

# The female athlete triad: a case series and narrative overview

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**Objective:** *To illustrate the varying presentations of the female athlete triad and to inform the practitioner of the potential sequelae of this common condition.*

**Clinical Features:** *Four patients presented with a variety of signs and symptoms of the female athlete triad including low caloric intake, osteoporosis, amenorrhea and/or endothelial dysfunction.*

**Intervention and Outcome:** *A conservative treatment approach was utilized in each case including education on the female athlete triad, education on increased caloric intake and a referral to the family physician.*

**Conclusion:** *Health care practitioners should be aware of the different clinical presentations of the female athlete triad. A narrative review of the literature is provided to educate practitioners on the components of the female athlete triad, proper diagnosis and appropriate management.*

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**KEY WORDS:** triad, athlete, female, osteoporosis, amenorrhea, endothelial

**Objectif :** *illustrer les différentes manifestations de la triade de l'athlète féminine et d'informer le praticien des séquelles potentielles de cette affection courante.*

**Caractéristiques cliniques :** *quatre patients ont manifesté une variété de signes et de symptômes de la triade de l'athlète féminine, y compris un faible apport calorique, l'ostéoporose, l'aménorrhée ou une dysfonction endothéliale.*

**Intervention et résultat :** *une approche de traitement conservateur a été utilisée dans chaque cas, y compris une formation sur la triade de l'athlète féminine, une formation sur l'augmentation de l'apport calorique et un renvoi au médecin de famille.*

**Conclusion :** *les professionnels de la santé devraient connaître les différentes manifestations cliniques de la triade de l'athlète féminine. Un examen narratif de la documentation est offert pour renseigner les praticiens sur les composantes de la triade de l'athlète féminine, le bon diagnostic et la prise en charge appropriée.*

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**MOTS CLÉS :** triade, athlète, femme, ostéoporose, aménorrhée, endothéliale

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## Introduction

In the early 1900s females were excluded from sport, specifically the Olympic games, because it was thought that sport might be too stressful for the female body, particularly the reproductive organs. Fortunately, the landscape of female athletics has changed dramatically in the past three decades. The change in female athletics is largely due to the induction of Title IX in the United States of America in 1972.<sup>1,2,3</sup> Since the passage of Title IX female athletic participation has drastically increased worldwide. The passage of Title IX mandated equal access for sport participation in schools for males and females alike.<sup>1,2,3</sup> Since the induction of Title IX in 1972 there has been a one thousand percent increase in the number of female athletes participating in sport. Female athletes have shown to increase self-esteem and self-confidence and reduce risky behaviours such as drug abuse and teen pregnancy in females. However, females face a unique set of psychological pressures in sport. Western society has placed a strong emphasis on ultra-thinness as the ideal body shape and size for females. This cultural ideal places females at an increased risk of developing disordered eating patterns in an effort to conform to the ultra-thin ideal of Western society.<sup>1</sup> The female athlete is not immune to societal pressures of ultra-thinness. A desire to improve performance, a win at all cost mentality, combined with an overly controlling parent or coach, may increase the athlete's risk for developing disordered eating patterns, ultimately leading to the female athlete triad.

In 1992, the American College of Sports Medicine (ACSM) task force on women's issues provided the first definition of the female athlete triad.<sup>4,5</sup> Initially, the female athlete triad was recognized as three separate but inter-related entities; eating/low energy availability, menstrual disturbance/amenorrhea, and bone loss/osteoporosis.<sup>4,5,6</sup> The ACSM position stand states that females that are at risk for developing the female athlete triad are those that are required to have frequent weigh-ins, consequences for weight gain in sport, pressure to win at all costs, and societal pressures to look a particular way. The female athlete triad most commonly presents in sports that have subjective scoring of the female's performance, endurance sports, sports that emphasize low body weight, sports that have multiple weight categories and prepubertal athletic participation, and finally, sports that require the athlete to wear revealing or tight clothing.<sup>4</sup>

The updated 2007 ACSM position stand now recognizes that the female athlete triad is a spectrum of symptoms and conditions ranging between health and disease.<sup>4</sup> The three spectrums include energy availability, menstrual function, and bone mineral density.<sup>4,7,8</sup> The position stand states that the three spectrums occur on a sliding scale ranging from optimal energy availability, eumenorrhea, and optimal bone mineral density to low energy availability with or without an eating disorder, functional hypothalamic amenorrhea, and osteoporosis respectively.<sup>4</sup> Low energy availability may occur unintentionally in female athletes with or without an eating disorder.<sup>7</sup> The three distinct clinical entities may occur alone or in combination with the other disorders. All three clinical entities may also occur at a subclinical level. The athletes' condition may move along each spectrum at a different rate, in one direction or the other, according to her diet and exercise habits.<sup>4,7,8</sup>

This case series presents various scenarios of the female athlete triad syndrome presenting with musculoskeletal pain to chiropractors. To our knowledge this is the first case series and narrative overview on the female athlete triad in the chiropractic literature. This is important due to the large number of female athletes that present to chiropractors and because of the increased female participation in recent years (added with the competition and societal pressures previously mentioned), chiropractors are likely to see these patients more commonly in practice. Therefore, the purpose of this paper is to present the variety of presentations of the female athlete triad syndrome in young premenopausal athletes and provide practitioners with a narrative overview.

## Case One

A 27 year-old female runner presented to a chiropractor with right-sided lateral ankle pain of two weeks duration. No specific mechanism of injury was reported. The pain was localized to the lateral aspect of the right ankle, 3.5cm proximal to the inferior pole of the lateral malleolus. The pain was described as a "sharp" sensation directly over the lateral malleolus. The pain had progressively increased one week prior to presentation to the chiropractor. Relieving factors included rest, cessation of running, ice and nonsteroidal anti-inflammatory drugs (NSAIDs). The pain was aggravated with full weight bearing in walking and running, as well as during the toe-off phase of ambu-



Image 1  
Ankle radiograph – AP  
Arrow shows sclerotic line through  
the distal fibula



Image 2  
Ankle radiograph – Medial oblique  
Arrow shows sclerotic line through  
the distal fibula



Image 3  
Ankle radiograph – AP bright light  
Arrow shows sclerotic fracture line.  
Arrowhead shows periosteal reaction

lation. Systems review was unremarkable. No constitutional signs or symptoms were noted.

The patient reported introducing running back into her routine after a three-month absence. At initial examination she was recreationally running five kilometers, three times per week. Four years prior to examination the patient was diagnosed with secondary amenorrhea from her medical physician. She was not being treated for amenorrhea. However, she was advised by her medical physician to start a regime of calcium and vitamin D supplementation.

On physical examination, observation revealed mild edema 3.5cm proximal to the distal aspect of the lateral malleolus. There was no ecchymosis, deformity, or scarring at the level of reported pain. Gait was unremarkable for pain or discomfort in the lateral ankle. Active and passive range of motion of the right ankle revealed limitation in dorsiflexion and inversion by 25% due to pain. All other active and passive ranges of motion were full and pain free. Orthopedic examination of the right ankle revealed pain on the proximal aspect of the distal fibula with the anterior drawer test (test for the cruciate ligaments)

with no associated laxity. No other ankle orthopedic tests were provocative for pain. Bony tenderness was elicited 3.5cm proximal to the distal aspect of the fibula. Malleolar squeeze elicited pain on the lateral aspect of the ankle. The tuning fork test (256Hz) was positive 3.5cm proximal to the distal aspect of the lateral malleolus. A neurological examination of the lower extremity was unremarkable including sensation, manual muscle testing, and deep tendon reflexes.

Right ankle radiographs were performed by the chiropractor and revealed a faint linear sclerotic line traversing the distal fibular metaphysis, 3.5cm proximal to the tip of the lateral malleolus, associated with a focal cortical distortion. Joint effusion was noted in the talotibial joint with anterior displacement of teardrop fat pad anterior to the talotibial joint. Soft tissue swelling was also noted lateral to the lateral malleolus on the radiograph. This patient was diagnosed with a recent stress fracture of the right distal fibular metaphysis (please refer to images 1, 2, and 3).

This patient was subsequently diagnosed with the female athlete triad due to her recent stress fracture and her

hypothalamic amenorrhea. She was managed by her chiropractor with education on the female athlete triad and advice to seek nutritional counseling to increase her caloric intake. This patient's stress fracture was managed conservatively with rest, ice, rehabilitation, manual therapy, and cessation of running for three weeks. At three weeks post-injury, follow-up radiographs of the right ankle were performed. The radiographs showed a dense sclerotic line traversing the metaphysis of the fibula 3.5cm proximal to the distal aspect of the lateral malleolus with associated callus formation.

### Case Two

A 27 year-old recreational level athlete (and chiropractor) presented to a chiropractic clinic with a history of 10 previous fractures. All fractures occurred during athletic pursuits. Her first fracture was a broken clavicle at age four. Another fracture was at the age of nine where she had pins and plates surgically placed into her tibia after a comminuted distal tibial fracture. She then fractured the base of the first metacarpal on the left at age 11. At age 13 she fractured the shaft of her first metacarpal on the left and the fourth distal phalange on the left foot. At age 14 she fractured her other clavicle, age 15 she fractured the shaft of her fifth metacarpal on the left hand. She fractured her nose twice, once at age 16 and once at age 18. Finally, at age 25 she fractured her fifth distal phalange on the left. All fractures were identified on routine radiographs. Due to the large number of fractures the patient does not remember how all fractures occurred but does report that they were all sustained during athletic pursuits.

At the age of 13 this patient was referred by her general practitioner for a DEXA scan to rule out osteopenia. The DEXA scan was read as unremarkable. However, her z-score was  $-2.2$ . There was no family history of osteopenia or osteoporosis. This patient was asked during her initial evaluation a series of questions in regard to the female athlete triad. She reported never being diagnosed with an eating disorder or disordered eating habits in the past. She did not report to ever keeping a food diary. She reached menarche at the age of 13 and has had 12 cycles per year since the onset of menarche. She also reports to have never been diagnosed with oligomenorrhea or amenorrhea. There is no history of menstrual dysfunction. She reports to have never been concerned with the female ath-

lete triad and that no medical professional has previously asked her questions in regard to the triad.

Due to significant fracture history, this patient was diagnosed with the female athlete triad due to a z score of  $-2.2$ . Education was provided to the patient in regards to increasing caloric intake. This patient may have been inadvertently not ingesting enough calories for her level of activity. She was referred to an osteoporosis specialist for further investigation of her low bone mineral density and a significant fracture history from her family physician.

### Case Three

A 23-year old female professional contemporary dancer presented to a chiropractor with left foot pain localized to the first, fourth and fifth metatarsal heads. The pain was aggravated with weight-bearing, walking, running, and dancing. At times, it would reach an intensity of 8 on a 10-point scale, particularly during the 'demi-point' (i.e. tip-toe) dance position. The pain in the foot was relieved with rest and taking time away from dance. No constitutional signs or symptoms were reported. Systems review was unremarkable.

Upon physical examination, no swelling was noted with observation of the left foot. Active and passive range of motion of the left ankle and metatarsal joints were full and pain free. Joint palpation of the first, fourth, and fifth metatarsal heads reproduced the chief complaint. There was no pain on palpation of the surrounding foot musculature. Tuning fork test of the metatarsal heads was unremarkable. The patient was subsequently diagnosed with metatarsalgia due to over training of the left first, fourth, and fifth metatarsals.

The patient reported to the chiropractor that she sustained previous stress fractures in her proximal tibia bilaterally one year earlier and a fractured base of her fifth metatarsal due to excessive dancing. During treatment for the metatarsalgia, the patient reported performing a plank (core stability exercise) and feeling immediate discomfort on the angle of the eighth rib on the right. She immediately had pain on palpation of the eighth rib, pain with inhalation and exhalation. The patient reported to the emergency room due to the extreme pain. Radiographs and an ultrasound examination of her ribs confirmed a fracture of the anterolateral aspect of the eighth rib on the right. The medical physician referred her for a DXA scan of the entire body that was read as unremarkable by the radiolo-

gist (no osteopenia or osteoporosis). The patient was then prescribed a course of oral contraceptive medication from her family physician.

Suspecting the female athlete triad, the chiropractor proceeded with a more thorough medical history. The dancer reported no previous history of amenorrhea or oligomenorrhea. She reported a normal menstrual cycle since the age of 12. The patient reported eating two meals a day and dancing six and a half hours per day five days per week. The chiropractor asked the patient to perform a seven-day diet diary to assess for disordered eating habits. The patient denied any previous clinical eating disorders, but reported that her family physician had diagnosed her with 'non-cognitive disordered eating' (i.e. inadvertent low caloric intake) in the past. This dancer was diagnosed with the female athlete triad by the chiropractor. The case was managed with education on the female athlete triad, communication with the patient's family physician on the suspicion of the triad, and dietary counseling to increase caloric intake.

#### Case Four

A 16-year old National level ice dancer presented to the chiropractor with pain in the left ankle. The pain was constant in nature and was localized to the medial malleolus. She previously presented to a sports physician and was diagnosed with medial malleolar bursitis. The bursitis was previously managed with aspiration of the bursa and a corticosteroid injection, this procedure was performed twice with no relief of signs or symptoms. There was no referred pain or numbness and tingling surrounding the left medial malleolus. Further history revealed that she has not menstruated and had no secondary sex characteristics at the age of 16. Questions surrounding her diet and exercise habits revealed that she trains approximately five hours per day, seven days per week, and consumes limited calories. A diet analysis was then performed, revealing a significant caloric deficiency. At 16 years of age she has not reached menarche and has not shown any secondary sex characteristics. The chiropractor immediately referred her to the medical physician for a physical examination due to the suspicion of the female athlete triad. The examination revealed that she was 78lbs and five feet in height. Primary amenorrhea was diagnosed and subsequently the female athlete triad. The patient's medial malleolar bursitis was managed conservatively by the chiropractor, and

the medical physician recommended increased caloric intake to manage the triad. Approximately one year later the patient is yet to increase her caloric intake and subsequently has not advanced to menarche.

#### Discussion

The components of the female athlete triad are the following:

##### 1. *Energy Availability*

Maintaining a low body weight for the sake of performance and aesthetic purposes is a common feature among young female athletes. Energy availability refers to the amount of energy that remains in the body to be used for training and sport performance. Female athletes experience energy deficient states with high-energy expenditure due to training without adequate compensation in energy intake. Energy availability occurs along a spectrum ranging from optimal energy to low energy with or without an eating disorder or disordered eating.<sup>9</sup> The prevalence of inadvertent low energy is unknown. However, the prevalence of disordered eating among athletes is 28-62%.<sup>9</sup> Clinical eating disorders are also common in female athletes including anorexia nervosa, bulimia nervosa, and eating disorders not otherwise specified according to the DSM IV. The prevalence of eating disorders according to the DSM IV in female athletes is 25-31%. Some female athletes may have no energy available for training and sport participation because they intentionally restrict daily caloric intake while others may fall into a negative energy balance because they are unaware of the calories needed for their specific sport.<sup>4,8-12</sup>

All cases presented in this case series were managed with increasing caloric intake due to disordered eating patterns potentially caused by a negative energy balance from excessive training schedules. None of the athletes presented were diagnosed with a clinical eating disorder from the DSM IV.

##### 2. *Menstrual Function*

Menstrual function ranges from eumenorrhea (normal menstruation) to amenorrhea (no menstruation > 3 months). In adolescent female athletes under the age of eighteen the prevalence of menstrual dysfunction is 45-50%.<sup>9</sup> The prevalence of menstrual dysfunction in adult female athletes over the age of eighteen is estimated to

be 12-79%.<sup>9</sup> Comparatively, the prevalence of menstrual dysfunction in adult non-athletes is approximately two to five percent.<sup>9</sup> The prevalence of oligomenorrhea is extremely difficult to determine in adolescent females since menstrual cycle intervals of >35 days are encountered in approximately 65% of females during their first 12 months following menarche.<sup>9,13</sup> Ovulatory status and menstrual cycle lengths are highly variable for the first five years post-menarche in females.<sup>9,13</sup>

Eumenorrhea is described as menstrual cycles lasting 28+7 days in duration.<sup>5,14</sup> To maintain eumenorrhea females need to consume approximately 45kcal/kg free fat mass (FFM) per day.<sup>5,14</sup> FFM is described as the weight of the athlete minus the weight of their fat and water mass. Oligomenorrhea is defined as menstrual cycles lasting >35 days in duration and can occur in females consuming <30kcal/kg FFM per day. Lastly, the most severe form of menstrual dysfunction is amenorrhea which is described as menstrual cycles lasting >90 days in duration.<sup>4,5,9,14</sup> There are two specific types of amenorrhea, primary and secondary. Firstly, primary amenorrhea occurs in females that are 15 years of age or older with the absence of menstruation with the presence of other secondary sex characteristics. Furthermore, primary amenorrhea can also be described as females that are 14 years of age with no secondary sex characteristics present. Case four represents a case of primary amenorrhea. This female figure skater was 16 years of age with no secondary sex characteristics and had not reached menarche. Secondly, secondary amenorrhea occurs in females with a cessation of menstruation for >90 days that once menstruated.<sup>4,5,9,14</sup> The latter is common in female athletes and can be termed functional hypothalamic amenorrhea (FHA). Case one represents a case of secondary amenorrhea. This female runner had menstruated previously; her cycles had stopped for a duration of 4 years. This patient was diagnosed with functional hypothalamic amenorrhea.

FHA occurs in female athletes due to low energy availability due to intentional or unintentional caloric restriction.<sup>13,15</sup> FHA is associated with increased exercise and weight loss resulting in hypoestrogenism, ultimately resulting in a failure to obtain peak bone mass.<sup>13</sup> Low energy availability in the female athlete results in changes in physiological and neuroendocrine response including a decrease in leptin, T3, insulin, IGF-1, and plasma glucose, and a resultant increase in ghrelin, cortisol, and growth

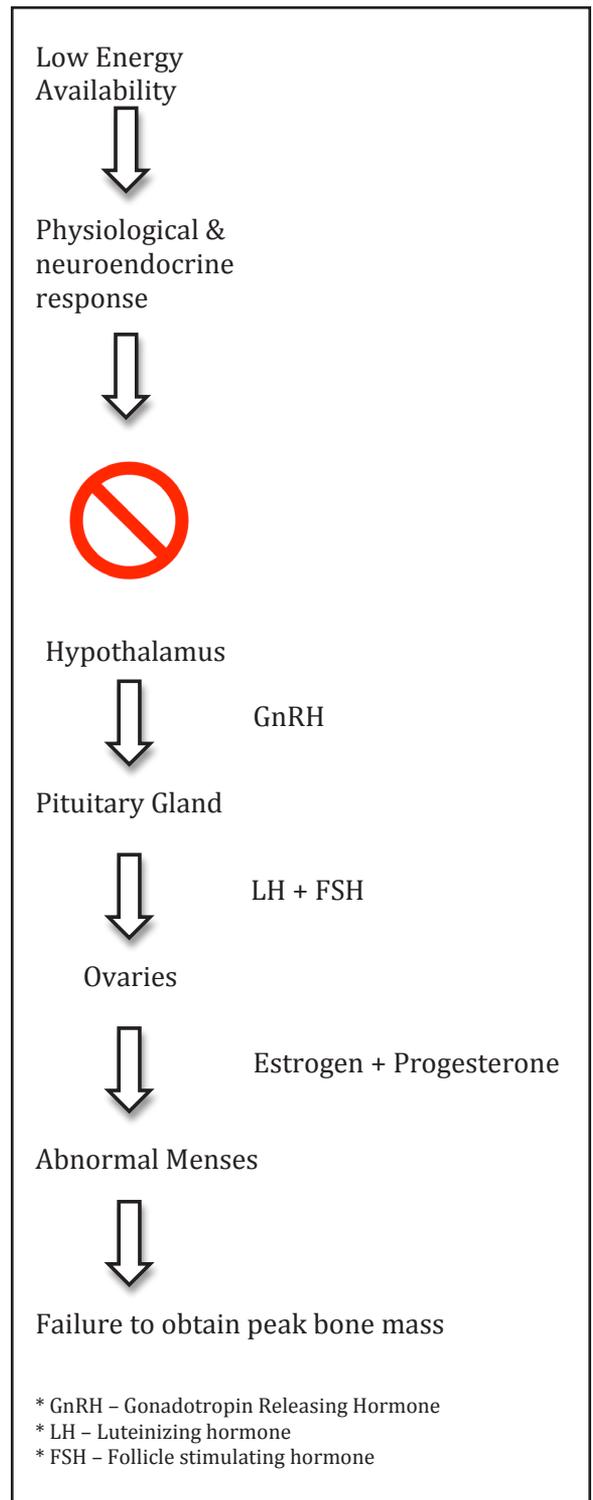


Image 4  
 Functional Hypothalamic Amenorrhea<sup>13-18</sup>

hormone. Physiological and neuroendocrine changes within the body will signal to the hypothalamus to stop producing gonado-tropin-releasing hormone (GnRH). A decrease in GnRH halts the releases of Luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary gland. Further, an overall decrease in LH and FSH suppresses the ovaries from producing estrogen and progesterone leading to abnormal menses in the female athlete.<sup>13,15,16,17,18,19,20</sup> (See Image 4).

### **3. Bone Mineral Density**

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Osteoporosis develops not only through the loss of bone mineral density during adulthood but it can also develop through the failure to accumulate sufficient bone mass during adolescent years.<sup>5,13,21,22</sup> In postmenopausal women osteopenia is defined as a T-score between  $-1$  and  $-2.5$  and osteoporosis is  $< -2.5$ . However, the terms osteopenia and osteoporosis in premenopausal females are not used in the same manner.<sup>13</sup> Z-scores are defined as the number of standard deviations above or below the mean for the patient's age, sex and ethnicity on a bone mineral density scan (DXA). T-scores are defined as the number of standard deviations above or below the mean for a healthy 30-year-old adult of the same sex and ethnicity as the patient.<sup>22</sup>

According to the International Society for Clinical Densitometry (ISCD) t-score on DXA scans are not to be used in the adolescent premenopausal population instead z-scores are to be used for comparison.<sup>23</sup> Low bone mass is defined as bone mineral density lower than expected for age-matched norms. Osteoporosis in young females should only be made with a z-score below  $-2$  together with the presence of a stress fracture, a clinically significant fracture history, disordered eating patterns, or hypogonadism.<sup>5,9,13,24</sup> Currently the epidemiological data relating to bone mineral density and fractures in premenopausal females is lacking and there is no agreement on standards for adjusting bone mineral density for bone size, pubertal stage, skeletal maturity, or body composition. Thus, fracture risk for premenopausal females cannot be predicted in the same manner as postmenopausal females.<sup>9,13</sup>

The ACSM recommends that DXA scans for premenopausal females suspected to have the female athlete triad in the following situations; oligomenorrhea/amenorrhea >

six months in duration, disordered eating/eating disorders for equal to or more than six months in duration, and the presence of a stress fracture or a fracture from minimal trauma.<sup>4</sup> Thus, the diagnosis of osteoporosis in young females is not made on densitometric criteria alone.<sup>9</sup> Clinically significant fracture history is defined as a long bone fracture of the lower extremity, a compression fracture of the spine, or two or more long bone fractures of the upper extremities. DXA scans are recommended for the lumbar spine and forearm in female athletes due to the weight bearing nature of sport. Female athletes will have an increase in bone mineral density in hips and ultimately of full body. The lumbar spine and the forearm should be carefully monitored in young female athletes because of the presence of rich trabecular bone and are submitted to little or no weight bearing during sport.<sup>4,9,25-28</sup>

Case two represents a case of a female athlete with a clinically significant fracture history. According to the ISCD it was clinically relevant to order a DXA scan for this athlete due to her clinically significant fracture history and fractures from minimal trauma. This athlete's DXA results showed a z-score of  $-2.2$  and a diagnosis of premature osteoporosis was made.

Emerging research states that the female athlete triad is no longer a triad but it is now a tetrad of interconnected conditions.<sup>29,30,31</sup> The new emerging component is endothelial dysfunction leading to an increased risk of heart disease. It has been proposed that endothelial dysfunction is caused by a decrease in estrogen ultimately from low energy availability.<sup>1,29,30,31</sup> Endothelial dysfunction is concerning because the sentinel event in cardiovascular disease pathogenesis is impaired endothelial function. Vessels contain estrogen receptors allowing for estrogen to play a regulatory role in vascular function. Estrogen stimulates the production of endothelial nitric oxide synthase, leading to increased production of endothelial-derived nitric oxide ultimately leading to vasodilation.<sup>1,29</sup> Amenorrhea is similar to menopause because low estrogen levels, whether in a pre or post-menopause, will theoretically cause impaired endothelial cell function and resultant impaired arterial dilation leading to cardiovascular disease.<sup>1,29,30,31</sup>

There are many clinical implications to reduced flow mediated dilation within vessels in athletes. Firstly, a loss of flow mediated dilation in conduit arteries may lead to a restriction in exercise-induced dilation of the ves-

sels and limit maximum blood perfusion to the tissues being supplied.<sup>1,31</sup> This process may lead to a reduction in exercise capacity and performance by restricting the amount of blood flow to critical muscles involved in exercise. Further, chronic endothelial dysfunction can lead to premature vascular changes by leading to accelerated development of atherosclerosis further leading to an increased risk of cardiovascular events.<sup>1,31</sup>

The triad may increase the risk of cardiovascular disease.<sup>1,31,32</sup> However, the strongest evidence in regard to health consequences of the female athlete triad is related to stress fractures.<sup>13</sup> The most common site for stress fractures in females is the tibia, accounting for 25-63% of all stress fractures. When a female athlete has menstrual irregularities it may increase the risk of stress fractures. However, it does seem to be controversial of whether age of menarche and oral contraceptive use play a role in stress fracture risk.<sup>13,33</sup>

### *Pre-participation Screening*

Identification of the triad takes thorough screening of all female athletes. Pre-participation screening for the triad should be performed prior to participating in any level of sport. The screening should include questions on menstrual history, exercise level, and diet history and past injuries including energy expenditure.<sup>34</sup> Important questions to ask all females prior to sport participation is age of menarche and number of menstrual periods in the past 12 months to determine if the athlete eumenorrheic, oligomenorrheic, or amenorrheic. Secondly, pre-participation screening questions must include inquiries in regard to exercise patterns, training intensity and frequency for the sport, past repetitive injuries, including history of fractures, and DXA scan scores if available.<sup>34</sup>

### *Management*

The management of the female athlete triad is controversial in the current body of literature.<sup>13</sup> The primary health care provider needs to be astute and willing to work collaboratively with a multidisciplinary team including sports psychologists, sports dieticians, coaches, therapists, physicians, and parents. Sports dieticians facilitate the design of healthy nutritional choices and maintaining an ideal body weight. Primary care providers can educate females in regard to preventing caloric deficit and maintaining a positive energy balance. Sports psychologists manage the

eating disorders and the effects on the psyche including self-esteem and self-confidence. Coaches can modify the athletes exercise intensity if needed. Parents can monitor progress, assess for compliance, and provide support and encouragement. Therapists including physiotherapists, chiropractors, and athletic therapists can assist with pain control, education on the condition and nutritional counseling. Finally physician's can be used for advanced imaging techniques and approach referrals.

Currently there is little knowledge about the clinical management of the female athlete triad, specifically, how to manage low bone mineral density and fracture risks in young females.<sup>9</sup> Haberland et al was the first group to conduct a survey on the clinical management of athletic amenorrhea in female athletes.<sup>35</sup> The results of the survey suggested that 92% of physician's surveyed used oral contraceptives and other hormonal therapeutic regimens to treat athletic amenorrhea despite the paucity of data demonstrating their efficacy in preserving bone mass.<sup>9,35,36,37</sup> One of the most recent surveys revealed that 80% of clinicians believe there are insufficient guidelines for the management of the female athlete triad, specifically for the evaluation of menstrual dysfunction, the use of bone density scans for diagnosing osteopenia in premenopausal females and treatment modalities.<sup>4</sup>

The efficacy of estrogen therapy in the form of oral contraceptives for improving bone health in premenopausal female athletes is extremely controversial in the current body of literature.<sup>9</sup> Some authors reported no change in bone mineral density after several months of oral contraceptive usage.<sup>26,36,37</sup> However, there are some studies reporting an increase in bone mineral density in the lumbar spine, hips, radius, and whole body with oral contraceptive use compared to healthy controls.<sup>38-42</sup> Studies need to control for weight gain during oral contraceptive usage due to the ultimate goal of managing the triad is to return of regular menses through proper nutrition and maintaining a reasonable body weight. Gibson et al. performed a pilot study and determined that to have an effect of 80% studies need 1180 subjects to participate, many studies are under-powered.<sup>37</sup> Further studies are required to determine if oral contraceptives can be used to replace bone loss once it has already occurred. There is consensus that oral contraceptives can be used to prevent further bone loss in female athletes. However, bone loss may be irreversible in premenopausal females.

Another pharmacological intervention for athletes suffering from the female athlete triad syndrome and functional hypothalamic amenorrhea (FHA) causing low bone mineral density is the use of bisphosphonates.<sup>9,43,44,45</sup> Bisphosphonates have been proposed to prevent further bone loss from occurring in young females athletes with FHA.<sup>43,44,45</sup> Bisphosphonates have not been shown to be superior in preventing bone loss when compared to vitamin D and calcium supplementation.<sup>43,45</sup> More research is needed to determine bisphosphonates full effects on bone mineral density in premenopausal females. Further, bisphosphonates are currently not approved by the Food and Drug Administration (FDA) for the use by premenopausal females.<sup>9</sup>

FHA impairs the attainment of peak bone mass in young premenopausal females.<sup>15</sup> It has been hypothesized that FHA may lead to an increased risk of fractures later in life due to a failure to reach peak bone mineral density in peak years.<sup>15</sup> There are several studies that have looked at the effects of increasing caloric intake and increasing weight gain for increasing bone mineral density in females with FHA.<sup>46-51</sup> The results of the aforementioned studies show promising results for increasing caloric intake as a successful and essential strategy for improving bone mineral density in premenopausal females with FHA with a resumption of regular menstruation with weight gain.<sup>15,46-51</sup> There is a need for further long-term studies to determine the effects of caloric intake and future fracture risks.<sup>15</sup>

Folic acid has been studied recently as a treatment for decreased flow mediated dilation in female athletes with FHA.<sup>52-54</sup> Folates have been hypothesized to participate in the endogenous regeneration of tetrahydrobiopterin, an essential cofactor in the production of endothelial nitric oxide synthase (eNOS). A decrease in eNOS will lead to significant decreases in nitric oxide (NO), an essential cofactor for maintaining healthy cardiovascular function.<sup>52-54</sup> Further, folic acid has a known homocysteine-lowering effect that may contribute to improvements in endothelial function and overall cardiovascular health.<sup>52-54</sup> Folic acid may also have a direct antioxidant effect in the conduit vasculature of the heart, increasing NO bioavailability, which may increase cardiovascular FMD.<sup>52-54</sup> Folic acid in 10mg dosage has been shown to improve endothelial function in various disease states but before amenorrheic female athletes can be added to this group, a

large cohort study followed for several years needs to be performed.<sup>52-54</sup>

## Summary

In summary, the female triad may actually be a tetrad of coexisting conditions including disordered eating, menstrual dysfunction, low bone mineral density, and endothelial dysfunction. A female athlete presenting with one component of the triad/tetrad should be assessed for other components by a health care practitioner to ensure proper management of the condition. It is important to note that the tetrad is not an inevitable consequence of training or of being an athlete. Rather, it mandates a call to educate young female athletes and those involved in their training of the consequence of the tetrad. It is important to educate athletes, parents, and coaches about the requirement for optimal energy intake, energy balance, and fuel intake. Oral contraceptive medication may be considered to prevent further loss of bone mineral density in athletes with FHA over the age of 16 and only if bone mineral density is decreasing despite nutrition. Bisphosphonates are approved for postmenopausal females but should not be used in young females with FHA because it is not FDA approved for use. Prevention, recognition, and treatment of the tetrad must be a priority to ensure that female athletes maximize the benefits of regular exercise and achieve optimal health as well as optimal performance.

## References:

1. Lanser EM, Zach KN, Hoch AZ. The female athlete triad and endothelial dysfunction. *PM & R : the journal of injury, function, and rehabilitation.* 2011;3(5):458-65.
2. Lynch SL, Hoch AZ. The female runner: Gender Specifics. *Clin Sports Med.* 2010; 29:477-498.
3. Mencias T, Noon M, Hoch AZ. Female athlete triad screening in National Collegiate Athletic Association Division I athletes: is the preparticipation evaluation form effective? *Clinical Journal of Sport Medicine.* 2012;22(2):122-5.
4. Otis CL, Drinkwater B, Johnson M, et al. American College of Sports Medicine position stand. The female athlete triad. *Med Sci Sports Exerc.*1997;29:1669-1671.
5. Nattiv A, Loucks AB, Manore MM, et al. American College of Sports Medicine position stand. The female athlete triad. *Medicine and Science in Sports and Exercise.* 2007;39(10):1867-82.
6. Nattiv A, Agostini R, Drinkwater B, Yeager KK. The female athlete triad. The inter-relatedness of disordered

- eating, amenorrhea, and osteoporosis. *Clin Sports Med*. 1994 Apr; 13(2):405-18.
7. Loucks AB. Energy availability, not body fatness, regulates reproductive function in women. *Exerc Sport Sci Rev*. 2003; 31(3):144-148.
  8. Thein-Nissenbaum JM, Carr KE. Female athlete triad syndrome in the high school athlete. *Physical Therapy in Sport*. 2011;12(3):108-16.
  9. Ducher G, Turner AI, Kukuljan S, Pantano KJ, Carlson JJ, Williams NI, De Souza MJ. Obstacles in the optimization of bone health outcomes in the female athlete triad. *Sports Medicine*. 2011;41(7): 587-607.
  10. Pantano KJ. Strategies used by physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine. 2009;10(1):3-11.
  11. Raymond-Baker P, Petroczi A, Quested E. Assessment of nutritional knowledge in female athletes susceptible to the female athlete triad syndrome. *J Occupational Medicine and Toxicology*. 2007; 2(10): 1-11.
  12. Brunet M. Female athlete triad. *Clinics in Sports Medicine*. 2005;24(3):623-36.
  13. Manore MM, Kam LC, Loucks AB. The female athlete triad: components, nutrition issues, and health consequences. *J Sports Sciences*. 2007;25 Suppl 1(January 2012):S61-71.
  14. Loucks AB, Nattiv A. Essay: The female athlete triad. *The Lancet*. 2005;366:S49-S50.
  15. Vescovi JD, Jamal SA, De Souza MJ. Strategies to reverse bone loss in women with functional hypothalamic amenorrhea: a systematic review of the literature. *Osteoporosis International*. 2008;19:465-478.
  16. Wade GN, Jones JE. Neuroendocrinology of nutritional infertility. *Am J Physiol Regul Integr Comp Physiol*. 2004; 287:R1277-96.
  17. Loucks AB, Thuma JR. Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. *J Clin Endocrinol Metab*. 2003; 88(1):297-311.
  18. Laughlin GA, Yen SS. Nutritional and endocrine-metabolic aberrations in amenorrheic athletes. *J Clin Endocrinol Metab*. 1996;81:4301-4309
  19. Thong FS, McLean C, Graham TE. Plasma leptin in female athletes: Relationship with body fat, reproductive, nutritional, and endocrine factors. *J Applied Physiology*. 200;88:2037 – 2044.
  20. Ackerman KE, Skrinar GS, Medvedova E, Misra M, Miller KK. Estradiol levels predict bone mineral density in male collegiate athletes: a pilot study. *Clinical Endocrinology*. 2012; 76(3):339-345.
  21. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis and Therapy. Osteoporosis prevention, diagnosis, and therapy. *J Am Med Assoc*. 2001;285:785 – 795.
  22. Burr DB. The contribution of the organic matrix to bone's material properties. *Bone*. 2002;31:8 – 11.
  23. International Society for Clinical Densitometry Position Development Conference. The diagnosis of osteoporosis in men, premenopausal women and children. *J Clin Densitom*. 2004; 7:17-26.
  24. Khan KM, Liu-Ambrose T, Sran MM, et al. New criteria for female athlete triad syndrome? *Br J Sports Med*. 2002; 36:10-3.
  25. Hind K. Recovery of bone mineral density and fertility in a former amenorrheic athlete. *J Sports Sci Med*. 2008; 7:415-8.
  26. Gremion G, Rizzoli R, Slosman D et al. Olio-amenorrheic long-distance runners may lose more bone in spine than in femur. *Med Sci Sports Exerc*. 2001 Jan; 33 (1); 15-21.
  27. Braam LA, Knapen MH, Geusens P, Brouns F, Vermeer C. Factors affecting bone loss in female endurance athletes: A two year follow-up study. *Am J Sports Med*. 2003;31(6):889–895.
  28. Gordon CM, Lawrence NM. Amenorrhea and bone health in adolescent and young women. *Obstetrics & Gynecology*. 2003; 15(5): 377-384.
  29. Hoch AZ, Papanek P, Szabo A, et al. Association between the female athlete triad and endothelial dysfunction in dancers. *Clinical Journal of Sport Medicine*. 2011;21(2):119-25.
  30. Hoch AZ, Lal S, Jurva JW, Gutterman DD. The female athlete triad and cardiovascular dysfunction. *Phys Med Rehab Clinics of North America*. 2007; 18(3): 385-400.
  31. Rickenlund A, Eriksson MJ, Schenck-Gustafsson K, Hirschberg AL. Oral contraceptives improve endothelial function in amenorrheic athletes. *The Journal of Clinical Endocrinology and Metabolism*. 2005;90(6):3162-7.
  32. De Souza MJ, Williams NI. Physiological aspects and clinical sequelae of energy deficiency and hypoestrogenism in exercising women. *Hum Reprod Update*. 2004; 10(5):433-48.
  33. Shaffer RA, Rauh MJ, Brodine SK, Trone DW, Macera CA. Predictors of stress fracture susceptibility in young female recruits. *Am J Sports Med*. 2006; 34(1):108-115.
  34. Hobart J a, Smucker DR. The female athlete triad. *American Family Physician*. 2000;61(11):3357-64, 3367.
  35. Haberland CA, Seddick D, Maracus R, et al. A physician survey of therapy for exercise-associated amenorrhea: a brief report. *Clin J Sport Med*. 1995; 5(4):246-50.
  36. Warren MP, Chua AT. Exercise-induced amenorrhea and bone health in the adolescent athlete. *Ann NY Acad Sci*. 2008; 1135:244-52.
  37. Gibson JH, Mitchell A, Reeve J, et al. Treatment of reduced bone mineral density in athletic amenorrhea: a pilot study. *Osteoporos Int*. 1999; 10(4):284-9.
  38. Castelo-Branco C, Vicente JJ, Pons F, et al. Bone mineral density in young, hypothalamic oioamenorrheic women treated with oral contraceptives. *J Reprod Med*. 2001 Oct; 46(10):875-9.
  39. Rickenlund A, Carlström K, Ekblom B, et al. Effects of

- oral contraceptives on body composition and physical performance in female athletes. *The Journal of Clinical Endocrinology and Metabolism*. 2004;89(9):4364-70.
40. DeCree C, Lewin R, Ostyn M. Suitability of epyroterone acetate in the treatment of osteoporosis associated with athletic amenorrhea. *Int J Sports Med*. 1988 June; 9(3):187-92.
  41. Cumming DC. Exercise-associated amenorrhea, low bone density, and estrogen replacement therapy. *Arch Intern Med*. 1996; 156:2193–2195.
  42. Warren MP, Miller KK, Olson WH, Grinspoon SK, Friedman AJ. Effects of an oral contraceptive (norgestimate/ethinyl estradiol) on bone mineral density in women with hypothalamic amenorrhea and osteopenia: an open-label extension of a doubleblind, placebo-controlled study. *Contraception*. 2005; 72:206–211.
  43. Nakahara T, Nagai N, Tanaka M, et al. The effects of bone therapy on tibial bone loss in young women with anorexia nervosa. *The International Journal of Eating Disorders*. 2006;39(1):20-6.
  44. Miller KK, Grieco KA, Mulder J, Grinspoon S, Mickley D, Yehezkel R, Herzog DB, Klibanski A. Effects of risedronate on bone density in anorexia nervosa. *J Clin Endocrinol Metab*. 2004 Aug;89(8):3903-6.
  45. Golden NH, Iglesias EA, Jacobson MS, Carey D, Meyer W, Schebendach J, Hertz S, Shenker IR. Alendronate for the treatment of osteopenia in anorexia nervosa: a randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2005; 90:3179–3185.
  46. Dominquez J, Goodman L, Sen Gupta S, et al. Treatment of anorexia nervosa is associated with increases in bone mineral density, and recovery is a biphasic process involving both nutrition and return of menses. *Am J Clin Nutr*. 2007; 86:92-9.
  47. Viapiana O, Gatti D, Dalle Grave R, Todesco T, Rossini M, Braga V, Idolazzi L, Fracassi E, Adami S. Marked increases in bone mineral density and biochemical markers of bone turnover in patients with anorexia nervosa gaining weight. *Bone*. 2007; 40:1073–1077.
  48. Compston JE, McConachie C, Stott C, Hannon RA, Kaptoge S, Debiram I, Love S, Jaffa A. Changes in bone mineral density, body composition and biochemical markers of bone turnover during weight gain in adolescents with severe anorexia nervosa: a 1-year prospective study. *Osteoporos Int*. 2006; 17:77–84.
  49. Bolton JG, Patel S, Lacey JH, et al. A prospective study of changes in bone turnover and bone density associated with regaining weight in women with anorexia nervosa. *Osteoporos Int*. 2005 Dec; 16(12): 1955-62.
  50. Zanker CL, Cooke CB, Truscott JG, et al. Annual changes of bone density over 12 years in an amenorrheic athlete. *Med Sci Sports Exerc*. 2004; 36(1):137-42.
  51. Fredericson M, Kent K. Normalization of bone density in a previously amenorrheic runner with osteoporosis. *Med Sci Sports Exerc*. 2005; 37(9):1481-6.
  52. Hoch AZ, Lynch SL, Jurva JW, Schimke JE, Gutterman DD. Folic acid supplementation improves vascular function in amenorrheic runners. *Clinical Journal of Sport Medicine*. 2010;20(3):205-10.
  53. Hoch AZ, Pajewski NM, Moraski L, et al. Prevalence of the female athlete triad in high school athletes and sedentary students. *Clin J Sport Med*. 2009;19(5):421-428.
  54. Hoch AZ, Pajewski NM, Hoffmann RG, et al. Possible relationship of folic acid supplementation and improved flow-mediated dilation in premenopausal, eumenorrheic athletic women. *J Sports Sci Med*. 2009;8:123–129.