OCP to ensure a natural return of their menstrual cycles and improvement in BMD.

Because of inconclusive data regarding OCPs, research has recently shifted toward finding other ways of delivering estrogen replacement that may be more effective in improving bone density. Transdermal estrogen may have a better impact on bone than an OCP because of its minimal effect on insulin-like growth factor 1, a bone trophic hormone essential for bone formation and remodeling. Oral estrogen is known to decrease systemic insulin-like growth factor 1, while transdermal formulations maintain or increase concentrations of this growth factor.[61,130] Transdermal estrogen replacement may be more effective than OCPs in maintaining or increasing BMD and preventing future fracture risk, as has been demonstrated in postmenopausal women.[38,107,128] Because research on transdermal estrogen has been performed mainly in postmenopausal women and not in young amenorrheic athletes, further research is needed to determine its utility as a treatment option in the triad.

In lieu of reliable data, treatment options other than estrogen and progestin have been explored. Mantzoros and colleagues examined leptin analog administration in women with functional hypothalamic amenorrhea. The majority of participants receiving daily subcutaneous leptin injections resumed menses.[27] However, thus far, intervention studies have been small and of short duration and therefore inconclusive regarding long-term effects on BMD.[27,131]

It is generally accepted that optimizing vitamin D and calcium intake in young women is important for bone health, especially since vitamin D levels are often found to be low in this age group.[30,50,51] There is still debate regarding the optimal daily intake of vitamin D, but based on the 2011 report on dietary requirements for calcium and vitamin D from the Institute of Medicine, it is suggested that adolescents should ingest 1300 mg of calcium and 600 IU of vitamin D daily.[103] For premenopausal women, the recommended daily doses are 1000 mg of calcium and 600 IU of vitamin D.[103]

Bisphosphonates (antiresorptive bone medications) are not recommended for bone density treatment in adolescents or young women. While bisphosphonates do improve bone density in the postmenopausal population[39] and adult women with AN,[46,88] they are not generally accepted as an option for reproductive age women, as they remain active in bones for many years and have a potential teratogenic effect in pregnancy. In addition, the low BMD in postmenopausal women is most often from increased bone loss, while the low BMD in the triad is usually from a lack of bone mass accretion during maturation. The efficacy of bisphosphonates in a younger population may not be as robust, and evidence of their use in the triad is lacking. However, bisphosphonates may have a role in a very select, high-risk population and may be used in conjunction with a physician specializing in osteoporosis management in young athletes. Bisphosphonate use should be closely monitored and accompanied by intense nutritional and exercise guidance.[29]

There has also been a recent movement toward the use of mechanical stimulation to treat bone loss because it mimics impact physical activity. Pulsed electromagnetic fields increase BMD in ovariectomized rats,[75] as well as in postmenopausal women.[120] Vibratory platforms can reduce and possibly prevent bone mass loss after only 20 minutes of quiet standing[104,114] and were correlated with BMD increases in 1 study of adolescent girls.[45] Therefore, these methods of bone stimulation may be a treatment option for low BMD in athletes with the triad who must decrease their physical activity. These techniques may allow women to experience some of the benefits of impact loading without hours of exercise that may be detrimental to their bone health. Research is needed to determine the proper dose and effectiveness of this therapy in young athletes.

One of the greatest barriers to the treatment of young women with the triad is overcoming the psychological component of their condition. Athletes are often determined, competitive people, with perfectionist personalities. Changing their mentality and altering their regimen of diet and exercise can be quite difficult. For athletes who present with classic symptoms of a clinical eating disorder, it is paramount to involve appropriate mental healthcare professionals in their care and management (eg, consideration of a psychiatric medication prescription with follow-up and/or cognitive behavioral therapy). Having athletes with disordered eating agree to a "contract" that outlines their responsibilities as well as the goals of treatment may be helpful.[14,117] Such a document can include consequences, such as exclusion from training and competition, if certain parameters of the contract are not followed.

Currently, the best approach to the triad is early detection and prevention. Preparticipation physical examinations are a particularly good time to screen for signs and symptoms. An athlete presenting with 1 component of the triad should always be evaluated for the other 2. Clinicians should screen for the cardinal signs of the triad: recent decline in performance, changes in mood, dramatic weight loss, and frequent injury, particularly fractures. Health care professionals as well as coaches and athletic administrators should aim to educate athletes on how to optimize their energy availability and bone health to prevent injury. Open lines of communication can also be helpful in recognizing a problem early so that an intervention can occur before the consequences are too difficult to reverse.

CONCLUSION

The female athlete triad is a potentially serious condition affecting many young women. Low bone density is a dangerous consequence of the triad, and the degree of low BMD in young patients is greatly dependent on age of onset and duration of amenorrhea.[47] Low energy availability plays a crucial role in menstrual function and bone health. There are several different theories about the best approach to treating this complicated condition. However, it is universally accepted that triad prevention, early recognition, and a multidisciplinary treatment plan with a focus on proper nutrition and resumption of menses are extremely important and should be priorities among health care professionals, coaches, and other adults involved in the lives of female athletes.

REFERENCES

1. Abraham SF, Beumont PJ, Fraser IS, Llewellyn-Jones D. Body weight, exercise and menstrual status among ballet dancers in training. *Br J Obstet Gynaecol.* 1982;89(7):507-510.
2. Ackerman KE, Nazem T, Chapko D, et al. Bone microarchitecture is impaired in adolescent amenorrheic athletes compared with eumenorrheic athletes and nonathletic controls. *J Clin Endocrinol Metab.* 2011;96(10):3123-3133.
3. American College of Obstetricians and Gynecologists. Hormonal contraception. ACOG technical bulletin. Number 198-October 1994 (replaces No. 106, July 1987). *Int J Gynaecol Obstet.* 1995;48(1):115-126.
4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* Text rev. 4th ed. Washington, DC: American Psychiatric Association; 2000.
5. American Society for Reproductive Medicine. Current evaluation of amenorrhea. *Fertil Steril.* 2008;90(5)(suppl):S219-S225.
6. Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders: a meta-analysis of 36 studies. *Arch Gen Psychiatry.* 2011;68(7):724-731.
7. Azziz R, Carmina E, Dewailly D, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. *Fertil Steril.* 2009;91(2):456-488.
8. Bachmann GA, Kemmann E. Prevalence of oligomenorrhea and amenorrhea in a college population. *Am J Obstet Gynecol.* 1 1982;144(1):98-102.
9. Bachrach LK. Consensus and controversy regarding osteoporosis in the pediatric population. *Endocr Pract.* 2007;13(5):513-520.
10. Bachrach LK. Measuring bone mass in children: can we really do it? *Horm Res.* 2006;65(suppl 2):11-16.
11. Barrack MT, Rauh MJ, Barkai HS, Nichols JF. Dietary restraint and low bone mass in female adolescent endurance runners. *Am J Clin Nutr.* 2008;87(1):36-43.
12. Barrack MT, Van Loan MD, Rauh MJ, Nichols JF. Body mass, training, menses, and bone in adolescent runners: a 3-yr follow-up. *Med Sci Sports Exerc.* 2011;43(6):959-966.
13. Barrow GW, Saha S. Menstrual irregularity and stress fractures in collegiate female distance runners. *Am J Sports Med.* 1988;16(3): 209-216.
14. Beals KA. *Disordered Eating Among Athletes: A Comprehensive Guide for Health Professionals.* Champaign, IL: Human Kinetics; 2004.
15. Beals KA, Meyer NL. Female athlete triad update. *Clin Sports Med.* 2007;26(1):69-89.
16. Becker AE, Grinspoon SK, Klibanski A, Herzog DB. Eating disorders. *N Engl J Med.* 1999;340(14):1092-1098.
17. Bennell K, Matheson G, Meeuwisse W, Brukner P. Risk factors for stress fractures. *Sports Med.* 1999;28(2):91-122.
18. Bennell KL, Malcolm SA, Thomas SA, et al. Risk factors for stress fractures in track and field athletes: a twelve-month prospective study. *Am J Sports Med.* 1996;24(6):810-818.
19. Bennell KL, Malcolm SA, Thomas SA, Wark JD, Brukner PD. The incidence and distribution of stress fractures in competitive track and field athletes: a twelve-month prospective study. *Am J Sports Med.* 1996;24(2):211-217.
20. Bennell KL, Malcolm SA, Wark JD, Brukner PD. Skeletal effects of menstrual disturbances in athletes. *Scand J Med Sci Sports.* 1997;7(5):261-273.
21. Berga SL, Mortola JF, Girton L, et al. Neuroendocrine aberrations in women with functional hypothalamic amenorrhea. *J Clin Endocrinol Metab.* 1989;68(2):301-308.
22. Blundell JE, King NA. Effects of exercise on appetite control: loose coupling between energy expenditure and energy intake. *Int J Obes Relat Metab Disord.* 1998;22(suppl 2):S22-S29.
23. Brunet ME, Cook SD, Brinker MR, Dickinson JA. A survey of running injuries in 1505 competitive and recreational runners. *J Sports Med Phys Fitness.* 1990;30(3):307-315.
24. Burrows M, Liu D, McKay H. High-resolution peripheral QCT imaging of bone micro-structure in adolescents. *Osteoporos Int.* 2010;21(3):515-520.
25. Byrne S, McLean N. Elite athletes: effects of the pressure to be thin. *J Sci Med Sport.* 2002;5(2):80-94.
26. Castelo-Branco C, Vicente JJ, Pons F, et al. Bone mineral density in young, hypothalamic oligoamenorrheic women treated with oral contraceptives. *J Reprod Med.* 2001;46(10):875-879.
27. Chou SH, Chamberland JP, Liu X, et al. Leptin is an effective treatment for hypothalamic amenorrhea. *Proc Natl Acad Sci U S A.* 19 2011;108(16):6585-6590.
28. Christo K, Cord J, Mendes N, et al. Acylated ghrelin and leptin in adolescent athletes with amenorrhea, eumenorrheic athletes and controls: a cross-sectional study. *Clin Endocrinol (Oxf).* 2008;69(4):628-633.
29. Cohen A. Should bisphosphonates be used in premenopausal women? *Maturitas.* 2010;66(1):3-4.
30. Constantini NW, Arieli R, Chodick G, Dubnov-Raz G. High prevalence of vitamin D insufficiency in athletes and dancers. *Clin J Sport Med.* 2010;20(5):368-371.
31. Cumming DC. Exercise-associated amenorrhea, low bone density, and estrogen replacement therapy. *Arch Intern Med.* 1996;156(19):2193-2195.
32. Dale E, Gerlach DH, Wilhite AL. Menstrual dysfunction in distance runners. *Obstet Gynecol.* 1979;54(1):47-53.
33. De Souza MJ, Williams NI. Physiological aspects and clinical sequelae of energy deficiency and hypoestrogenism in exercising women. *Hum Reprod Update.* 2004;10(5):433-448.
34. Drinkwater BL, Bruemner B, Chesnut CH 3rd. Menstrual history as a determinant of current bone density in young athletes. *JAMA.* 1990;263(4):545-548.
35. Drinkwater BL, Nilson K, Chesnut CH III, Bremner WJ, Shainholtz S, Southworth MB. Bone mineral content of amenorrheic and eumenorrheic athletes. *N Engl J Med.* 1984;311(5):277-281.
36. Drinkwater BL, Nilson K, Ott S, Chesnut CH 3rd. Bone mineral density after resumption of menses in amenorrheic athletes. *JAMA.* 1986;256(3): 380-382.
37. Dusek T. Influence of high intensity training on menstrual cycle disorders in athletes. *Croat Med J.* 2001;42(1):79-82.
38. Ettinger B, Ensrud KE, Wallace R, et al. Effects of ultralow-dose transdermal estradiol on bone mineral density: a randomized clinical trial. *Obstet Gynecol.* 2004;104(3):443-451.
39. Fogelman I, Ribot C, Smith R, Ethgen D, Sod E, Reginster JY. Risedronate reverses bone loss in postmenopausal women with low bone mass: results from a multinational, double-blind, placebo-controlled trial. BMD-MN Study Group. *J Clin Endocrinol Metab.* 2000;85(5):1895-1900.

40. Forwood MR, Baxter-Jones AD, Beck TJ, Mirwald RL, Howard A, Bailey DA. Physical activity and strength of the femoral neck during the adolescent growth spurt: a longitudinal analysis. *Bone.* 2006;38(4):576-583.
41. Fredericson M, Kent K. Normalization of bone density in a previously amenorrheic runner with osteoporosis. *Med Sci Sports Exerc.* 2005;37(9):1481-1486.
42. Gibson JH, Mitchell A, Reeve J, Harries MG. Treatment of reduced bone mineral density in athletic amenorrhea: a pilot study. *Osteoporos Int.* 1999;10(4):284-289.
43. Gilsanz V, Chalfant J, Kalkwarf H, et al. Age at onset of puberty predicts bone mass in young adulthood. *J Pediatr.* 2011;158(1):100-105.
44. Gilsanz V, Chalfant J, Kalkwarf H, et al. Age at onset of puberty predicts bone mass in young adulthood [published online ahead of print August 24, 2010]. *J Pediatr.*
45. Gilsanz V, Wren TA, Sanchez M, Dorey F, Judex S, Rubin C. Low-level, high-frequency mechanical signals enhance musculoskeletal development of young women with low BMD. *J Bone Miner Res.* 2006;21(9):1464-1474.
46. Golden NH, Iglesias EA, Jacobson MS, et al. Alendronate for the treatment of osteopenia in anorexia nervosa: a randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab.* 2005;90(6):3179-3185.
47. Golden NH, Lanzkowsky L, Schebendach J, Palestro CJ, Jacobson MS, Shenker IR. The effect of estrogen-progestin treatment on bone mineral density in anorexia nervosa. *J Pediatr Adolesc Gynecol.* 2002;15(3):135-143.
48. Gordon CM. Clinical practice: functional hypothalamic amenorrhea. *N Engl J Med.* 2010;363(4):365-371.
49. Gordon CM, Bachrach LK, Carpenter TO, et al. Dual energy X-ray absorptiometry interpretation and reporting in children and adolescents: the 2007 ISCD Pediatric Official Positions. *J Clin Densitom.* 2008;11(1):43-58.
50. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. *Arch Pediatr Adolesc Med.* 2004;158(6):531-537.
51. Gracia-Marco L, Vicente-Rodriguez G, Casajus JA, Molnar D, Castillo MJ, Moreno LA. Effect of fitness and physical activity on bone mass in adolescents: the HELENA Study [published online ahead of print March 11 2011]. *Eur J Appl Physiol.*
52. Gulekli B, Davies MC, Jacobs HS. Effect of treatment on established osteoporosis in young women with amenorrhoea. *Clin Endocrinol (Oxf).* 1994;41(3):275-281.
53. Haenggi W, Casez JP, Birkhaeuser MH, Lippuner K, Jaeger P. Bone mineral density in young women with long-standing amenorrhea: limited effect of hormone replacement therapy with ethinylestradiol and desogestrel. *Osteoporos Int.* 1994;4(2):99-103.
54. Hans D, Downs RW Jr, Duboeuf F, et al. Skeletal sites for osteoporosis diagnosis: the 2005 ISCD Official Positions. *J Clin Densitom.* 2006;9(1):15-21.
55. Harber VJ, Petersen SR, Chilibeck PD. Thyroid hormone concentrations and muscle metabolism in amenorrheic and eumenorrheic athletes. *Can J Appl Physiol.* 1998;23(3):293-306.
56. Harel Z, Gold M, Cromer B, et al. Bone mineral density in postmenarchal adolescent girls in the United States: associated biopsychosocial variables and bone turnover markers. *J Adolesc Health.* 2007;40(1):44-53.
57. Hergenroeder AC, Smith EO, Shypailo R, Jones LA, Klish WJ, Ellis K. Bone mineral changes in young women with hypothalamic amenorrhea treated with oral contraceptives, medroxyprogesterone, or placebo over 12 months. *Am J Obstet Gynecol.* 1997;176(5):1017-1025.
58. Hull MG, Knuth UA, Murray MA, Jacobs HS. The practical value of the progestogen challenge test, serum oestradiol estimation or clinical examination in assessment of the oestrogen state and response to clomiphene in amenorrhoea. *Br J Obstet Gynaecol.* 1979;86(10):799-805.
59. International Society for Clinical Densitometry. Updated 2005 official positions for the international society for clinical densitometry. http://www.iscd.org/Visitors/positions/OfficialPositionsText.cfm. Accessed May 1, 2011.
60. Iwamoto J, Takeda T. Stress fractures in athletes: review of 196 cases. *J Orthop Sci.* 2003;8(3):273-278.
61. Kam GY, Leung KC, Baxter RC, Ho KK. Estrogens exert route- and dose-dependent effects on insulin-like growth factor (IGF)-binding protein-3 and the acid-labile subunit of the IGF ternary complex. *J Clin Endocrinol Metab.* 2000;85(5):1918-1922.
62. Kanis JA, McCloskey EV, Johansson H, Oden A, Melton LJ 3rd, Khaltaev N. A reference standard for the description of osteoporosis. *Bone.* 2008;42(3):467-475.
63. Kawai M, Modder UI, Khosla S, Rosen CJ. Emerging therapeutic opportunities for skeletal restoration. *Nat Rev Drug Discov.* 2011;10(2):141-156.
64. Keen AD, Drinkwater BL. Irreversible bone loss in former amenorrheic athletes. *Osteoporos Int.* 1997;7(4):311-315.
65. Khan AA, Bachrach L, Brown JP, et al. Standards and guidelines for performing central dual-energy x-ray absorptiometry in premenopausal women, men, and children. *J Clin Densitom.* 2004;7(1):51-64.
66. Khan AA, Hanley DA, Bilezikian JP, et al. Standards for performing DXA in individuals with secondary causes of osteoporosis. *J Clin Densitom.* 2006;9(1):47-57.
67. Khan KM, Liu-Ambrose T, Sran MM, Ashe MC, Donaldson MG, Wark JD. New criteria for female athlete triad syndrome? As osteoporosis is rare, should osteopenia be among the criteria for defining the female athlete triad syndrome? *Br J Sports Med.* 2002;36(1):10-13.
68. Kreipe RE, Forbes GB. Osteoporosis: a "new morbidity" for dieting female adolescents? *Pediatrics.* 1990;86(3):478-480.
69. Lattakova M, Borovsky M, Payer J, Killinger Z. Oral contraception usage in relation to bone mineral density and bone turnover in adolescent girls. *Eur J Contracept Reprod Health Care.* 2009;14(3):207-214.
70. Lauder TD, Dixit S, Pezzin LE, Williams MV, Campbell CS, Davis GD. The relation between stress fractures and bone mineral density: evidence from active-duty army women. *Arch Phys Med Rehabil.* 2000;81(1):73-79.
71. Lewandowski KC, Cajdler-Luba A, Salata I, Bienkiewicz M, Lewinski A. The utility of the gonadotrophin releasing hormone (GnRH) test in the diagnosis of polycystic ovary syndrome (PCOS). *Endokrynol Pol.* 2011;62(2):120-128.
72. Lieberman EH, Gerhard MD, Uehata A, et al. Estrogen improves endothelium-dependent, flow-mediated vasodilation in postmenopausal women. *Ann Intern Med.* 1994;121(12):936-941.
73. Lilenfeld LR, Kaye WH, Greeno CG, et al. A controlled family study of anorexia nervosa and bulimia nervosa: psychiatric disorders in first-degree relatives and effects of proband comorbidity. *Arch Gen Psychiatry.* 1998;55(7):603-610.
74. Lindberg JS, Powell MR, Hunt MM, Ducey DE, Wade CE. Increased vertebral bone mineral in response to reduced exercise in amenorrheic runners. *West J Med.* 1987;146(1):39-42.
75. Lirani-Galvao AP, Bergamaschi CT, Silva OL, Lazaretti-Castro M. Electrical field stimulation improves bone mineral density in ovariectomized rats. *Braz J Med Biol Res.* 2006;39(11):1501-1505.
76. Lloyd T, Triantafyllou SJ, Baker ER, et al. Women athletes with menstrual irregularity have increased musculoskeletal injuries. *Med Sci Sports Exerc.* 1986;18(4):374-379.
77. Lobo RA, Paul WL, Goebelsmann U. Dehydroepiandrosterone sulfate as an indicator of adrenal androgen function. *Obstet Gynecol.* 1981;57(1):69-73.
78. Loucks AB. Energy balance and body composition in sports and exercise. *J Sports Sci.* 2004;22(1):1-14.
79. Loucks AB, Horvath SM. Athletic amenorrhea: a review. *Med Sci Sports Exerc.* 1985;17(1):56-72.
80. Loucks AB, Mortola JF, Girton L, Yen SS. Alterations in the hypothalamic-pituitary-ovarian and the hypothalamic-pituitary-adrenal axes in athletic women. *J Clin Endocrinol Metab.* 1989;68(2):402-411.
81. Loucks AB, Thuma JR. Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. *J Clin Endocrinol Metab.* 2003;88(1):297-311.
82. Manore MM. Dietary recommendations and athletic menstrual dysfunction. *Sports Med.* 2002;32(14):887-901.
83. Manore MM, Kam LC, Loucks AB. The female athlete triad: components, nutrition issues, and health consequences. *J Sports Sci.* 2007;25(suppl 1):S61-S71.
84. McKay H, Liu D, Egeli D, Boyd S, Burrows M. Physical activity positively predicts bone architecture and bone strength in adolescent males and females [published online ahead of print September 14, 2010]. *Acta Paediatr.*
85. Meczekalski B, Podfigurna-Stopa A, Genazzani AR. Hypoestrogenism in young women and its influence on bone mass density. *Gynecol Endocrinol.* 2010;26(9):652-657.
86. Meczekalski B, Podfigurna-Stopa A, Warenik-Szymankiewicz A, Genazzani AR. Functional hypothalamic amenorrhea: current view on neuroendocrine aberrations. *Gynecol Endocrinol.* 2008;24(1):4-11.
87. Medicine PCotASfR. Current evaluation of amenorrhea. *Fertil Steril.* 2004;82(suppl 1):S33-S39.
88. Miller KK, Grieco KA, Mulder J, et al. Effects of risedronate on bone density in anorexia nervosa. *J Clin Endocrinol Metab.* 2004;89(8):3903-3906.
89. Misra M, Klibanski A. Anorexia nervosa and osteoporosis. *Rev Endocr Metab Disord.* 2006;7(1-2):91-99.

90. Montero A, Lopez-Varela S, Nova E, Marcos A. The implication of the binomial nutrition-immunity on sportswomen's health. *Eur J Clin Nutr.* 2002;56(suppl 3):S38-S41.
91. Myburgh KH, Hutchins J, Fataar AB, Hough SF, Noakes TD. Low bone density is an etiologic factor for stress fractures in athletes. *Ann Intern Med.* 1990;113(10):754-759.
92. Nattiv A, Agostini R, Drinkwater B, Yeager KK. The female athlete triad: the inter-relatedness of disordered eating, amenorrhea, and osteoporosis. *Clin Sports Med.* 1994;13(2):405-418.
93. Nattiv A, Loucks AB, Manore MM, Sanborn CF, Sundgot-Borgen J, Warren MP. American College of Sports Medicine position stand: the female athlete triad. *Med Sci Sports Exerc.* 2007;39(10):1867-1882.
94. Nehlsen-Cannarella SL. Cellular responses to moderate and heavy exercise. *Can J Physiol Pharmacol.* 1998;76(5):485-489.
95. Nichols DL, Sanborn CF, Essery EV. Bone density and young athletic women: an update. *Sports Med.* 2007;37(11):1001-1014.
96. Otis CL, Drinkwater B, Johnson M, Loucks A, Wilmore J. American College of Sports Medicine position stand: the female athlete triad. *Med Sci Sports Exerc.* 1997;29(5):i-ix.
97. Perregaux D, Chaudhuri A, Mohanty P, et al. Effect of gender differences and estrogen replacement therapy on vascular reactivity. *Metabolism.* 1999;48(2):227-232.
98. Pettersson F, Fries H, Nillius SJ. Epidemiology of secondary amenorrhea: I. Incidence and prevalence rates. *Am J Obstet Gynecol.* 1973;117(1):80-86.
99. Rencken ML, Chesnut CH 3rd, Drinkwater BL. Bone density at multiple skeletal sites in amenorrheic athletes. *JAMA.* 1996;276(3):238-240.
100. Rickenlund A, Carlstrom K, Ekblom B, Brismar TB, Von Schoultz B, Hirschberg AL. Effects of oral contraceptives on body composition and physical performance in female athletes. *J Clin Endocrinol Metab.* 2004;89(9):4364-4370.
101. Rickenlund A, Eriksson MJ, Schenck-Gustafsson K, Hirschberg AL. Amenorrhea in female athletes is associated with endothelial dysfunction and unfavorable lipid profile. *J Clin Endocrinol Metab.* 2005;90(3):1354-1359.
102. Riggs BL, Khosla S, Atkinson EJ, Dunstan CR, Melton LJ 3rd. Evidence that type I osteoporosis results from enhanced responsiveness of bone to estrogen deficiency. *Osteoporos Int.* 2003;14(9):728-733.
103. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab.* 2011;96(1):53-58.
104. Rubin C, Recker R, Cullen D, Ryaby J, McCabe J, McLeod K. Prevention of postmenopausal bone loss by a low-magnitude, high-frequency mechanical stimuli: a clinical trial assessing compliance, efficacy, and safety. *J Bone Miner Res.* 2004;19(3):343-351.
105. Rubin CD. Emerging concepts in osteoporosis and bone strength. *Curr Med Res Opin.* 2005;21(7):1049-1056.
106. Russell M, Stark J, Nayak S, et al. Peptide YY in adolescent athletes with amenorrhea, eumenorrheic athletes and non-athletic controls. *Bone.* 2009;45(1):104-109.
107. Samsioe G. Transdermal hormone therapy: gels and patches. *Climacteric.* 2004;7(4):347-356.
108. Sanborn CF, Horea M, Siemers BJ, Dieringer KI. Disordered eating and the female athlete triad. *Clin Sports Med.* 2000;19(2):199-213.
109. Sanborn CF, Martin BJ, Wagner WW Jr. Is athletic amenorrhea specific to runners? *Am J Obstet Gynecol.* 15 1982;143(8):859-861.
110. Scholes D, Ichikawa L, LaCroix AZ, et al. Oral contraceptive use and bone density in adolescent and young adult women. *Contraception.* 2010;81(1):35-40.
111. Schwartz B, Cumming DC, Riordan E, Selye M, Yen SS, Rebar RW. Exercise-associated amenorrhea: a distinct entity? *Am J Obstet Gynecol.* 15 1981;141(6):662-670.
112. Shaffer RA, Rauh MJ, Brodine SK, Trone DW, Macera CA. Predictors of stress fracture susceptibility in young female recruits. *Am J Sports Med.* 2006;34(1):108-115.
113. Singh KB. Menstrual disorders in college students. *Am J Obstet Gynecol.* 1981;140(3):299-302.
114. Slatkovska L, Alibhai SM, Beyene J, Cheung AM. Effect of whole-body vibration on BMD: a systematic review and meta-analysis. *Osteoporos Int.* 2010;21(12):1969-1980.
115. Soyka LA, Fairfield WP, Klibanski A. Clinical review 117: Hormonal determinants and disorders of peak bone mass in children. *J Clin Endocrinol Metab.* 2000;85(11):3951-3963.
116. Sundgot-Borgen J. Risk and trigger factors for the development of eating disorders in female elite athletes. *Med Sci Sports Exerc.* 1994;26(4): 414-419.
117. Sundgot-Borgen J. Weight and eating disorders in elite athletes. *Scand J Med Sci Sports.* 2002;12(5):259-260.
118. Sundgot-Borgen J, Torstveit MK. Aspects of disordered eating continuum in elite high-intensity sports. *Scand J Med Sci Sports.* 2010;20(suppl 2):112-121.
119. Sundgot-Borgen J, Torstveit MK. Prevalence of eating disorders in elite athletes is higher than in the general population. *Clin J Sport Med.* 2004;14(1):25-32.
120. Tabrah F, Hoffmeier M, Gilbert F Jr, Batkin S, Bassett CA. Bone density changes in osteoporosis-prone women exposed to pulsed electromagnetic fields (PEMFs). *J Bone Miner Res.* 1990;5(5):437-442.
121. Tenforde AS, Fredericson M. Influence of sports participation on bone health in the young athlete: a review of the literature. *PM R.* 2011;3(9): 861-867.
122. Theintz G, Buchs B, Rizzoli R, et al. Longitudinal monitoring of bone mass accumulation in healthy adolescents: evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab.* 1992;75(4):1060-1065.
123. Torstveit MK, Rosenvinge JH, Sundgot-Borgen J. Prevalence of eating disorders and the predictive power of risk models in female elite athletes: a controlled study. *Scand J Med Sci Sports.* 2008;18(1):108-118.
124. Torstveit MK, Sundgot-Borgen J. The female athlete triad exists in both elite athletes and controls. *Med Sci Sports Exerc.* 2005;37(9):1449-1459.
125. Veldhuis JD, Evans WS, Demers LM, Thorner MO, Wakat D, Rogol AD. Altered neuroendocrine regulation of gonadotropin secretion in women distance runners. *J Clin Endocrinol Metab.* 1985;61(3):557-563.
126. Viswanathan V, Eugster EA. Etiology and treatment of hypogonadism in adolescents. *Pediatr Clin North Am.* 2011;58(5):1181-1200.
127. Walsh JM, Wheat ME, Freund K. Detection, evaluation, and treatment of eating disorders the role of the primary care physician. *J Gen Intern Med.* 2000;15(8):577-590.
128. Warming L, Ravn P, Christiansen C. Levonorgestrel and 17beta-estradiol given transdermally for the prevention of postmenopausal osteoporosis. *Maturitas.* 2005;50(2):78-85.
129. Warren MP, Brooks-Gunn J, Fox RP, Holderness CC, Hyle EP, Hamilton WG. Osteopenia in exercise-associated amenorrhea using ballet dancers as a model: a longitudinal study. *J Clin Endocrinol Metab.* 2002;87(7):3162-3168.
130. Weissberger AJ, Ho KK, Lazarus L. Contrasting effects of oral and transdermal routes of estrogen replacement therapy on 24-hour growth hormone (GH) secretion, insulin-like growth factor I, and GH-binding protein in postmenopausal women. *J Clin Endocrinol Metab.* 1991;72(2):374-381.
131. Welt CK, Chan JL, Bullen J, et al. Recombinant human leptin in women with hypothalamic amenorrhea. *N Engl J Med.* 2 2004;351(10):987-997.
132. Willenberg HS, Bahlo M, Schott M, Wertenbruch T, Feldkamp J, Scherbaum WA. Helpful diagnostic markers of steroidogenesis for defining hyperandrogenemia in hirsute women. *Steroids.* 2008;73(1): 41-46.
133. Yeager KK, Agostini R, Nattiv A, Drinkwater B. The female athlete triad: disordered eating, amenorrhea, osteoporosis. *Med Sci Sports Exerc.* 1993;25(7):775-777.