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# Bone Health in Adolescent Athletes with a Focus on Female Athlete Triad

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## Abstract

Peak bone mass (PBM) is a negative predictor of osteoporosis and life-long fracture risk. Because osteoporosis is such a prevalent disease with life-threatening consequences later in life, it is important to try to maximize PBM. Adolescence is a critical time for bone acquisition. This review discusses some of the differences in male and female skeletal development and modifiable factors that enhance bone accrual in this age group, particularly in athletes. Hormonal influences, physical activity effects, and nutritional contributions are presented, with a focus on the adolescent athlete. Emphasis is placed on the importance of appropriate energy availability in this age group. The Female Athlete Triad (the inter-relationship of decreased energy availability, menstrual irregularity, and low bone density) is an important issue for adolescent, athletic women, and is therefore reviewed, including prevention and treatment strategies. Recommendations for maximizing bone density in both male and female adolescents are discussed.

### Keywords

Athlete; adolescent; physical activity; bone density; bone microarchitecture; hormones; estrogen; hypogonadism; growth hormone; IGF-1; cortisol; leptin; ghrelin; PYY; nutrition; female athlete triad

## Introduction

Osteoporosis is a leading cause of morbidity and mortality in the elderly. Roughly 40% of women and 13% of men over the age of 50 years will experience an osteoporotic fracture in their lifetime[1]. Peak bone mass (PBM) is a predictor of osteoporosis and fracture risk later in life [2], thus maximizing PBM is a key factor in maintaining bone health throughout the lifespan. For example, a 10% increase in adult BMD at the femoral neck (FN) may decrease fracture risk at that site by 50% [3]. Approximately 90% of PBM is achieved by the end of the second decade of life [4, 5], with 26% of adult bone mineral content (BMC) being acquired during the 2 years around peak height velocity (PHV) [6].

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There is a strong hereditary component to developing PBM, with 60% to 80% of the variance in PBM being explained by genetic factors [7–10]. However, because adolescence is such a critical time for bone acquisition, it is important to understand the various modifiable factors that enhance bone accrual. Growth hormone (GH) and insulin-like growth factor- 1 (IGF-1), gonadal steroids (estradiol and testosterone), leptin, DHEAS, 3,5,3'- triiodothyronine (T3), cortisol, catecholamines, parathyroid hormone (PTH), along with other hormones, affect bone turnover and PBM. Mechanical loading through weight-bearing exercise is vital during childhood and adolescence to achieve PBM [11, 12]. In addition, nutritional contributions, such as overall caloric consumption, and calcium and vitamin D intake are crucial to maintaining an appropriate energy balance, and for bone signaling and skeletal development [13, 14].

The Female Athlete Triad (Triad) and/or its individual components (decreased energy availability, menstrual dysfunction, and low bone density) are problems amongst adolescent, athletic women [13, 15], and specifically, low bone density with impaired bone accrual during the adolescent and young adult years in these women may result in long-lasting consequences if not addressed early [13, 15].

This review will discuss sex differences in bone accrual, as well as hormonal, mechanical and nutritional factors that influence bone health. The Triad will be reviewed, as well as general prevention and treatment strategies for the various components of the triad. Finally, recommendations for maximizing bone density in both male and female adolescent athletes will be discussed.

## Sex Differences in Bone Accrual

PBM refers to bone mass attained during the stable period after both peak height and bone mass are achieved, prior to subsequent bone loss [16]. Peak growth velocity (PGV) precedes maximal BMC acquisition, with rates and timing of PHV and peak total body BMC velocity varying between the sexes. Before puberty, there are minimal differences in BMC attainment between girls and boys. Growth velocity of the total body is rapid immediately after birth, slows in infancy, and increases again at 12 months (primarily in the legs, but not the spine) in both sexes [17]. At age 7, girls have reached approximately 80% of their adult height and 40% of their PBM, while boys have reached 70% of the adult height and 35% of their PBM [18, 19]. Growth velocity in the legs continues to be about twice that of the axial skeleton until puberty. During puberty, the increase in sex steroids leads to a slowing of long bone growth of the appendicular skeleton as the epiphyses begin to fuse [17]. In a 6-year longitudinal study by Bailey, *et al.* [20], 113 boys and girls were followed pre- and post-puberty. PHV occurred on average at age 11.77 years in girls and 13.44 years in boys, while peak total body BMC velocity occurred slightly later (age 12.54 years and 14.05 years in girls and boys respectively) [20]. Thus, as with the onset of puberty itself, the PHV and peak total body BMC velocity in boys lag behind that of girls. In the above mentioned study and others, PHV and the peak total body BMC velocity were higher and longer in duration in boys than girls, as were the resultant peak height and peak BMC [20–22].

The age at which young adults attain PBM is both sex-and skeletal site-specific. Studies in women using quantitative computed tomography (qCT) have demonstrated that the size and density of vertebral bone peak soon after sexual and skeletal maturity [23–25]. This is consistent with data suggesting that trabecular bone loss occurs as early as the third decade of life and that the cross-sectional area of vertebral bodies in women is constant from ages 15 to 90 years [24, 26–28]. Reports on cross-sectional changes in men's vertebrae are less consistent. Some authors have suggested no change in vertebral cross-sectional area (CSA) shortly after peak height is obtained, while others have reported that CSA increases with age

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throughout adulthood [24, 28]. The CSA of vertebral bodies in prepubertal girls is 11% smaller than age, height, and weight-matched prepubertal boys [29]. This discrepancy increases , with a 25% difference at skeletal maturity, controlling for body size differences [30].

Data regarding attainment of peak appendicular bone mass in both sexes are more controversial, as a result of various technologies used to assess bone density, architecture, and quality (such as DXA, qCT and bone biopsy). Of note, during the peripubertal period, cortical width increases by periosteal bone apposition in males, whereas there is a greater suppression of endosteal bone resorption in females [17]. Using high resolution peripheral quantitative CT, studies have shown that pubertal males have greater total bone area, cortical thickness, trabecular number and density, and bone strength index compared with females [31]. Overall, males develop longer and wider bones, with a mildly thicker cortex than females. Lower fracture rates in men compared to women can at least partially be attributed to the greater CSA and periosteal bone thickening throughout the male skeleton.

## Hormones That Influence Bone Accrual

Adult men with a history of delayed puberty have lower BMD of the lumbar spine, radius, and proximal femur than age-matched counterparts who had normal timing of pubertal onset [32–34]. Adolescent girls with amenorrhea have lower BMD, as measured by DXA or CT, than their eumenorrheic counterparts [35–37]. Hip structural analyses in girls with anorexia nervosa, who by definition are amenorrheic, have shown the femoral neck and shaft to have decreased resistance to axial and bending loads [38]. MRI techniques have demonstrated a greater abundance of yellow marrow (as opposed to red marrow) in the peripheral skeleton in girls with anorexia nervosa compared to healthy controls, suggesting preferential differentiation of the mesenchymal stem cell pool into premature adipocytes rather than osteoblasts [39]. In addition, high resolution CT techniques have shown girls with anorexia nervosa to have lower bone trabecular volume and trabecular thickness, and higher trabecular separation at the ultradistal radius compared with normal weight girls of comparable age [40].

Historically estrogen was thought to be the key hormone for bone development in females and testosterone the critical hormone for bone in males, but this view is shifting. Mounting evidence demonstrates that endogenous estrogens and androgens exert independent, positive effects on bone growth and development in both male and female adolescents [41, 42]. The important role of estrogen in skeletal development in males was identified through case studies of young adult men with adequate testosterone and signs of normal virilization, but mutations in two important genes, namely those encoding aromatase and estrogen receptor alpha. Individuals with these genetic mutations have tall stature, open epiphyses, low BMD, and high concentrations of bone turnover markers, presumably due to a lack of estrogen or estrogen action [43, 44]. In aromatase-deficient men, estrogen replacement leads to epiphyseal closure, increased BMD, and a decrease in concentrations of bone turnover markers [45, 46]. Estrogen replacement also prevents bone loss in men following orchiectomy for prostate cancer or sex reassignment [47–49]. In addition to the indirect effects of testosterone, whereby it inhibits bone resorption through its aromatization to estradiol, testosterone has a direct effect on bone density and structure, and increases bone size by enhancing periosteal bone apposition [50–52]. Finally, in both men and women, plasma concentrations of DHEAS, a precursor for both androgens and estrogens, are 100–500 fold greater than testosterone concentrations, and 1000–10,000 fold higher than estradiol concentrations [53, 54].

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GH, IGF-I, IGF-II, and IGF binding proteins (IGFBPs) affect skeletal growth, bone remodeling and mineralization by direct and indirect actions on bone [21]. For example, GH stimulates prechondrocyte proliferation in the growth plate, enhances pre-osteoblast proliferation and osteoblast differentiation, and induces local and systemic production of IGF-I [21, 55]. In addition, exogenous administration of GH suppresses production of IGFBP-4 (which opposes the anabolic effects of IGF-I on bone) and stimulates production of IGFBP-2, -3, and -5 (which stimulate bone cells directly and/or through IGF-I). IGF-I affects chondrocyte and osteoblast differentiation and action, and also enhances renal conversion of 25(OH) vitamin D to the active hormone $1,25(OH)_2$ vitamin D, increasing calcium and phosphorus absorption in the gut [7, 56]. In addition, IGF-I increases renal tubular reabsorption of phosphorus, [7, 56]. Sex steroids, T4, and glucocorticoids impact the secretion of GH and IGF-I, but also have other effects on skeletal development [21, 57, 58]. Glucocorticoids inhibit calcium absorption through a vitamin D independent mechanism and inhibit osteoblast action and survival through potentially an osteoclast mediated mechanism [58–60]. Thyroid hormones increase bone turnover by increasing osteoblastic and osteoclastic activity [57].

The specific and multiple hormonal interactions affecting BMD are still being elucidated. In particular, many of the hormones that signal energy availability [such as leptin, ghrelin, peptide PYY (PYY), insulin, adiponectin and cortisol] appear to have an impact on bone metabolism and change across puberty. Rodent studies indicate that leptin (an adipose-derived peptide that is anorexigenic) stimulates efferent neural signaling from the hypothalamus to receptors on osteoblasts, thereby regulating cancellous bone formation. It also has direct and beneficial effects on cortical bone [61]. *In vitro* studies have reported that ghrelin receptors are expressed on osteoblasts [62], and ghrelin (a hormone secreted by the stomach and is orexigenic) stimulates osteoblastic activity [63, 64]. In addition, stimulation of the Y2 receptor by PYY (a hormone secreted by the L-cells of the distal gut that suppresses hunger) is believed to be deleterious to bone, based on the Y2 receptor knock-out mouse having increased bone mass associated with increased bone formation [65, 66]. Data regarding the relationship between adiponectin (another adipose-derived peptide) and BMD in childhood, adolescence, and young adulthood have been mixed [65, 67, 68], with *in vitro* and animal data indicating an increase in both osteoblastic and osteoclastic activity with adiponectin [69, 70]. Finally, high cortisol levels are deleterious to bone at multiple levels, and may increase in conditions of energy deficit [71]. Many of these hormones change across puberty and may impact bone accrual through the pubertal years. For example, leptin levels peak early in puberty in boys and then decrease, whereas girls have a continued increase in leptin levels through puberty, with peak levels attained in late puberty [72]. Ghrelin levels decrease across pubertal stages [73], while PYY levels are the lowest around the timing of peak growth, when GH levels peak [74].

The impact of long standing exercise on hormones affecting bone metabolism remains under investigation. However, changes in some of these hormones have been described even in the short-term, although the implication of many of these short-term changes remains unclear at this time. For example, short bouts of high-intensity physical activity lead to temporary increases in cortisol and ghrelin, and decreases in leptin [75]. However, with training, the hypothalamic-pituitary-adrenal (HPA) axis response to a given exercise intensity is reduced. When athletes overtrain by dramatically increasing the volume and/or intensity of physical activity over a short period of time, they develop sustained fatigue. Basal cortisol levels increase, but the HPA axis loses its ability to increase cortisol in response to exercise [76]. Thus, exercise has various effects on the hormonal milieu depending on the intensity, duration, and volume of activity. These parameters, along with types of exercise and their effects on adolescent BMD need to be further explored.

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Endocrine status is highly dependent on energy availability (dietary energy intake minus exercise energy expenditure, normalized to fat-free mass). Energy availability is the amount of dietary energy left for other physiologic functions after exercise [13]. In adolescents with anorexia nervosa, a restrictive eating disorder associated with very low weight and marked reductions in bone density and bone acquisition, hypothalamic production of many hormones is disrupted [77]. Leptin concentrations are low as a result of weight loss and decreased fat mass [78]. There is a state of hypogonadotropic hypogonadism with low concentrations of estradiol and testosterone. In addition, individuals with anorexia nervosa have a nutritionally acquired resistance to GH and consequent low IGF-I levels [79]. Serum concentrations of cortisol, ghrelin, PYY and possibly adiponectin are elevated, while insulin and leptin are suppressed [80].

As long as energy availability is maintained at an optimal level, and overtraining does not occur, the various endocrine axes in adult and adolescent athletes appear to function normally, with normal gonadal function and normal levels of IGF-I. However, when energy availability continues to decrease, perturbations occur in various hormonal axes, hypothalamic amenorrhea develops, and hormonal patterns mimic those in anorexia nervosa [65, 81, 82]. Such amenorrheic athletes, in comparison to eumenorrheic athletes, not only have lower levels of leptin, but elevated ghrelin and cortisol levels, and decreased T3, glucose, FSH, estradiol, progesterone and insulin, and a lower ratio of IGF-I to IGFBP-I (a binding protein of IGF-I), indicating less bioavailable IGF-I [65, 81, 83].

There is a high prevalence of disordered eating in adolescent athletes (18.2% reported in one study [84]), and this is more common amongst those who are amenorrheic compared to those who are eumenorrheic (62% versus 11% [15]). Higher rates of disordered eating behavior have been noted in runners, gymnasts, and dancers compared to other kinds of athletes, non-athletes and controls, although the condition may be associated with other kinds of athletic activity [85–87]. Male athletes, such as wrestlers and jockeys are also at risk for disordered eating behavior and unhealthy weight loss practices [88, 89].

Various other diseases during adolescence that impact hormones may also have a profound effect on PBM. Cushing's disease (hypercortisolemia), hyperparathyroidism , hyperthyroidism, asthma (from chronic use of steroids), diabetes (from low IGF-I levels and associated eating disorders), and celiac disease (from decreased vitamin D absorption and possibly low IGF-I levels), all pose a risk to skeletal health [90]. Co-existence of these conditions in athletes increases their risk of impaired bone health. The interplay among these hormones and others continues to be investigated, but it is clear that the disruption of one or more hormonal axis can have a tremendous effect on BMD during the critical adolescent years.

## Physical Activity

Healthy athletes typically have bone density that is 5–30% greater than their sedentary counterparts [91, 92]. If the elevated BMD is maintained, this could lead to a 50–80% fracture risk reduction [2, 92–94]. In the study by Bailey *et al.* [20], there was a 9% and 17% greater total body BMC for active boys and girls respectively, compared to their inactive peers, 1 year after the age of peak total BMC velocity. In cross-sectional studies of adolescent male and female athletes, BMD has been reported to be greater in athletes who participated in high impact (e.g. gymnastics and volleyball) or odd impact loading sports (e.g. squash and soccer), compared to those who participated in repetitive/low impact sports (e.g. cross-country/swimming and cycling) , and compared to controls [95–99]. Differences in sex, age, and maturity, as well as type, intensity, frequency, and duration of exercise among various studies make it difficult to summarize the precise effects of specific activities

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on BMD during pubertal development. However, much of the literature demonstrates that site-specific loading positively correlates with site-specific increases in BMD [100]. This is quite evident in racquet sports, where DXA has shown significantly higher BMD in the dominant versus non-dominant arms of the players [101].

In the Gothenburg Osteoporosis and Obesity Determinants (GOOD) study, a cross-sectional study of 1068 young men (mean age 18.9 ± 0.02), the amount of physical activity (in hours per week) was positively associated with areal BMD (aBMD) of the total body, radius, femoral neck, and lumbar spine, as well as with cortical bone size (increased thickness and periosteal circumference) and trabecular volumetric BMD (vBMD), but not with cortical vBMD or length of the long bones. The lowest effective amount of exercise was ≥ 4 hours/week. Greater differences were seen in those subjects who began their training before age 13 as opposed to later in life, suggesting the importance of weight-bearing during childhood and puberty. The greatest differences in BMD were seen in weight-loaded bone sites in boys who participated in the highest quartile of physical activity hours/week compared to the sedentary group [102]. When the cortical bone geometry of the tibia in this same cohort was analyzed by dividing the group into past versus current physical activity level (those who were always inactive, those formerly active but now inactive, and those continuing to be active), subjects who stopped their sports activity for up to 6.5 prior years had persistently greater cortical periosteal circumference and CSA than those always inactive [103]. This suggests positive effects of exercise on bone even after sports involvement has ceased.

In a longitudinal cohort study comparing bone mass in elite and subelite track and field athletes and less active controls, 50 power athletes, 61 endurance athletes, and 55 nonathlete controls (men and women aged 17–26 years) were followed over 12 months using DXA. Baseline results showed that power athletes had higher BMD at lower and upper limbs and lumbar spine compared with controls, while endurance athletes had higher BMD than controls in lower limb sites only. Power athletes of both sexes had greater BMD at the lumbar spine than endurance athletes. Over the 12 months, athletes and controls within each gender showed significant increases in total body BMC and femur BMD. Changes in bone density were independent of exercise status except at the lumbar spine, where power athletes gained significantly more bone density than the other groups [104]. Although age adjustments were not performed, the age range of the subject population was narrow.

Physical activity helps maximize bone mass during childhood, adolescence and early adulthood, maintain bone through mid-life, diminishes bone loss with aging, and improves stability and strength to minimize falls and fractures in the elderly [105, 106]. However, these benefits come from slow skeletal adaptations to training over time. Because it takes three to four months to complete the bone remodeling cycle of resorption, formation, and mineralization, exercise intervention lasting at least six to eight months is likely required to achieve a change in bone mass that is detectable [107].

Hind and Burrows [108] reviewed controlled-trials involving exercise interventions in children and adolescents. Of the 22 included trials, 9 were conducted in children during prepuberty (Tanner I), 8 during early puberty (Tanner II-III) and 5 during mid-late puberty (Tanner IV-V). Exercise interventions included games, dance, resistance training and jumping exercises, ranging in duration from 3 to 48 months. All trials in early puberty, 6 in prepuberty, and 2 in mid-late puberty, reported positive effects of exercise on bone. In studies with interventions > 6 months, BMD increases were 0.9–4.9% in pre-pubertal, 1.1–5.5% in early pubertal, and 0.3–1.9% in mid-late pubertal exercisers compared to controls [108]. While most studies indicated a positive effect of exercise on bone in boys, data in girls were more conflicting in these studies [108]. Additionally, recent data using high resolution peripheral qCT indicate effects of physical activity on bone microarchitecture,

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with an effect of impact loading physical activity on total bone area in males, and on total and trabecular bone density and trabecular number in females [109].

While there is no doubt that exercise of the appropriate type and volume optimizes bone health, there are risks associated with excessive exercise. Stress fractures, for example, are common in distance runners whose bone remodeling cannot keep up with the repetitive loading they place on their legs [110]. Total BMC and BMD is lower in adolescent male cyclists compared to non-athletes, even with comparable calcium intake [111]. The negative effects of excessive exercise on bone are more pronounced when energy availability is inadequate [15]. Such activity and undernutrition may lead to an exercise-related hypogonadal condition in males [112] or a more frequent hypothalamic amenorrhea in females. The Triad (discussed in more detail subsequently), is often seen in adolescent and young adult athletes, with concerns for low PBM and impaired bone health in later life[13].

Of note, even in a hypogonadal state, mechanical loading of the skeleton plays a significant role in bone accrual. Runners may experience ground reactive forces 3–5 times their body weight, while gymnasts experience forces 12 times their weight [113, 114]. Thus, it is not surprising that even when amenorrheic, gymnasts tend to maintain their bone mass, and may even have higher bone mass than non-athletic controls [115]. Thus the type of exercise is relevant to bone remodeling and PBM.

Future prospective studies controlling for exercise type, duration, and energy availability, as well as larger sample sizes, qualitative and quantitative imaging, and bone turnover markers are needed to better understand the impact of optimal versus excessive athletic activity on bone. Because the optimal exercise type duration and frequency still need to be elucidated for male and female adolescent athletes, the best current recommendation for adolescents may be to find weight-bearing activities they enjoy and will continue to incorporate into their routine ≥ 3 days/week for a total of ≥ 4 hours/week. This recommendation should also emphasize the importance of adequate energy availability, ensuring adolescent athletes remain in a neutral or positive energy balance to maximize the effects of physical activity on bone, while preventing hypogonadism.

## Nutritional Factors Influencing Bone Accrual

As mentioned previously, anorexia nervosa, which involves extreme restrictive eating behavior, can have serious deleterious consequences to bone [37]. However, in addition to consumption of adequate calories, there are other nutrients that are also relevant to bone health. During PHV there is an increased rate of fractures in boys and girls, as peak total BMD velocity lags behind PHV, leading to a transient period of increased skeletal fragility [116]. Proper nutrition is critical to preventing fractures and contributing the building blocks for PBM accretion, which include calcium, phosphorus and proteins.

Calcium: Calcium intake and BMD were lower in adolescents with distal forearm fractures compared to controls, with higher calcium intake having a protective effect against fractures in this age group [117–121]. Prospective, placebo-controlled calcium supplementation trials (1000 mg calcium/day) in healthy adolescent boys and girls with inadequate baseline calcium intake have reported increases in total body BMD [122, 123]. While dairy products are obvious sources of calcium, many foods including juices, cereals, and cereal bars, contain added calcium with the percent recommended daily allowance (%RDA) listed on foods being based on 1000 mg daily. Calcium carbonate contains 40% of elemental calcium and is a commonly used calcium supplement (e.g. Tums™, Oscal™, Caltrate™). Calcium carbonate should be taken with food, as some individuals with achlorhydria cannot absorb this calcium salt well on an empty stomach [124]. Because adverse effects of calcium carbonate may include bloating and constipation, calcium phosphate (e.g. Posture™) is

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another option, and is associated with less constipation and fewer gastrointestinal side effects. Calcium citrate (e.g. Citracal™), which contains 24% elemental calcium, is more bioavailable than calcium carbonate and can be taken on an empty stomach.

The Institute of Medicine's recommendations for daily calcium intake in children ages 9–18 is 1300 mg daily. Unless an individual has an underlying disorder of calcium homeostasis, 2,500 mg is considered the upper limit of safety [125]. As maximal absorption of elemental calcium in a single dose is approximately 500 mg, higher doses are not more effective. Daily intake needs to be divided into multiple doses throughout the day. As a cautionary note, in athletes who are amenorrheic, calcium intake per recommendations is not sufficient to optimize bone density [123]. While an optimal intake of calcium is necessary for all athletes, optimizing energy availability, overall nutritional status, and reproductive function is vital for bone health.

Vitamin D: As little as 10 to 15 minutes of direct sunlight can generate 10,000 to 20,000 IU of vitamin D. However, there are many factors that significantly affect vitamin D synthesis, including latitude, amount of skin exposed, and skin pigmentation [126]. For example, children who have darker skin pigmentation require 5–10 times as much sunlight exposure to achieve the same serum concentrations of 25OH vitamin D than children with lighter skin [126, 127].

Vitamin D intake reduces the risk of stress fractures, infectious illnesses, inflammation, and impaired muscle function [14], however athletes in general, and particularly adolescents often consume less than the recommended amount of vitamin D[15, 128, 129]. In a study by Gordon et al., of 307 adolescents presenting for an annual exam in a Boston clinic, 42% were vitamin D deficient [25OH vitamin D concentration < 20 ng/ml (50 nmol/l)]. Blood concentrations were 24% lower in the winter compared to the summer [130]. Analysis of the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) and the Continuing Survey of Food Intakes by Individuals 1994–1996, 1998 (CSFII 1994–1996, 1998) it was found that adolescent girls had much lower dietary intake of vitamin D than boys, with about 50% of young teenage girls (9–13 years) and 32% of older adolescent girls (14–18 years) consuming even 200 IU/daily [129, 131].

Few foods in the American diet have naturally occurring vitamin D, with oily fish containing the highest concentration (e.g. 3.5 oz. fresh, wild salmon has 600–1000 IU vitamin $D_3$). Foods that are fortified with vitamin D include dairy products, breakfast cereals, infant formula, and margarine [14]. Over the counter supplements are available as multivitamins, calcium + D tablets, softchews, chocolate tablets, and other easy to consume forms. Prescription doses of 50,000 IU vitamin $D_2$ tablets and liquid D are also available. In 2008, the American Academy of Pediatrics increased their recommended daily intake of vitamin D from 200 to 400 IU for adolescents [132]. Many experts believe this recommendation is still not high enough, suggesting 400 to 1000 IU daily may be necessary to maintain adequate 25OH D levels [133].

25OH vitamin D concentrations < 20 ng/ml (50 nmol/l) are considered by most bone experts to represent vitamin D “deficiency”, with levels of 21–29 ng/ml (52–72 nmol/l) considered “insufficient”, and levels >30 ng/ml(>70 nmol/l) “sufficient” [14, 129]. While the ideal blood concentration of vitamin D remains to be determined, intoxication is currently defined as concentrations >150 ng/ml (375 nmol/l) [14].

25OH vitamin D levels should be checked in adolescent athletes [134]. Many athletes get adequate sun-exposure, and recommendations to optimize cutaneous production of vitamin D should be tempered with recommendations to wear sunscreen to protect themselves from the other negative consequences of ultraviolet radiation. If serum 25OH vitamin D is low,

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various dosing regimens can be used to replete D (e.g.2000–5000 IU daily or 50,000 IU weekly for 6–8 weeks) prior to maintenance dosing. Individuals with concentrations <20 ng/ml should also be evaluated for other causes of deficiency (e.g. malabsorpion from celiac disease).

For now adolescent athletes should be advised to eat a varied diet of nutrient-dense food; getting adequate fruit, vegetables, complex carbohydrates, fats, proteins, and overall calories. Most research on nutrition and bone health in this age group has focused on calcium, and more recently, vitamin D. Clearly meeting the minimum requirements for energy, protein, calcium, and vitamin D intake has osteogenic benefits.

## Female Athlete Triad

The Female Athlete Triad (Triad), a term coined in 1992 by the American College of Sports Medicine, refers to a constellation of three clinical entities that are often interrelated and present in some adolescent and adult female athletes. The Triad includes decreased energy availability, menstrual irregularity, and low bone mass [135]. The concept of the Triad has since evolved to include different stages of a continuum. At one end of the spectrum are athletes with mildly disordered eating (e.g. missing certain nutrients, skimping on calories), who have oligomenorhea or a subclinical menstrual disorder (e.g. luteal phase defects), and possibly a stress fracture. At the far end of the spectrum are women who have eating disorders such as anorexia nervosa or bulimia, long-standing amenorrhea, osteoporosis [13]. While the full Triad is certainly a health concern, even the presence of one or two of its individual components is concerning and merits evaluation.

Although the exact prevalence of the overall Triad is unknown, studies have reported high incidences of its individual components, including disordered eating in up to 62% of adolescent athletes, and amenorrhea in up to 69% of female athletes in certain sports [13, 136–138]. Girls are more at risk if they are involved in activities that emphasize a “thin aesthetic” build (e.g. ballet), sports that emphasize a low BMI in the belief that it maximizes speed (e.g. running), or those with a weight limit (e.g. lightweight rowing). However, the Triad can affect girls in any sport. For example, in a study involving female high school athletes from 6 schools and representing 8 different sports , 23.5% reported amenorrhea [84].

The occurrence of amenorrhea in some female athletes has been attributed to a negative energy balance, which disrupts the HPG axis. Loucks et al. demonstrated a decrease in LH pulse frequency in healthy women following just 5 days of low energy availability [139]. More recently, DeSouza and colleagues studied BMD and bone turnover markers in exercising women who were energy and estrogen replete, energy replete and estrogen deficient, energy deficient and estrogen replete, or energy and estrogen deficient. When the energy status of exercising women was adequate, there were no significant changes in bone formation or resorption, regardless of estrogen status. Those with estrogen and energy deficiency had decreased lumbar BMD, suppressed bone formation and increased bone resorption [140].

In comparing adolescent amenorrheic (AA) and eumenorrheic (EA) runners and age-matched controls (HC), our group found lower BMD Z-scores at the spine and total body in the AA compared to the other two groups. Spine Z-scores were <-1 in 38% of AA, 11% of EA, and 11% of HC. The hip Z-scores were statistically lower in the amenorrheic athletes than the eumenorrheic athletes, but not the controls. This suggests a greater deleterious effect of amenorrhea at the spine, and/or a partially compensatory effect of site-specific weight-bearing at the hip. IGF-I concentrations were lower in the amenorrheic athletes compared to control subjects, with IGF-I, body composition, and menstrual status being

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significant predictors of BMD [15]. Important predictors of amenorrhea in athletes include low fat mass, lower leptin, and increases in ghrelin and PYY [65, 81].

The association of hypothalamic amenorrhea and low bone mass highlights the importance of assessing BMD in athletes who exhibit signs of Triad. Currently, there are mixed data regarding the efficacy of interventions other than nutritional and psychological support. Studies of hormonal replacement via oral contraceptives have had mixed results [141]. While estrogen replacement should reduce osteoclastic bone resorption and improve bone density [142], concomitant decreases in IGF-I levels from use of oral estrogen [143, 144], and decreases in free testosterone levels [145], may offset these potential benefits [146]. Finally, cyclic menses induced by OCPs may prevent athletes and their providers from assessing whether or not they are at a healthy weight, or whether strategies are necessary to improve the state of energy availability. The impact of transdermal estrogen on bone density in female adolescent amenorrheic athletes has not been assessed.

Thus, for now, early detection and prevention are the best strategies. An athlete with one component of the Triad should be evaluated for the other two. Female adolescent athletes (and their doctors, coaches, and parents) should suspect low energy availability when an athlete exhibits weight loss, decline in performance, mood changes, frequent illness or injury, fractures, or menstrual dysfunction. The importance of proper nutrition and regular menses should be a topic that athletes, the adults supervising their training, and healthcare providers feel comfortable discussing.

## Conclusion

Adolescence is a critical period for attainment of PBM, an important predictor of future fracture risk. Encouraging teens to consume adequate calories and nutrients such as calcium and vitamin D is important for healthy progression through puberty and for optimal skeletal health. Enhancement of normal skeletal development can be achieved with the addition of frequent, weight-bearing exercise in the presence of adequate nutrition. While we do not yet have an ideal exercise prescription, it is now widely believed that activities that confer high-impact forces in unusual loading patterns are osteogenic. Ground reaction forces in addition to the pull of muscles on bone can enhance bone building during adolescence and beyond. Because prevention is better understood and has fewer potential negative side effects than adult treatments for low bone density, we need to enforce good habits early to prevent development of any of the components of the Triad, and to optimize bone mass acquisition in adolescent athletes.

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