Risk Biotypes and the Female Athlete Triad

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Introduction

Data support the many benefits of female competitive athletic participation. Regular exercise increases overall strength and aerobic fitness, thus improving girls' cardiovascular health and lowering their risk of chronic degenerative diseases, such as atherosclerosis and diabetes [1–4]. Sports participation enhances female athletes' self-esteem, self-efficacy, and reduces feelings of depression [5]. Various reports document higher academic performance, cognitive function, and degree completion rates among girls and young women who engage in competitive sports [6, 7]. Furthermore, female athletes partake in tobacco or illicit drug use, and sexual promiscuity to a lesser degree than nonathletes [8, 9]. Therefore, female athletic involvement promotes many positive health, cognitive, and psychogenic effects [10].

The 2012 London Olympic Games were the first Olympics to include only sports in which both females and males could participate. Every sporting event at the London Games had a women's and men's division, and every participating nation was represented by at least one female athlete. In fact, for the first time in US history, there were more female American Olympic participants than male. At the 2014 Sochi Olympics, women finally were added to ski jumping. As women have lobbied for gender equity throughout the globe, and have demonstrated what the female body can do, they have pushed their bodies to new physical limits.

It is well-established that women can safely run ultradistant marathons, swim the English Channel, and climb Mount Everest. American volleyball player, Kerri Walsh-Jennings, even showed the world that she could win an Olympic gold medal while pregnant! But in the process of women pushing their bodies and benefitting from sport, some of the negative consequences of exercise participation in the setting of underfueling have emerged. Thus, this chapter will discuss the effects of inadequate energy availability in sport, the Female Athlete Triad (Triad) , and those athletes most susceptible. Also presented will be the risk biotypes and treatment and prevention strategies to help keep girls and women safely in the game.

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The "Female Athlete Triad" Definition

The "Female Athlete Triad," a term first coined in 1992 by the Task Force on Women's Issues of the American College of Sports Medicine (ACSM), described the interrelationships of three distinct conditions: disordered eating (DE) , amenorrhea, and osteoporosis [11]. The ACSM's original position statement on the Triad, published in 1997, reported that athletes with DE or eating disorders (EDs) may develop menstrual disturbances due to an inadequate energy intake relative to the energy expended from exercise [12]. The original position proposed that low energy availability may disrupt the gonadotropin releasing hormone (GnRH) pulse generator of the hypothalamus, thus disturbing luteinizing hormone (LH) pulse frequencies from the pituitary, and therefore negatively affecting sex steroids from the gonads. The low concentrations of ovarian hormones found in amenorrheic and oligomenorrheic athletes have been associated with decreased bone mineral density (BMD) and increased rates of bone loss [12].

With more clinical experience and research performed over the subsequent 10 years, the ACSM updated the Triad position statement in 2007 [10]. In the 2007 position paper, the Triad was described as a "spectrum" of energy availability, menstrual function, and BMD. At the ideal end of the spectrum, an athlete has optimal energy availability, eumenorrhea, and optimal bone health, which may then decline to "reduced energy availability with or without DE," low BMD, and/or subclinical menstrual disorders, including oligomenorrhea, luteal deficiency, and anovulation. At the pathologic end of the spectrum are the combination of "low energy availability with or without an ED," functional hypothalamic amenorrhea [FHA; absence of menses caused by suppression of the hypothalamic–pituitary–ovarian (HPO) axis without a known anatomic or organic disease cause], and osteoporosis [10]. This position statement emphasized the concept of a continuum, clarifying that athletes are at risk for developing aspects of the Triad that could have negative consequences without being at the extreme end of the Triad spectrum.

More recently, in 2014, the Female Athlete Triad Coalition published a consensus statement on treatment and return to play for female athletes with the Triad [13]. The purpose of the consensus statement was to provide more comprehensive guidelines regarding screening, assessment, treatment, and management of the components of the Triad and to recommend an algorithm for return to play of Triad athletes at different stages of severity [13]. Additionally, in 2014, the International Olympic Committee (IOC) produced a consensus statement suggesting a change in terminology to "Relative Energy Deficiency in Sport (RED-S)," to reflect a broader scope of the syndrome, including many aspects of physiological function, health, and athletic performance [14]. Because the 2007 Triad Position Statement and the 2014 Triad Coalition Consensus Statement also mention additional potential consequences of the Triad, including increased risk of injury and consequences to endocrine, gastrointestinal, renal, and neuropsychiatric systems as well as effects on musculoskeletal and cardiovascular health [12, 15], for the purposes of this chapter, we will continue to use the term "Triad."

The Interrelationship of the Three Components of the Triad

When discussing the three main components of the Triad, it is widely accepted that maintaining an appropriate level of energy availability (30–45 kcal/kg of fat-free mass/day), by consuming an adequate level of energy relative to exercise energy expenditure, is paramount to optimize health, performance, and injury risk. An energy deficit develops when an athlete is unable to consume sufficient energy to compensate for the calories burned from exercise. Among some athletes, the energy deficit is intentional, as in those with DE/EDs. However, others develop a caloric deficit inadvertently because of a lack of education and knowledge of the nutritional needs related to their sport and exercise. Regardless of the cause of energy deficit, the results can be similar.

Studies by Loucks, De Souza, and others have clearly demonstrated a link between decreased

energy availability and menstrual dysfunction [15–17]. We now know that menstrual disturbances are common in female athletes and range from subtle disturbances, such as luteal phase defects (LPD) and anovulation in asymptomatic, eumenorrheic women, to more severe menstrual dysfunction, including oligomenorrhea and amenorrhea. Exercise-associated amenorrhea, a form of FHA, is a disruption in hormone cycling that includes abnormal patterns of GnRH secretion at the hypothalamus. FHA in athletes has been causally linked to decreased energy availability, as energy is diverted away from the reproductive axis to more vital bodily processes, such as cell maintenance and immune function. Suppression of the HPO axis is coupled with energy-conserving mechanisms [10]. For example, amenorrheic athletes have consistently demonstrated lower resting energy expenditure (REE) and triiodothyronine (T3) than their eumenorrheic counterparts [18, 19].

Normal GnRH pulsatility is critical for LH and FSH release from the anterior pituitary. LH and FSH subsequently induce production of a variety of hormones including estradiol, progesterone, androstenedione, testosterone, inhibin, activin, and insulin-like growth factor I (IGF-1). In addition, many hormones and neurotransmitters can modulate GnRH secretion, illustrating the complexity of GnRH control. These include the gonadal steroids, which have positive and negative effects on GnRH pulsatility, as well as prolactin, corticotropin-releasing hormone (CRH), neuropeptide Y (NPY), catecholamines, and opiates. Some factors, including CRH and NPY, also impact areas that affect caloric consumption and appetite. Additionally, appetite regulating hormones, such as leptin, ghrelin, and peptide YY (PYY), can impact GnRH pulsatility, as can hormones such as insulin and IGF-1 [20].

Prior research suggests that many of these complex hormonal processes are disrupted in athletes with FHA. Specifically, amenorrheic athletes have a decrease in GnRH, FSH, LH, estradiol, androgens, insulin, glucose, IGF-1, T3, and leptin [21]. All of the aforementioned hormones have been implicated in bone metabolism. Estrogens have an important antiresorptive effect on bone, as do androgens such as testosterone. Estradiol levels in female athletes correlate highly with lumbar, hip, and whole body BMD in various studies [22]. While the exact mechanism is unclear, clinical and animal data suggest an anabolic role for insulin on bone metabolism [23]. IGF-1 exerts an anabolic effect on bone and the effects of growth hormone are primarily mediated through IGF-1. Hypothyroidism decreases metabolic rate, and while some studies have demonstrated increases in BMD in those with hypothyroidism, bone quality was poor, leading to a positive association between hypothyroidism and increased fracture risk [24]. T3 is important for local IGF-1 secretion in bone, which may account for poor bone quality in patients with hypothyroidism [25].

Leptin acts as a key messenger of nutritional status and influences appetite, energy balance, and reproduction [26]. It exerts centrally and peripherally mediated effects on bone. Centrally, mouse models suggest that leptin induces cortical bone formation, but also induces trabecular bone loss, acting via sympathetic signaling, the GH-IGF-1 axis, kisspeptin, and NPY [27]. Peripherally, leptin increases the expression of osteogenic genes versus adipogenic genes in bone marrow stromal cells, increases osteoblast proliferation, decreases osteoclastogenesis, and has a positive effect on the appendicular skeleton [28].

Athletes with FHA also exhibit an increase in fasting PYY, ghrelin, cortisol, and growth hormone resistance [21, 29, 30]. PYY, an anorexigenic peptide hormone secreted by neuroendocrine L cells of the distal intestine, typically increases in response to caloric intake. Utz et al. demonstrated a strong inverse relationship between mean overnight PYY levels and lumbar, hip, and radius BMD in adult women with anorexia nervosa [31]. In a study of adolescent amenorrheic and eumenorreic athletes and eumenorrheic controls, PYY negatively predicted the bone formation marker, P1NP, as well as lumbar bone mineral apparent density, a surrogate for volumetric bone density [32]. More research is needed to better understand the relationship of PYY and bone.

Ghrelin is secreted primarily by the P/D1 cells in the gastric fundus and is another hormone that reflects energy status. Levels are high in conditions of fasting and hypoglycemia and decrease after food, particularly carbohydrate intake [33]. Ghrelin negatively correlates with BMI, body fat percentage, fat mass, body weight, insulin, T3, and leptin in cross-sectional and longitudinal studies of individuals at the extremes of the weight spectrum: anorexia nervosa and obesity, as well as in athlete studies across the menstrual spectrum: amenorrhea to eumenorrhea [34–38]. De Souza et al. have reported that fasting ghrelin levels are elevated by about 85 % in amenorrheic exercising females compared with sedentary ovulatory women, exercising ovulatory women, and even luteal phase defect/anovulatory exercisers [37]. Direct effects of ghrelin on bone have yet to be fully elucidated, however. Finally, cortisol secretion is higher in amenorrheic athletes than eumenorrheic athletes and controls, and correlates negatively with BMD in those with FHA as well as other hypercortisolemic populations [39].

Interestingly, among athletes with the Triad, treatment through dietary behavioral change and increased intake of energy has been shown to successfully reverse the menstrual cycle disruption and promote normal menstruation and fertility [40–43]. However, prior research indicates that an inability to accrue optimal levels of bone mass during the adolescent years may be irreversible and consequences to bone during the adolescent years may lead to lifelong low bone mass [44, 45].

Additional Consequences of the Triad

Along with effects on menstrual function and bone mass, other negative outcomes of the Triad include increased risk of bone stress or musculoskeletal injury, hindered performance, negative effects on the cardiovascular system (e.g., endothelial dysfunction), metabolic and reproductive dysfunction, and gastrointestinal disorders [10, 46]. Additionally, the Triad, particularly among those with ED or DE, may exhibit psychological comorbidities, including anxiety disorders, depression, low self-esteem, and/or body image disturbances [10]. The following paragraphs will explore three of these additional consequences in more detail: bone and musculoskeletal injury, hindered performance, and endothelial dysfunction.

Bone and Musculoskeletal Injury

The development of a bone stress injury, ranging from a low grade stress reaction to a frank stress fracture, depends on many factors, including those related to nutritional status, biomechanics, bone mass and bone metabolism, impact attenuation, training volume, training surface, among other influences. The Triad negatively impacts several factors, including nutritional status, bone metabolism, and bone mass. Research in healthy women indicates that energy availability below a critical threshold of 30 kcal/kg of fat-free mass/day lowers leptin, estradiol, and IGF-1 [39, 47, 48]. This hormone profile parallels changes in biomarkers of bone formation and resorption consistent with reduced bone formation and enhanced bone loss. This may reduce the body's ability to form new bone and repair microdamage from repetitive exercise loading, stress, and strain. Low energy availability may also contribute to micronutrient deficiencies, which may also limit new bone formation.

In adult women, there is a strong relationship between bone density and fracture risk. Prior reports indicate that in postmenopausal women, for every 1 SD decrease in bone density T-score, fracture risk doubles [49]. However, studies that evaluated the relationship between bone density levels and rate of bone stress injury in adolescents and young adult athletes yield conflicting results. Some research among cross country runners, track and field athletes, and female adolescents report an association between lower bone mass [50, 51] or a family history of osteoporosis [51, 52] and fracture risk; however other studies report no association [53–56]. Two prospective investigations, by Bennell et al. and Kelsey et al., who followed female adult runners for 1–2 years,

found a significant negative relationship between bone mass and risk of developing a stress fracture [50, 51]. In a recent study of over 250 active girls and young women, a BMD Z-score <−1.0 was one of the strongest factors associated with the development of bone stress injury. Furthermore, in a study of male and female collegiate athletes, Nattiv et al. found that low BMD negatively influenced time to full return to sport among athletes who had developed a bone stress injury [57].

In addition to low bone mass, DE and menstrual dysfunction (i.e., amenorrhea) correlate with bone stress injury. Five prior studies reported associations between DE and fracture history [53, 54, 58–60]. Runners with a history of stress fracture had higher cognitive dietary restraint [58] or restrictive eating [60], a more prevalent history of anorexia nervosa or bulimia nervosa [59], or scored higher on the EAT-40 [54] than those who never sustained a fracture. A study among ballet dancers also reported that those with stress fracture history more often reported an ED or restrictive eating [53]. FHA and oligomenorrhea have been repeatedly associated with stress fracture. Two prospective studies that evaluated track and field or cross country athletes for 2–5 years found that menstrual irregularity was a significant independent predictor of bone stress injury in their multivariate models [51, 60]. Another found that those who developed stress fractures had fewer menses in the past year [50]. Several other cross-sectional studies found an association between stress fracture history and a history of amenorrhea or oligomenorrhea [51, 52, 54, 55, 59, 61, 62]. Furthermore, a dose–response relationship between the number of Triad-related risk factors and bone stress injury incidence has been noted [63]. These findings provide strong support for the negative effect of the Triad on bone stress injury.

Additionally, the Triad has been linked to the development of soft tissue musculoskeletal injury. Rauh et al. prospectively assessed the rate of musculoskeletal injury among high school athletes participating in a variety of sport types [64]. Among the high school athletes, DE [classified using the Eating Disorder Examination Questionnaire (EDE-Q)], oligomenorrhea or amenorrhea in the past year, and low BMD (Z-score ≤−2.0) were independently associated with the development of a soft tissue or bone-related musculoskeletal injury [64]. This study provides preliminary evidence, but further research is needed to better clarify the relationships between the Triad and soft tissue musculoskeletal injury.

Performance

While some athletes with an intentional or inadvertent energy deficit may perform well in the short term, *persistent* undereating leads to numerous physiological effects that could negatively affect performance in endurance, power, and skill-based sports. Low energy and carbohydrate intake deplete muscle glycogen stores, leading to premature fatigue. Additionally, reduced carbohydrate intake lowers blood glucose, reducing the supply of energy to the brain, which may hinder cognitive function and promote mental fatigue [65]. Inadequate energy and protein intake wastes muscle stores and further leads to weakness and fatigue, increasing risk of injury. Consistent with these findings, consuming a low-fat diet has been associated with lower calorie intake and reductions in endurance performance among runners [66]. Though few studies specifically address the effect of chronic low energy availability or the Triad on exercise performance, a recent study by Vanheest and colleagues explored this relationship in junior elite swimmers [67]. The athletes were categorized as cyclic or ovarian suppressed based on gonadal hormone status. The ovarian suppressed swimmers had lower energy intake, energy availability, total T3, and IGF-1. The ovarian suppressed swimmers had a 9.8% decline in 400-m swim velocity compared with an 8.2% improvement in the cycling group after 12 weeks of training. Ovarian steroids (progesterone and estradiol), metabolic hormones (T3 and IGF-1), and energy status markers (energy intake and energy availability) were highly correlated with swim velocity [67]. This study demonstrated that when exercise training occurs in the presence of underfueling, it can result in ovarian suppression and energy conservation, and is associated with

poor sport performance [67]. Further research directly investigating the effect of low energy availability on athletic performance in athletes representing a variety of sport types is needed.

Endothelial Dysfunction

Triad has also been associated with endothelial dysfunction, a precursor in the development of cardiovascular disease [68]. Shear stress on vascular endothelium leads to nitric oxide (NO) release, which in turn promotes vascular smooth muscle cell (VSMC) dilatation. In addition, NO has anti-atherosclerotic properties including inhibiting platelet aggregation, smooth muscle proliferation, leukocyte adhesion, and LDL oxidation. Estrogen serves a cardioprotective effect by stimulating the endothelial NO synthase (eNOS) signaling system, binding to estrogen receptors of the endothelial cell caveolae, and also via a genomic mechanism, binding to estrogen receptors with a resultant increase in eNOS gene expression [69]. Flow-mediated dilation (FMD) of the brachial artery can be measured using ultrasound. Prior research has found a 95% positive predictive value of abnormal brachial dilation in predicting coronary endothelial dysfunction [70].

Hoch et al., in their study of 32 collegiate running athletes, found significantly lower FMD in amenorrheic athletes compared with oligomenorrheic and eumenorrheic athletes [71]. Rickenlund et al. studied FMD and lipid profiles in endurance athletes with amenorrhea, oligomenorrhea, and eumenorrhea, along with sedentary eumenorrheic controls. FMD was significantly decreased in the amenorrheic athletes versus the other groups, and the amenorrheic athletes also had the worst lipid profiles (higher total cholesterol and LDL) of the three athlete groups [72]. In a study of teenage amenorrheic and eumenorrheic volleyball players and eumenorrheic nonathlete controls, FMD was again lowest in the amenorrheic athletes [73]. Serum estradiol levels were lowest in the amenorrheic athletes, and levels positively predicted vascular function. In the amenorrheic athletes who became eumenorrheic after quitting their strenuous sporting activity, restored vascular function was associated with increased serum estrogen levels [73]. In a study of 22 professional ballet dancers, 64% had decreased FMD. The authors found that FMD correlated significantly with serum estrogen and whole body and lumbar BMD [74].

Risk Biotypes and Prevalence

All female athletes are potentially at risk of developing the Triad; however, athletes who participate in sports emphasizing leanness or low body weight may be at increased risk. In a study by Torstveit and Sundgot-Borgen, which included 669 elite female Norwegian athletes, 70.1% of athletes competing in leanness sports were classified as being at risk for the Triad compared with 55.3% of athletes in non-leanness sports [75].

Multiple studies have shown that athletes are more susceptible to developing EDs than nonathletes [76–79]. Besides the sociocultural demands placed on females to maintain an "ideal" body shape, elite athletes are confronted with the stress of optimizing performance, meeting the specific requirements of their sport, and being evaluated by coaches and judges on a regular basis [80]. These factors can lead to harmful dieting, the potential development of EDs, low energy availability, hormone disturbances, and low bone mass among leanness sport athletes. For instance, the age of menarche in athletes competing in activities that demand low weight is significantly later than that of nonathletes [81]. Other studies reported higher prevalence of menstrual dysfunction in athletes competing in leanness sports (24.8%) compared with those competing in non-leanness sports (13.1%) [82, 83]. In a study of 788 Iranian female competitive athletes (mean age 21.1 ± 4.5 years), Dadgostar et al. found that girls and young women who participated in weight class or endurance sports had a 2–3 times higher risk of developing oligomenorrhea or amenorrhea [84, 85]. Furthermore, other research has shown that females participating in leanness sports have lower BMD than non-leanness sports [86, 87] (See Table 13.1).

Table 13.1 Examples of leanness sports: sports in which leanness and/or a specific body weight are considered important for performance

Endurance sports	Cross-country skiing, cycling, rowing, running, speed skating, and swimming
Aesthetic sports	Cheerleading, dance, figure skating, gymnastics, and synchronized swimming
Weight-class sports	Boxing, judo, kickboxing, lightweight rowing, mixed martial arts, taekwondo, weightlifting, and wrestling
Anti-gravitational sports	Cycling, swimming, and synchronized swimming

Leanness sports often include those that (1) involve high volume training, (2) require revealing uniforms, (3) use weight categories, and/or (4) emphasize a prepubertal body for optimal performance or aesthetics [10]. The following paragraphs include further details about various leanness sport categories and data regarding the increased prevalence of low energy availability (with or without DE/EDs), clinical or subclinical menstrual disturbances, and/or low bone mass for each group.

Endurance Athletes

Studies suggest that endurance athletes exhibit a higher risk of developing DE or EDs, menstrual dysfunction, and low bone mass compared with those participating in other sport types. While the loading nature of endurance sports can be characterized as less osteogenic than ball or other sports involving high- and odd-impact loads, endurance athletes are also at high risk of developing an energy deficit, which negatively impacts bone.

Runners Prior research indicates a higher prevalence of DE/ED among endurance runners, particularly elite competitive runners participating at the collegiate or postcollegiate level. Thompson et al. reported that among a sample of 300 collegiate cross country runners, 19.4% either currently or previously had had an ED [88], while Hulley et al. found that 16% of their sample of elite women distance runners had a current ED [89]. These ED estimates are considerably higher than the 0.5−2% occurrence of anorexia nervosa or bulimia nervosa, respectively, among normal, healthy young adults [17]. Beals and Hill evaluated the eating attitudes and behaviors, menstrual function, and bone mass among 112 US collegiate athletes. They observed that the leanness sport group (consisting largely of endurance runners) reported a significantly higher frequency of moderate to extreme body dissatisfaction, binge eating, and trended ($P=0.08$) toward reporting a self-diagnosed ED more frequently than non-leanness athletes [83]. However, among a sample of 423 high school athletes, Nichols et al. did not find a higher prevalence of DE among girls participating in a leanness (consisting largely of runners) compared with those participating in a non-leanness sport [90]. How the questions were initially asked and the presence or absence of follow-up questioning may have contributed to the differing results.

Previous studies document higher estimates of menstrual dysfunction among endurance runners spanning various ages and levels of competition. Reports indicate that up to 66% of female competitive endurance runners exhibit menstrual disturbances [91–93], values that are approximately 3–5 times higher than the 5–15% [94, 95] prevalence reported in normal, healthy young women and girls. Gibson et al. observed a 66% prevalence of menstrual irregularity among 50 elite endurance runners, while Dusek et al., upon evaluation of 72 female athletes, found a 3 times higher prevalence of secondary amenorrhea among athletes compared with controls, with the highest prevalence of secondary amenorrhea (65%) reported among female endurance runners [93, 96].

Additionally, it is established that adolescent, collegiate, and postcollegiate runners spanning a range of levels of competition exhibit lower bone mass than athletes in other sports. In studies among endurance runners, prevalence estimates of low bone mass are as high as 40%, using a Z-score <-1.0 cutoff. This is significantly higher

than the 5–10% prevalence reported among non-endurance runner athletes, and the 16% prevalence expected in a normal population distribution [91, 92]. Mudd et al., when comparing data from 99 collegiate athletes participating in 12 sport types, found that endurance runners had lower total body and lumbar spine BMD values when compared with gymnasts and softball players [97, 98]. Robinson et al. evaluated bone mass among a sample of collegiate gymnasts, runners, and nonathlete controls [98]. Runners exhibited significantly lower lumbar spine, femoral neck, and total body BMD compared with the other two groups [98].

Triathletes, Cyclists, and Swimmers There has been less research investigating Triad in triathletes, endurance cyclists, and swimmers. However, the current literature suggests that athletes participating in these sports also exhibit an elevated prevalence of Triad components. Studies report elevated levels of DE attitudes and behaviors, including food restriction and body image distortion, in triathletes [99, 100]. This is consistent with findings from Hoch et al., who reported a 60% prevalence of energy deficiency and 40% prevalence of current or previous amenorrhea among a group of club triathletes [101]. Interestingly, research assessing bone mass among triathletes has not found reduced bone mass in this group of athletes [102]. One explanation accounting for the lack of low BMD levels among the triathletes may be the fact that many club triathletes begin training and competing in the sport in adulthood, after peak bone mass is achieved. This may lessen any potential negative effects to bone that could have occurred if the athlete were exposed to the DE and subsequent energy deficits during adolescence. Most of these studies did not take into account the various weight-bearing activities the triathletes may have participated in during their childhood/adolescent periods. As individuals begin training for triathlon at a younger age, further investigations will be needed to better understand the unique risk profile among triathletes.

Little research has evaluated eating attitudes and behaviors, menstrual function, and bone mass among female endurance cyclists. Unlike other endurance sports, more has been reported in male rather than female cyclists. Among these studies, male cyclists exhibit an increased pressure to lose weight, have elevated scores on the eating attitudes test (EAT), and have a higher use of diet pills, laxatives, and self-induced vomiting, particularly during competition [102]. Additionally, studies report lower levels of bone mass among endurance cyclists, particularly among male master cyclists with an average of 20 years of participation in the sport. According to Nichols et al., male master cyclists had significantly lower lumbar spine and total hip BMD compared with age-matched controls and young adult cyclists [103]. Additionally, 15% of the male master cyclists exhibited BMD T-scores <-2.5, the cutoff used in the diagnosis of osteoporosis in older adults [103]. Further research is needed among female cyclists to better identify the prevalence of DE, menstrual dysfunction, and low bone mass.

The few studies evaluating swimmers also identified an elevated prevalence of DE. Da Costa and colleagues assessed eating attitudes and behaviors using three surveys among adolescent swimmers and reported a 44% prevalence of DE [104]. Anderson and Petrie utilized the Eating Disorder Diagnosis questionnaire and found that approximately 28% of collegiate swimmers met criteria for either subclinical DE or a clinical ED [105]. Additionally, among Norwegian elite athletes, swimmers exhibited lower BMD values than athletes in ball or power sports [106]. In a systematic review of 64 studies focused on swimmers' bone mass, structure, and metabolism, most of the studies found similar BMD values in swimmers versus sedentary controls, but many showed lower BMD in swimmers versus other sport groups, including gymnasts, runners, volleyball players, soccer players, and basketball players [107]. This indicates that while swimming does not exert a weight-bearing, osteogenic effect on bone, it does not appear to be associated with a high prevalence of low BMD. There may be a lower rate of menstrual dysfunction and higher fat mass in swimmers versus athletes in leaner sports, which complicates conclusions regarding the additive effects of non-weight-

bearing exercise in the setting of eumenorrhea. Future research is needed to investigate the prevalence of menstrual dysfunction among swimmers with better control for menstrual function and lean and fat mass.

Aesthetic Sports

One important concern of athletes participating in leanness activities is the focus on body appearance in their sports. For example, a high lean to fat mass ratio is important in sports such as figure skating, gymnastics, and sports dance for aesthetic reasons [80]. Aesthetic sports are associated with a negative self-perception during puberty because of body maturation, physiological, and behavioral changes [108]. Moreover, certain characteristics of some athletes such as competitiveness, concern with performance and body shape, and perfectionism, have also been associated with eating problems [109]. Therefore, all of these factors can influence athletes to start irregular eating behaviors, in order to improve performance and meet a specific body shape. Van Durme et al. showed that eating pathology is prevalent in aesthetic sports, especially in female athletes, and that eating concerns and sport-related factors such as competition anxiety could contribute to the dieting behavior of these athletes [110]. In general, studies of female skaters, dancers, and gymnasts have revealed a tendency toward energy-restricted diets, and high rates of clinical and subclinical EDs [79, 110–112]. One meta-analysis concluded that elite athletes in lean sports, especially dance, were at higher risk of developing EDs [109]. A large study of elite athletes showed that the prevalence of EDs in female athletes was as high as 42% in aesthetic sports compared with 24% in endurance, 17% in technical, and 16% in ball games sports [78]. Additionally, it is common to start aesthetic activities in early childhood. In a study of 5 and 7-year-old girls, those participating in aesthetic sports reported higher weight concerns than girls in nonaesthetic sports or no sports [113]. Over time, those who had reported high weight concerns or body dissatisfaction across ages 5 to 7 reported higher dietary restraint, poorer eating attitudes, and increased likelihood of dieting at age 9, regardless of their weight status [114]. A study in elite female synchronized skaters observed significant differences between perceived ideal and current body shape and reported a low mean energy intake of just 26 kcal/kg body weight [115], well below what would be required to fuel exercise expenditure and basic metabolic and reproductive functioning.

Menstrual dysfunction is more common in sports emphasizing thinness, with a prevalence ranging between 1.4 and 27.7% [86]. However, some studies have reported particularly higher prevalence of menstrual disorders in aesthetic athletes. A study including 311 female athletes reported menstrual irregularities in 38.1% of aesthetic athletes (including dance, sports, diving, and gymnastics) compared with 19% in endurance athletes and team/anaerobic sports [116]. A meta-analysis showed that 36.5–70% of professional ballet dancers had a lifetime history of menstrual disturbances and also reported a 4-year incidence of secondary amenorrhea as high as 85% [117]. Similarly, studies in gymnasts have shown high prevalence of menstrual irregularities (71.4–78%) and delayed puberty [87, 118]. Delayed puberty has also been reported in figure skaters, especially in elite and more specialized pair skaters [119].

Aesthetic sports have been variably associated with bone impairment. Some studies have suggested that despite the high prevalence of menstrual irregularities and EDs, female gymnasts and figure skaters have improved BMD in weight-bearing bone sites [120, 121]. Stress fractures in figure skaters have been linked more to the excessive forces placed on the skeleton rather than lower BMD [122]. Moreover, gymnasts have shown improved BMD compared with runners, despite menstrual status [98, 123, 124]. A possible explanation is that the mechanical loading of this sport, may counterbalance the negative effect of menstrual disorders and hypoestrogenism. Conversely, other studies of gymnasts and dancers found lower BMD than other athletes and controls, and concluded that the protective effects of exercise on bone is lost in the presence

of menstrual irregularities [125, 126]. A study in retired gymnasts showed greater spinal BMC and BMD, trabecular volumetric density, and strength in gymnasts without a history of amenorrhea, but not in those with a history of primary or secondary amenorrhea [126]. It is possible that weight-bearing exercise improves BMD when athletes do not have accompanying metabolic, menstrual or eating irregularities, and that bone impairment is more pronounced later in life, when the protective effect of exercise is lost.

Weight-Class Sports

Other athletes at higher risk of developing the Triad are those competing in sports with weight categories such as wrestling, judo, karate, and rowing. In these sports, athletes wish to gain a competitive advantage by obtaining the lowest possible body weight or weight category while maximizing strength [80]. It is known that athletes competing in combat sports periodically practice short-term weight fluctuations prior to a competition season. One study reported that almost 90% of judoists participating in international tournaments had a rapid weight loss of 5–10% of their body weight over a 7-day period [127]. Although weight reduction in these athletes is motivated mainly by optimization of performance, meeting sport-specific demands, and is often seasonal [128, 129], a high proportion of weight-class athletes are using extreme weight-control methods [130]. The rules of some sports may be associated with the risk of continuous dieting, energy deficit, and/or use of extreme weight loss methods that can be detrimental to health and performance [130]. Even though high-impact-loading sports have a protective effect on bone [131, 132] and wrestlers have increased BMD at the lumbar spine [133], chronic states of low energy availability and cyclic weight lost can have negative effects on health parameters such as nutritional status, hormonal status, and immune functions [128].

For instance, one study of adolescent female athletes showed that the exercise-induced osteogenic benefits were less when rowing training was associated with low estrogen and progesterone metabolite excretion [134]. Also a small study in lightweight female rowers showed that 76% of athletes had a history of menstrual irregularities and it was associated with lower lumbar BMD [135]. There is a lack of literature regarding the specific prevalence of Triad among female athletes competing in weight class sports. However, there are several studies in which these sports are included and categorized as "leanness sports," with the prevalence of all components of the Triad and stress fractures being higher than other sports [86, 87, 136]. Finally, small studies in male wrestlers have demonstrated hormonal alterations such as lower testosterone and estradiol levels, and found that estrogen was a more important predictor of BMD than testosterone in this population [137, 138]. This evidence suggests that female and male athletes competing in these sports could be at risk of hormonal, bone, and nutritional impairment.

Other Sports

There are other sports in which body composition and weight play an important role because of mechanical and gravitational factors. This is the case with ski jumping and high jump, which require vertical movements of the body, with fat mass being considered a disadvantage [80]. A lower body weight may result in improved speed in sports that require the body to be lifted against the earth's gravitational field [139]. For this reason, most ski jumpers are underweight and can present with EDs. For instance, the mean BMI in ski jumpers has decreased from 23.6 kg/m^2 in 1970 to 19.4 kg/m^2 in 2002, with values as low as 16.4 kg/m^2 in World Cup athletes that year[139]. In an effort to prevent the myriad negative health effects on such athletes, there have been recent changes in the regulations of this sport in order to make it less attractive and even disadvantageous to be severely underweight. For instance, athletes with lower weight must have shorter skis, which represent an aerodynamic disadvantage that may compensate for the lower weight.

Weight concerns are also quite relevant in horseracing. Jockeys are required to have very low weight and strict weight control during the competitive seasons. Unfortunately, weight control measures in these athletes include saunas, smoking, excessive exercise, skipping meals, and restricting food intake in the 24 h prior to racing that certainly are detrimental to health [140, 141]. In one study of jockeys, energy intake was well below the recommendation for such athletes [142]. Furthermore, other studies have shown low BMD and disrupted hormonal activity in jockeys [143–145]. Thus, it is important to maintain a high level of suspicion to identify athletes at risk of the Triad, especially in sports with emphasis on lean appearance.

Special Populations

Adolescents Adolescents represent a unique subpopulation of athletes, since they must meet the needs and demands of their sport and the physiological demands of growth and development. Key processes occurring during the adolescent years include the development of secondary sex characteristics, initiation of the menstrual cycle (in females), and the process of bone mineral accrual. If an adolescent athlete does not consume sufficient energy to compensate for the energy expended from their sport and growth, over time, various metabolic and hormonal adaptations ensue, creating an environment that suppresses bone mineral accumulation, sexual maturation, and normal menstrual cyclicity. This is due to a disruption of a variety of growth hormones (i.e., insulin-like growth factors), metabolic and appetite-regulating hormones (i.e., leptin, ghrelin, TSH, and T3), and gonadal hormones (i.e., follicle-stimulating hormone, luteinizing hormone, estradiol, androgens, and progesterone) [48, 146–149]. Furthermore, energy deficiency and stress may increase cortisol levels, which augments the negative effects to bone development, sexual maturation, and menstruation [146].

Several investigators have evaluated the prevalence of the Triad among adolescent athletes. Based on the original definition of the Triad (from the 1993 ACSM Position Statement) [150], including DE/EDs, amenorrhea, and osteoporosis, among 170 high school athletes participating in a range of interscholastic sports, there was an 18 % prevalence of DE/EDs based on the EDE-Q, 24 % prevalence of menstrual irregularity (amenorrhea or oligomenorrhea), and a 22 % prevalence of low bone mass (Z-score ≤ -1) [90]. In another study, by Hoch et al., using the updated definition of the Triad (the 2007 ACSM Position Statement) [10], which includes low energy availability as the first component, there was a 36 % prevalence of low energy availability (defined as 45 kcal/kg/lean body mass), a 54 % prevalence of menstrual abnormalities, and a 16 % prevalence of low bone mass (Z-score ≤ -2.0) [151]. In this latter study, the athletes exhibited a higher prevalence of menstrual abnormalities, but a lower prevalence of low bone mass compared with sedentary controls [151].

Barrack et al. identified female adolescent endurance runners as an athlete population with an elevated prevalence of low BMD and reported a 40 versus 10 % prevalence of BMD Z-scores ≤ -1.0, among runners compared with adolescent non-runner athletes [152]. In a subsequent investigation, risk factors associated with low bone mass among the adolescent runners included elevated dietary restraint, amenorrhea, and participating in five or more seasons of an endurance running sport [92]. In a 3-year follow-up among the high school runner sample (mean age of 16 years at baseline and age 19 years at follow-up) the authors found that despite an average approximate 10 pound weight gain during the 3 years, about 90 % of runners with low BMD at baseline continued to exhibit low bone mass at the follow-up assessment [153]. These findings underscore the importance of accruing sufficient bone mass during the adolescent years, since it may be difficult to significantly increase bone mass during and after the third decade of life [44].

Male Athletes While research efforts center on female athletes in the study of the Triad, the occurrence of a similar male athlete Triad,

consisting of (1) low energy availability, (2) disruptions in the hypothalamic pituitary gonadal, growth hormone, thyroid, and adrenal axes, and (3) insults to bone mass, has not been thoroughly evaluated. Currently, little research exists on male athlete groups at risk and the few studies that have evaluated adolescent and young adult male athletes are limited by a small sample size.

Current literature indicates that males participating in certain weight class sports are at risk of developing DE behaviors to cut weight. Wrestling stands as one of the highest profile sports associated with DE, as it is not uncommon for wrestlers to attempt competition in a weight class below their natural weight, as mentioned previously [102]. Behaviors reported among wrestlers to lose weight include self-induced vomiting, sauna use, excessive exercise, use of laxatives, diuretics, and wearing heavy clothing [102]. Misuse of these weight-cutting techniques has been associated with the death of at least three collegiate wrestlers [154]. As a result, new regulations have been implemented to promote the health and safety of the athletes, which included banning pathogenic behaviors and changing the timing of weigh-ins [102].

Other male athlete groups at risk of developing DE, altered hormone levels, and reduced bone mass include endurance runners and cyclists. As mentioned previously, male young adult endurance cyclists report increased pressure to lose weight, use of pathogenic behaviors, and DE, while male master cyclists exhibit reduced bone mass [102]. Several studies report significantly lower testosterone levels among male endurance runners compared with nonathlete controls [155–159], while other investigators identified lower lumbar spine BMD levels in male endurance runners compared with non-runner athletes [160] or nonathlete controls ([161]).

Interestingly, investigators report negative associations between running training volume and bone mass or sex hormones among male endurance runners [162, 163]. In these instances, running training volume may serve as a proxy for exercise energy expenditure, which may suggest that the insults to bone and reductions in the sex hormone levels may be due to an energy deficit, much like the effect of an energy drain on sex hormone levels and bone in the Female Athlete Triad. This is a notable finding since short-bout, explosive exercise movements are associated with increased testosterone levels [164]. These studies suggest that male, like female, endurance runners may be subject to similar hormone disruptions and bone-related risks.

While traditionally testosterone was thought to be the critical hormone in males for bone health, more recent research suggests that it is the conversion of androgens to estradiol that makes it beneficial to bone. In fact, in a study by Ackerman et al., estradiol levels, BMI, and resistance training were found to be more important determinants of BMD in male collegiate athletes (wrestlers, runners, and golfers) than testosterone [137]. Other male athlete sport groups with preliminary data potentially implicating them as an at-risk sport associated with behaviors and outcomes consistent with the Triad include ski jumping, sport climbing, sprint football, bodybuilding, weight lifting, rowing, and horseracing [102]. Future research is needed to more comprehensively outline male athletes´ risk profile and potential negative short- and long-term effects.

Treatment

A multidisciplinary approach is required to treat and prevent further complications of Triad. Involvement of a primary care physician and/or sport physician, dietician, psychiatrist or therapist, team coaches, and family members is necessary during recovery of athletes. There are nonpharmacological and pharmacological therapies for treating the Triad; however, there is still some controversy about which is the best approach.

In general, the primary goal of treatment is to normalize body weight and energy balance with lifestyle and dietary modifications. Diet and exercise regimen modifications should be the main focus to increase daily energy availability. When addressing these issues with athletes, a restrained and stepwise manner is advisable. For instance, modest exercise reduction (10–20%) and an increase of energy availability to at least

30–45 kcal/kg of fat-free mass per day are reasonable goals [10]. Caloric intake should be increased slowly to avoid raising the patient's fear of becoming fat and to avoid the negative sequelae of "refeeding syndrome." Referral to a sports nutritionist/dietitian will also promote a gradual increase in energy intake and optimize overall nutrient intake. Restoration of menstrual cycles and increases in BMD have been seen with weight gain in several studies [10, 165]. Though getting BMD to an optimal range is sometimes not possible, an improvement in BMD may be seen depending on the timing, severity, and duration of energy restriction [166]. Athletes should be advised to achieve a BMI $\geq$18.5 kg/m^2 or 90% of ideal body weight [13]. However, these weight goals may be difficult to attain and are not always sustained over time. It is also important to remember that some athletes may need to achieve even higher weight goals to restore normal menstrual function, because they may have a higher amount of lean muscle mass and a relatively lower amount of adipose tissue.

Another challenge for the physician is that many athletes are reluctant to follow activity and dietary recommendations. Therefore, pharmacological therapy may need to be considered in conjunction with behavior modifications. Oral contraceptive pills (OCPs) containing estrogen and progestin are commonly used in athletes suffering amenorrhea, although evidence regarding the effects on bone density is inconclusive [13, 167, 168]. Recently, research has focused on alternative ways of delivering hormonal therapy. Transdermal estrogen may have a better impact on bone than OCPs because of minimal effects on IGF-1, which is a bone trophic hormone essential for bone formation and remodeling [169]. Studies on postmenopausal women have shown that transdermal estrogens (alone or plus progesterone) are more effective than OCPs in increasing BMD and decreasing fracture risks [170, 171]. Spine and hip BMD improvement was also seen with transdermal estrogen and oral progesterone therapy in adolescent anorexia patients [172]. However, further studies proving the efficacy of transdermal estrogen in treating Triad are needed. Some small studies have also tested the subcutaneous analog leptin therapy for recovering menstrual cycles and improving BMD in those with FHA, but with its side effect of weight loss, adjusting dosing and confirmation of an overall benefit of leptin therapy through larger studies is absolutely required [173, 174].

Additionally, calcium, vitamin D, and sometimes potassium supplementation is recommended in athletes, especially those with restrictive eating behaviors. The daily doses suggested are 1300 mg/day of elemental calcium in divided doses in adolescents (1000 mg in women $\geq$19 years old), 400–800 IU of vitamin D, and 60–90 mg of potassium [169, 175]. In general, bisphosphonates are not recommended for BMD treatment in premenopausal populations, except in extreme circumstances and under the guidance of a bone metabolism specialist, such as an endocrinologist [13]. Antidepressant medications, specifically selective serotonin reuptake inhibitors (SSRIs), may be useful in certain cases. Several studies have shown SSRIs to be effective in the treatment of bulimia nervosa, significantly reducing the frequency of binge eating and purging; however, the evidence is less clear in the case of anorexia nervosa [176, 177]. Another advantage of using antidepressants is the treatment of comorbid conditions such as anxiety, depression, and obsessive compulsive disorder [13]. The main drawback of SSRIs is that they have been linked with weight loss in some individuals with negative effects on BMD [13, 178, 179].

The Triad is a challenging diagnosis and the management has several difficulties. Therefore, education and prevention are fundamental in reducing morbidity and mortality. Prevention and early detection are more effective strategies to reduce symptoms and decrease the risk of serious long-term complications.

Early Detection and Prevention

Awareness of the Triad is the first step. When 180 Australian female exercisers (ages 18–40 years) were surveyed about the Triad, only 10% could name all three components and 45% did not think amenorrhea could affect bone health. A total of

22% of those in lean-build sports answered that they would do nothing if they were amenorrheic [180]. Of 103 American female high school track athletes, more than 90% provided incorrect answers about the consequences of bone loss and the link to menstrual irregularity [181]. In a survey of 240 health care professionals and coaches, fewer than half the physicians could identify the three Triad components and only 8% of the coaches answered correctly [182]. Thus, more information needs to be disseminated to health professionals, coaches, and athletes, alike.

The preparticipation evaluation (PPE) is an excellent time to screen athletes for the Triad. The majority of the US National Collegiate Athletic Association (NCAA) Division 1 universities require a PPE, including a history and physical, prior to sports participation. However, only about a third require an annual update [183]. The Female Athlete Triad Coalition developed 12 questions for inclusion in the PPE [184]. However, only 9% of the NCAA Division 1 schools had ≥9 of the 12 recommended Triad-related questions as part of their PPEs, with 44% of the universities including ≤4 items [183, 184]. The most recent edition of the PPE history and physical examination form endorsed by the American Academy of Family Physicians, American Academy of Pediatrics, ACSM, and others, is the most commonly recommended tool for use with PPEs for middle school through college-aged athletes. It includes 7 of the 12 items recommended by the Female Athlete Triad Coalition, omitting some DE-related questions [185].

Recently, athlete-focused DE prevention programs have been evaluated. In an 8-week program called Athletes Targeting Healthy Exercise and Nutrition Alternatives (ATHENA), coaches and peers led sessions with high school athletes. Topics in the sessions included depression, self-esteem, healthy norms, societal pressures to be thin, and steroid use. Student athletes who participated in the ATHENA program reported less diet pill use and positive improvements in diet habits and exercise self-efficacy versus those who only received informational pamphlets on the topics. When followed for up to 3 years, athletes in ATHENA showed decreases in marijuana and alcohol use, but unfortunately not in eating pathology [186].

In cognitive dissonance-based prevention (DBP), participants confront the thin-ideal standard of female beauty through various activities and discussions in order to create cognitive dissonance. In a healthy weight intervention (HWI), participants learn to make small lifestyle changes to their dietary and exercise habits in order to maintain a healthy weight. Becker et al. compared an athlete-modified DBP (AM-DBP) and an athlete-modified HWI (AM-HWI) approach in a study of 157 female collegiate athletes [187]. Both interventions reduced thin-ideal internalization, dietary restraint, bulimic pathology, shape and weight concern, and negative affect at the 6-week follow-up, with sustained reductions in bulimic pathology, shape concern, and negative affect at 1 year. In addition, there was an increase in students spontaneously seeking medical consultation for the Triad [187].

In a small study of college athletes who had achieved recovery from EDs, participants were asked what advice they would give to coaches, parents, and other athletes at risk for EDs [188]. Coaches were advised to (1) become educated on EDs to increase awareness, (2) emphasize proper athlete nutrition, (3) focus on sport skill rather than body weight to achieve performance goals, (4) refrain from singling out athletes for their body weight or shape, (5) confront an athlete with an ED if even suspected, (6) provide emotional support, (7) refer the athlete to professional care (e.g., physician, psychologist, and/or nutritionist), (8) prohibit sports participation if health risks are evident, (9) try to pair the athlete up with another athlete who has recovered from an ED, and (10) notify the athlete's family. Advice to parents also involved providing emotional support, encouraging professional treatment, and becoming educated about EDs. Suggestions for other athletes with EDs included (1) keeping optimistic about recovery, (2) determining the underlying cause of and triggers for the ED, (3) getting professional treatment, (4) seeking out emotional support from others, (5) focusing on the benefits of recovery, (6) putting the ED in perspective in terms of how it is skewing life values,

and (7) focusing on what has been learned from the ED experiences [188]. Certainly enhancing awareness and taking the advice of those who have experienced aspects of the Triad are future directions in which we need to head.

Conclusion

The Triad and its individual components can occur in female athletes at any age and in any sport. Early awareness and education can help prevent struggles ranging from unsatisfying sports performances to lifelong emotional and physical health problems. Because we know there are certain sport populations at increased risk for the Triad, increased efforts need to be made to improve detection and care in these groups. Following suggestions provided by the IOC, the Female Athlete Triad Coalition, ACSM and other groups of professionals with expertise on this topic is important. In the past decade, researchers have gained a better understanding of the complexity of the Triad and the interrelationship of its components. This understanding needs to be more widely disseminated and further research needs to be conducted to enhance the care of those afflicted by the Triad.

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