Sex Differences in Sports Medicine

ELLEN CASEY
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SEX DIFFERENCES IN SPORTS MEDICINE

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This book is dedicated to my parents, Bill and Kristine,
for their endless encouragement. To my husband Chris and my children,
Nathaniel and Emersyn, for their support and love. And finally,
to my sports medicine colleagues, for our shared passion
in caring for athletes of all kinds.
—Ellen Casey, MD

I dedicate this book to my parents, Cecilia and Jae Rho, who came from a culture
and a generation that placed limits on women in sports and in medicine.
Throughout my life, I have inherited many wonderful things from my parents,
but they never passed these limitations on to me. In fact, they have always
encouraged me to go beyond where I can see.
—Monica Rho, MD

To my best friends—Gayle, Hannah, Aaron, and Jenny.
—Joel Press, MD

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PREFACE

The title of this book nearly became *Gender Differences in Sports Medicine.* Before embarking on this book, we used the terms *sex* and *gender* interchangeably. However, "gender" refers to the phenotype that comprises psychosocial, cultural, and behavioral factors, whereas "sex" refers to the genotype of the chromosomal complement present in cells, hormonal profiles, and sex organs. This book is aimed at addressing the biology behind the differences of men and women in sports medicine, which is why the preferred term we use in our title and in our chapters is "sex differences."

The theme of this book may immediately engender some feeling that the book is going to address one sex being superior to the other in the arena of sports medicine. In creating this book it is not our intent to add to the "battle of the sexes" or to determine superiority between them. *Sex Differences in Sports Medicine* is written for the sports medicine clinician who wants to take his or her approach to the next level of personalized care. A PubMed search on sex or gender differences in the musculoskeletal system reveals very little literature prior to the late 1990s. Before that time little thought was given to sex-specific differences in researching the musculoskeletal system. Since that time, and with the overwhelming effects of Title IX legislation increasing female participation in sports, there has been a noticeable shift in musculoskeletal research acknowledging sex disparity. We have been interested in these differences for many years. Inherently, when we treat men and women in our offices we attempt to utilize sex-specific approaches to their sports-related injuries. However, there has been no singular source of collected information on the sex-specific differences in sports medicine in textbook form.

A few years ago we created an academic symposium entitled "The Active Female Across the Lifespan." This course focused on the ever-changing female musculoskeletal system and how it impacts risk of injury and response to treatment of active females at key maturational phases. We invited nationally renowned speakers to the Rehabilitation Institute of Chicago, who eloquently explained the female musculoskeletal system. Educationally, the symposium was outstanding. However, as the directors of this course we could not help but notice that less than 5% of our course participants were male. We learned a significant lesson during the development of this course—in order to engender true understanding of sex-specific differences, you can neither focus on nor alienate one sex. Isolating one sex from the other tends to automatically segregate your audience. There are textbooks focused on topics relevant to the "female athlete." The intention of this book is to present the sex-specific differences of both men and women in order to provide sports medicine clinicians a well-rounded understanding of these issues.

We would like to thank all of the authors who contributed to this book. We have had a tremendous amount of support from them to make this a truly one-of-a-kind textbook. We asked for their creativity in creating the outline of their chapters, their diligence in presenting the most current research findings, and their dedication in synthesizing this information for mass consumption. Our authors share our common goal, which is to educate other clinicians about these sex-specific differences so that we can provide better care to our athletes. We hope that you, our readers, will take this information and incorporate it into your everyday clinical practice.

Ellen Casey, MD
Monica Rho, MD
Joel Press, MD

INTRODUCTION

Ever since humankind crawled out of the primordial soup or Adam and Eve came to be in the Garden of Eden, men and women have existed side by side. Although they both evolved over the same time period and were exposed to similar climate and evolutionary forces, differences in their structural make up exist. Anatomic changes have occurred to serve various evolutionary needs. Man, originally, was felt to be the hunter/gatherer while women were needed to raise the offspring and protect them as they grew. Over the centuries their roles have evolved as well as their overall activity levels. Ultimately, humans began to be engaged in physical activity, not only for survival, but for recreation and sport. The loads placed on the musculoskeletal system during sports and physical activity can have different and varying effects on men and women owing to numerous muscle, bone, and connective tissue differences. Understanding some of these differences may be a key to understanding the evaluation and treatment of many sports-related musculoskeletal disorders.

The only difference between male and female skeleton models is that the female has a more rounded pelvis, but in reality there are many subtle differences between male and female skeletons (1). First of all, bones develop at different rates in males and females. The bones in a female body mature earlier than those in the male body. Note the tallest person in the class picture in kindergarten is often a girl. Female bones complete their development around age 18, while male bones continue to mature until around age 21. This is part of the explanation behind the difference in the average size of male and female bones—because the male bones continue to grow and develop longer, they also become larger (on average) and have more pronounced corners. Thus the jawbone is generally larger and more pronounced in males and the brow is taller (1). Male skeletons also generally have longer, thicker bones in the arms, legs, and fingers. Women have a much broader pelvic bone than men to facilitate parturition. The effects of these subtle differences will be reflected on in later chapters on the sports-related injuries

Besides skeletal differences, changes in ligament and cartilage can vary between men and women, at least in part due to hormonal differences. Ligamentous laxity in general has been found to be greater in women and may explain issues of ankle instability, shoulder instability, and anterior cruciate ligament (ACL) injuries that occur more often in women (2). Cartilage changes are also noted to be different between the sexes and osteoarthritis of the knee develops more frequently in women compared with men (2). In asymptomatic women between ages 50 and 79 years, MRI studies showed that women lose cartilage in the tibia at four times the annual rate of men (2). More recent studies have shown sex-specific differences in peak torque, muscle stiffness, and musculoarticular stiffness of the knee joints in a young active population where females demonstrated less normalized peak torque, relaxed muscle stiffness, and contracted musculoarticular stiffness. These observed differences may contribute to higher knee injury incidence and prevalence in females when compared to males (3). There is also literature that suggests that there are sex-specific responses of knee extensor torque to maximal-effort contractions (4) and differences in leg stiffness (5).

To better understand the sex differences between men and women as they relate to sports injuries, we first need to understand the background of sports participation of men and women. Men and women have not equally participated in sports and recreational activities over mankind's life span. History shows that women were actually engaged in some sport three millennia ago. Homer (c. 800 BC) relates the story of Princess Nausicaa playing ball with her handmaidens next to a riverbank on the island of Scheria: "When she and her handmaids were satisfied with their delightful food, each set aside the veil she wore: the young girls now played ball; and as they tossed the ball. . . ." (Homer, lines 98–112) (6). The second-century BC grammarian

Agallis attributed the invention of ball games to Nausicaa, most likely because Nausicaa was the first person in literature to be described playing with a ball. It took thousands of years before women were involved in any sort of play activities that were more than recreational (7).

In 1874, as women were beginning to gain access to higher education, Dr. Edward Clarke published *Sex in Education; Or, A Fair Chance for Girls*, which sparked tenacious and acrimonious debate about the capacity of women for physical activity (6). Ultimately, in the late 1800s and early 1900s, women began to form informal athletic clubs that involved tennis, croquet, bowling, and archery. Early college sports for women were largely intramural (within colleges between students). Finally, the confluence of numerous movements, including passage of the Nineteenth Amendment allowing women to vote, the war effort of women in World War II as demonstrated by "Rosie the Riveter," the Civil Rights Act of 1964, feminist activism of the 1960s and 1970s, and the formation of associations for women's athletics led to the evolution of Title IX and its passage in 1972 (6). Title IX gave women the right to participate in sports on a plane equal to men. The impact on female participation in athletics has been dramatic (8). Increased participation also carries with it an increased number of athletes exposed to potential injuries. As women's participation in sports has been brought closer to levels observed in men, differences in injury types and frequencies need to be addressed.

For many years the debate as to the susceptibility of the different sexes to specific injuries has been clouded by reporting of actual number of athletes participating in sports, injury mechanisms, definitions of injuries, and the number of exposures to possible injuries (9–11). A retrospective study by Sallis et al. of patterns of injuries between men and women, which looked at over 3,700 athletes, spanning 15 years, showed that except for some minor sex differences in total injuries for two sports (swimming and water polo) and several differences in total injuries by anatomic location, very little difference exists in the pattern of injury between men and women competing in comparable sports (12). Wolf et al. also showed no significant relationship between occurrence of injury and gender in Division 1 collegiate swimming (13). Similar findings were noted in gymnastics (14) and cross-country skiers, swimmers, long-distance runners, and soccer players (15). However, although injury rates are similar between men and women for many sports, the anatomic locations of these injuries can vary. Arendt and Dick showed significantly higher anterior cruciate ligament injury rates in both basketball and soccer in females compared with males (16). Sallis's retrospective review also confirmed several differences in total injuries by anatomic location. Understanding some of these gender-specific issues related to sports injuries can help the sports medicine clinician address prevention, evaluation, diagnosis, and rehabilitation of sports injuries.

Men and women have evolved over the centuries to be very active in recreational and sporting activities. Patients of both sexes come to our clinics every day with various sports-related injuries. Often they will have specific issues that need to be evaluated with a good understanding of sex-related nuances and differences. It is the purpose of this book to provide an in-depth look at the musculoskeletal system and tease out some of the many sex-related issues that affect our patients in hopes of providing better care for them.

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SEX DIFFERENCES IN SPORTS MEDICINE

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1

SEX HORMONES

Mary Caldwell, Ellen Casey, Bethany Powell, and Sandra J. Shultz

INTRODUCTION

Hormones affect the entire neuromusculoskeletal system in various ways depending on age, sex, and hormone concentration. Hormonal changes, which can be seen in the pubertal or the aging athlete, as well as during the menstrual cycle, may influence sports-related injury or sports performance. Therefore, the clinician treating musculoskeletal conditions must understand the implications of these hormonal changes in the male versus female athlete. In order to best approach this topic, we begin with a discussion of the key hormones in sexual development as well as their production and concentration across the life span. We then focus on the individual and combined hormonal effects on the many tissues in the musculoskeletal system, including a brief basic science review of collagen metabolism and function. We combine the findings from clinical studies and animal models to explore how hormonal differences between males and females may have implications on sports performance and sports-related injury. We end with a review of what we know about the influence of hormonal contraceptives on the musculoskeletal system and the role of sex hormones in anterior cruciate ligament (ACL) injury to highlight the clinical relevance of this material.

REVIEW OF HORMONAL PRODUCTION

The hormones produced by the human body are generally divided into four classes: steroids, peptides, amino acids, and fatty acids. Steroid hormones, such as estrogen, progesterone, and testosterone, are all fat-soluble molecules made from cholesterol. Growth hormone (GH), relaxin (1), and insulin-like growth factor 1 (IGF-1) are all water-soluble polypeptide hormones (2). This chapter focuses primarily on the steroid hormones and polypeptide hormones as they share the responsibility for growth and biologic dimorphism (3–5).

Steroid Hormones: Estrogen, Progesterone, and Testosterone

Progesterone, estrogen, and testosterone are created through the process of steroidogenesis (6–8). Steroidogenesis can be considered a single process that is repeated in various glands, such as the skin, ovary, or testicle, with cell-type specific variations (9). Cholesterol is converted to pregnenolone and then the specific hormone produced depends on the tissue and enzymes present (9). A steroid hormone is classified by the receptor it binds. Hence, while androgens, progestogens, and estrogens are considered steroid hormones, they are all of a different subclass since they bind to different steroid hormone receptors (10). Understanding the conversion and production of each of these hormones with relation to one another is crucial to interpreting the clinical relevance of hormonal imbalances with regard to biologic dimorphism and implications in sports medicine (Figure 1.1).

Estrogen is produced from the conversion of testosterone or androstenedione via the enzyme aromatase (11). In both males and females, production and conversion occur in adipose tissue, skin, muscle (8, ch. 13;12), and brain (13). In males, 80% of estrogen is produced by the peripheral glands while 20% is produced by the leydig cells in the testes (8, ch. 16). In premenopausal women, 95% of estrogen production occurs in the granulosa cells of the developing follicle during the proliferative phase and the corpus luteum during the luteal phase (LP) of the menstrual cycle (8, ch. 13). The most common estrogens are estradiol, estrone, and estriol. Estradiol is created primarily in the ovary and is the major form of circulating estrogen in nonpregnant females of reproductive age (8, ch. 13). Estrone, also primarily produced in the ovary, is the dominant type of estrogen present in postmenopausal women and has

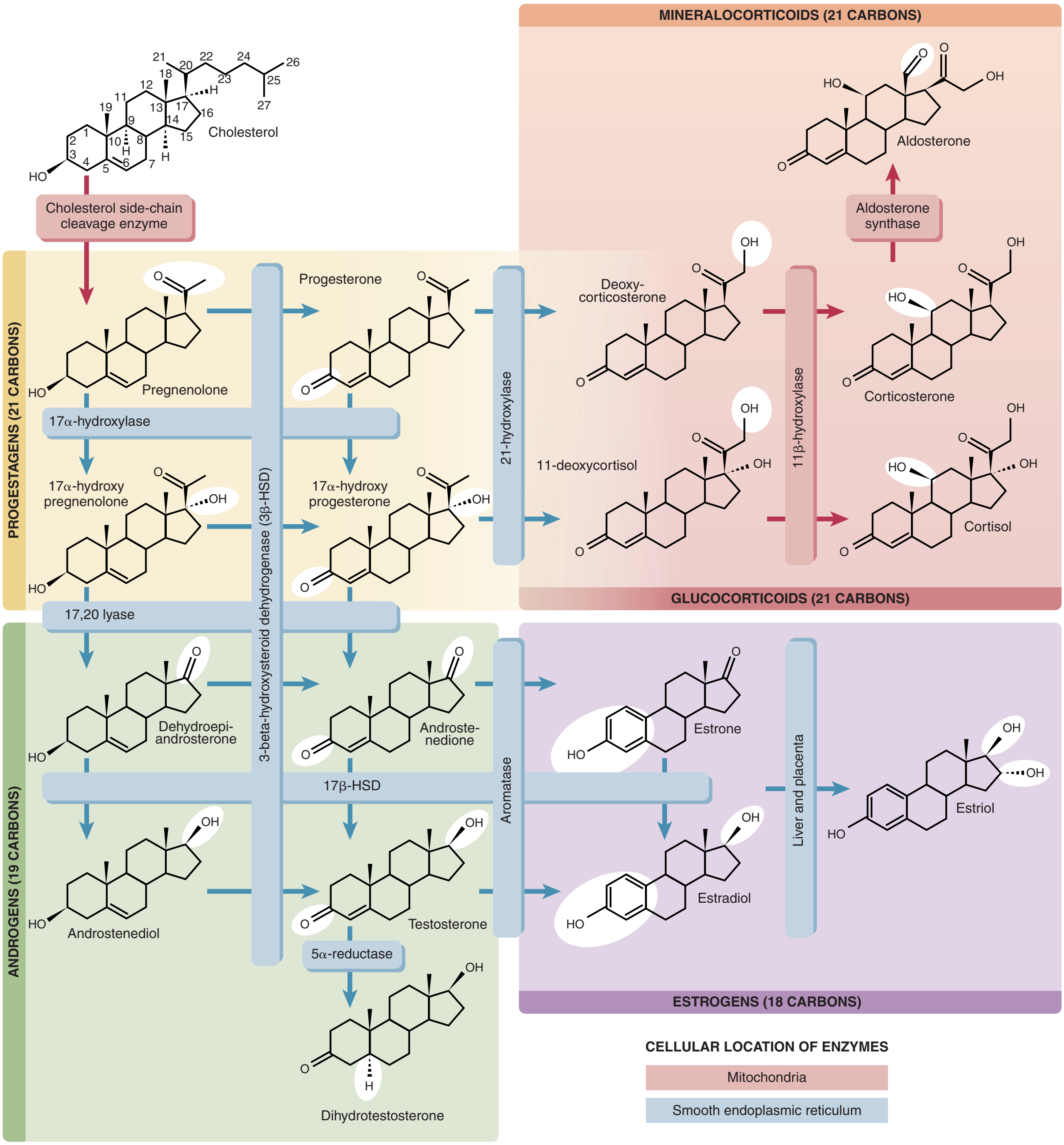

FIGURE 1.1: Steroidogenesis.

about one third of the potency of estradiol (8, ch. 13). Estriol is produced mainly in the placenta in pregnant women due to enzymes produced by the fetus and is biologically relevant only during pregnancy (8, ch. 13). Unless otherwise noted, estradiol is the form of estrogen discussed in this chapter. Estrogen acts primarily as an endocrine factor, but can also act as a paracrine factor. In the blood, 60% of estrogen is bound to albumin, 38% is bound to sex hormone-binding globulin (SHBG), and the remaining 2% is free (8, ch. 13) (Figure 1.2).

Progesterone is primarily produced by steroidogenesis in the corpus luteum during the LP of the menstrual cycle (8, ch. 13). During this phase, the granulosa cells convert thecal androgens to progesterone. The enzymes in the corpus luteum differ from the enzymes of the developing follicle, making progesterone synthesis favorable (8, ch. 13). In males, the leydig cells produce progesterone (8, ch. 12). Progesterone is also produced in the adrenal glands and nervous system by both sexes (6,7). Once progesterone enters the blood, 80% binds to albumin, 18% binds to corticosteroid-binding globulin, and 2% remains free (14) (Figure 1.2).

Testosterone is produced from steroidogenesis in the testes, ovaries, and adrenal glands. The testicular leydig cells in males produce over 95% of male testosterone, while in females, the ovaries produce the majority of testosterone. The adrenal glands also produce androgens called dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEA-S) that are later converted to testosterone in multiple tissues, including the skin and muscle (12,15,16). In males, a small amount of testosterone is further converted to a five times more potent androgen called dihydrotestosterone (DHT) (17). Recall that in both sexes, testosterone can be converted to estrogen via the enzyme aromatase (11) (Figure 1.3).

Polypeptide Hormones: Relaxin, Growth Hormone, and Insulin-Like Growth Factor 1

Relaxin can be divided into two common types in humans: H2 and H3. H2 relaxin mainly binds the relaxin family peptide (RFXP) 1 receptor and is produced primarily by the corpus luteum and placenta (18). This isoform is also produced by the heart, blood vessels, breast, skin, liver, bone, and prostate (18). H3 relaxin is produced by the brain and testes and binds RXFP3 and RFXP1, although it binds RFXP1 with lower affinity than H2 relaxin (18). Relaxin, in this chapter, refers to H2 relaxin unless otherwise noted (Figure 1.4).

GH is produced by the pituitary gland, which then stimulates production and release of IGF-1 from the liver (5). IGF-1 mediates the anabolic actions of GH (19). The relationship between GH and IGF-1 is referred to as the GH/IGF-1 axis (20). Besides liver production, osteocytes can also secrete IGF-1 in response to mechanical loading (3) (Figure 1.5).

HORMONAL REGULATION

The neuro-endocrine axis regulates the production of hormones throughout the life span, causing levels to vary with age and sex. The hypothalamus releases gonadotropin-releasing hormone (GnRH) (8, ch. 15), growth hormone-releasing hormone (GHRH), and growth hormone-inhibiting hormone (GHIH), which act on the anterior pituitary (21). GnRH regulates the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary gland (8, ch. 15), while GHRH and GHIH regulate the release of GH from the anterior pituitary gland (21) (Figures 1.2–1.5). GH then stimulates production and release of IGF-1 from the liver (5). Meanwhile, LH and FSH govern the production of estrogen, progesterone, and testosterone. Also, important in the regulation of estrogen and testosterone is sex hormone-binding globulin (SHBG). SHBG is produced primarily in the liver, but it is also produced in the uterus, brain, and testes. It essentially manages the bioavailability of the two main sex hormones (testosterone and estrogen). In general, SHBG decreases with high concentrations of androgens and increases with low concentrations of androgens (22). For example, if androgen levels are high, SHBG production is decreased proportionally, leading to appropriate activity of androgens. However, if there is too little SHBG for whatever reason, there can be excess androgen effects such as increased body hair and acne. Likewise, when androgen levels are low in response to the hypothalamic-pituitary-gonadal axis, SHBG production is increased to make a portion of the androgens biologically inactive (23,24). In contrast, SHBG levels increase with high-estrogen states such as pregnancy (22).

HORMONAL DIFFERENCES BY AGE, SEX, AND MENSTRUAL CYCLE

This section will discuss sex differences in hormonal concentrations throughout the life span. Please refer to Figure 1.6 for hormonal concentrations during the perinatal, prepuberty, puberty, male postpuberty, and female postmenopause time periods. Please refer to Figure 1.7 for hormonal concentrations during the female menstrual cycle.

(*text continued on page 9*)

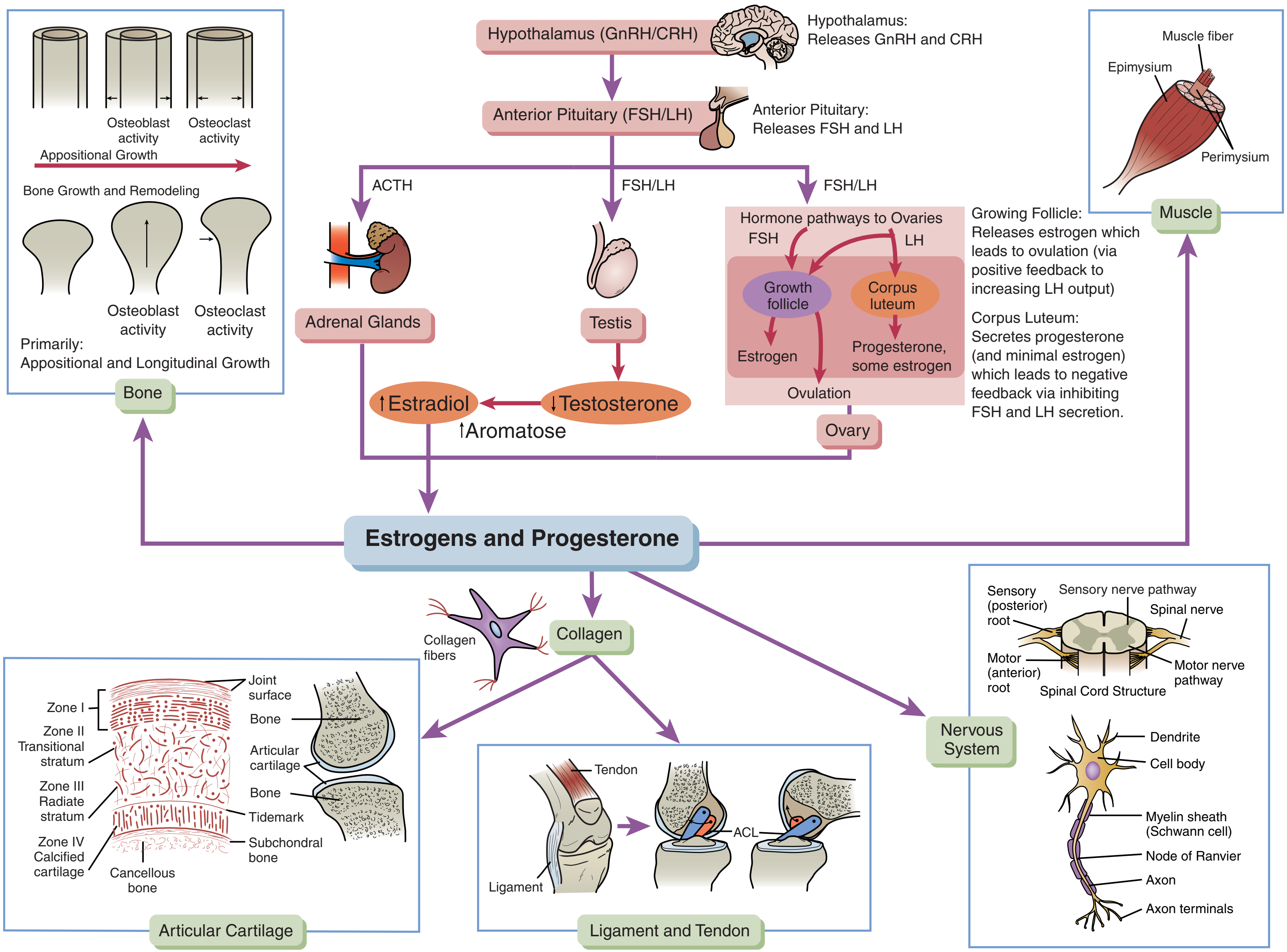

FIGURE 1.2: Estrogen and progesterone in the neuromusculoskeletal system.

ACTH, adrenocorticotropic hormone; ACL, anterior cruciate ligament, CRH, corticotropic releasing hormone; FSH, follicle stimulating hormone; GnRH, gonadotropin releasing hormone; LH, luteinizing hormone.

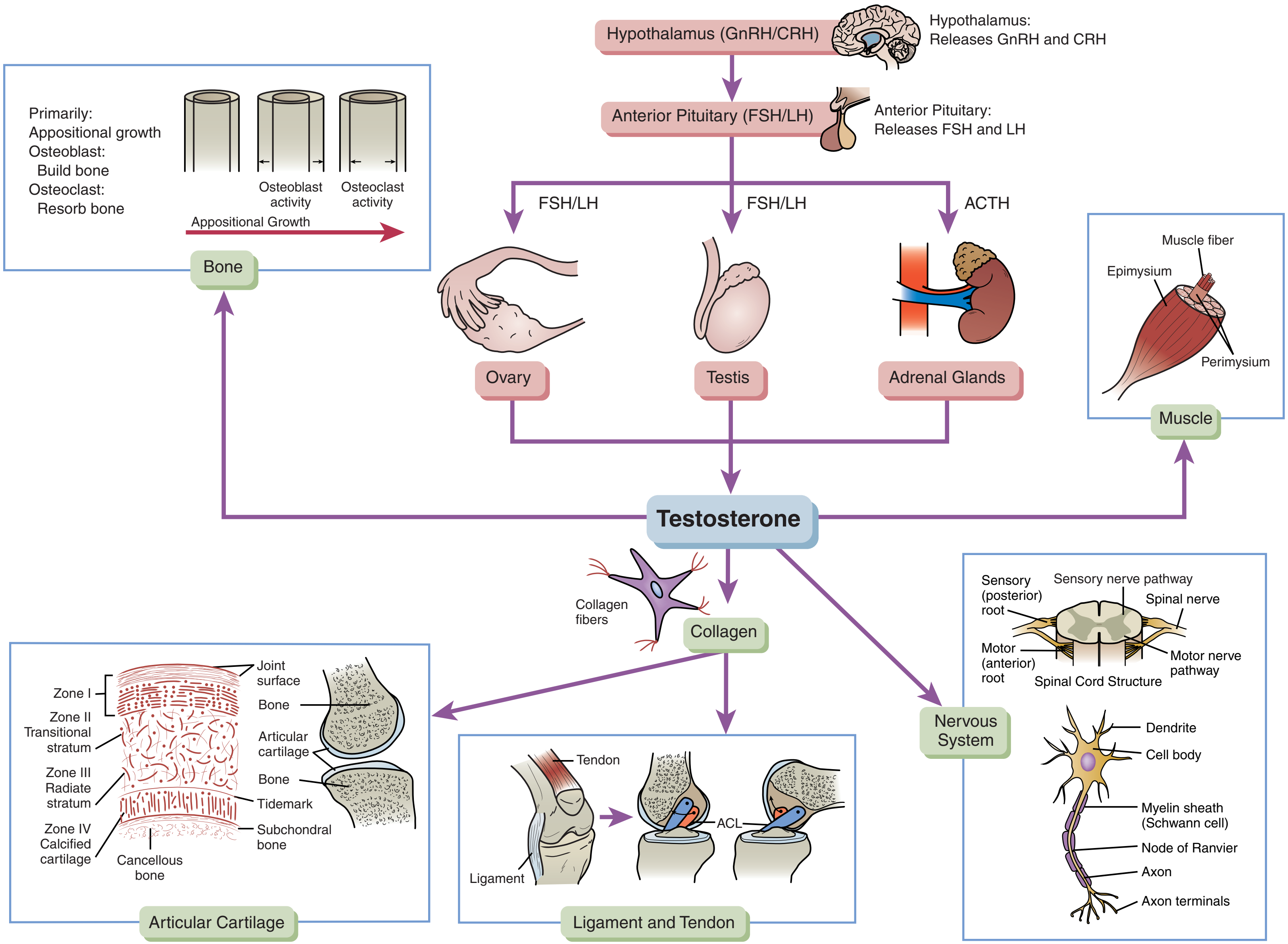

FIGURE 1.3: Testosterone in the neuromusculoskeletal system.

ACTH, adrenocorticotropic hormone; FSH/LH, follicle stimulating hormone/luteinizing hormone; GnRH, gonadotropin releasing hormone.

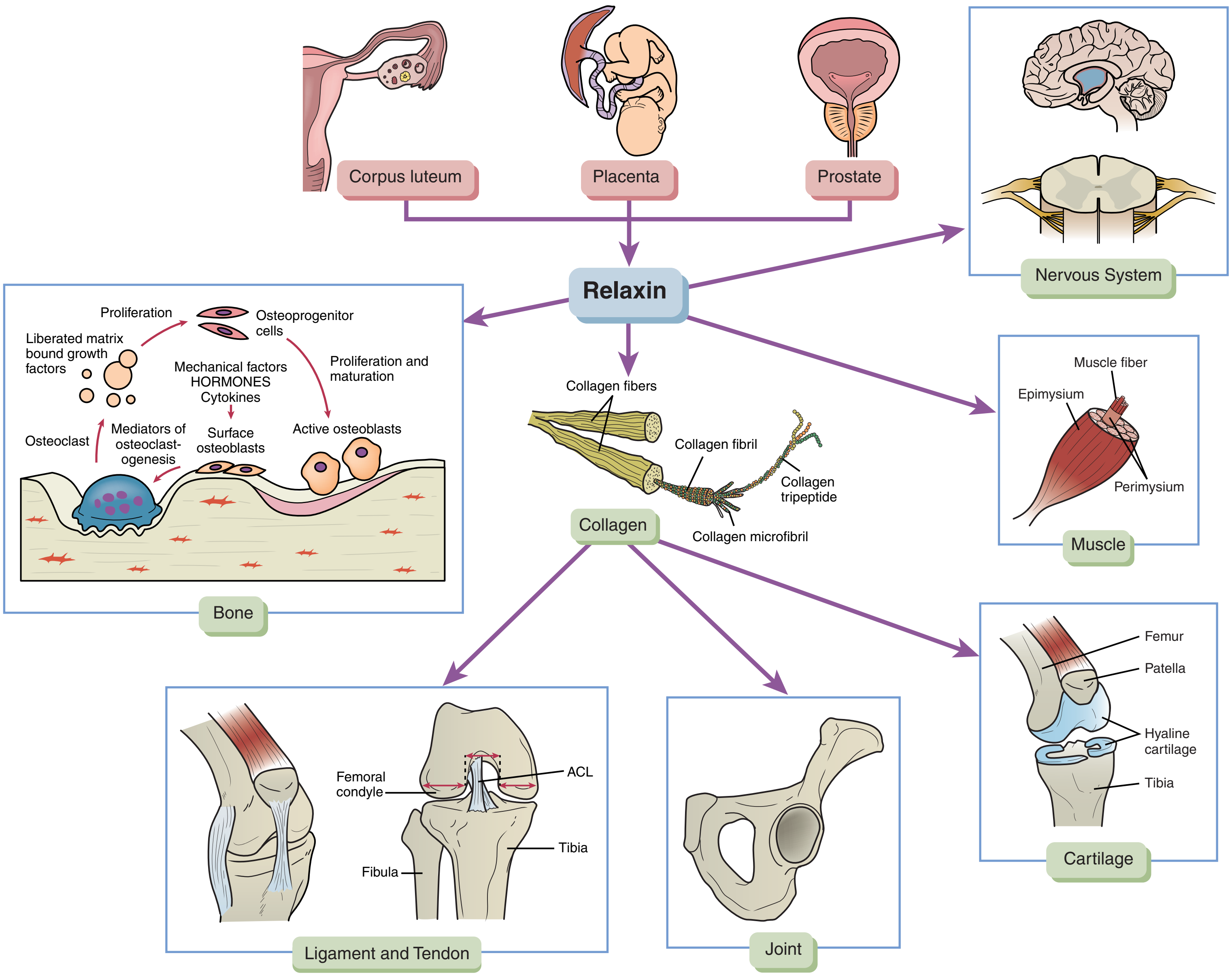

FIGURE 1.4: Relaxin in the neuromusculoskeletal system.

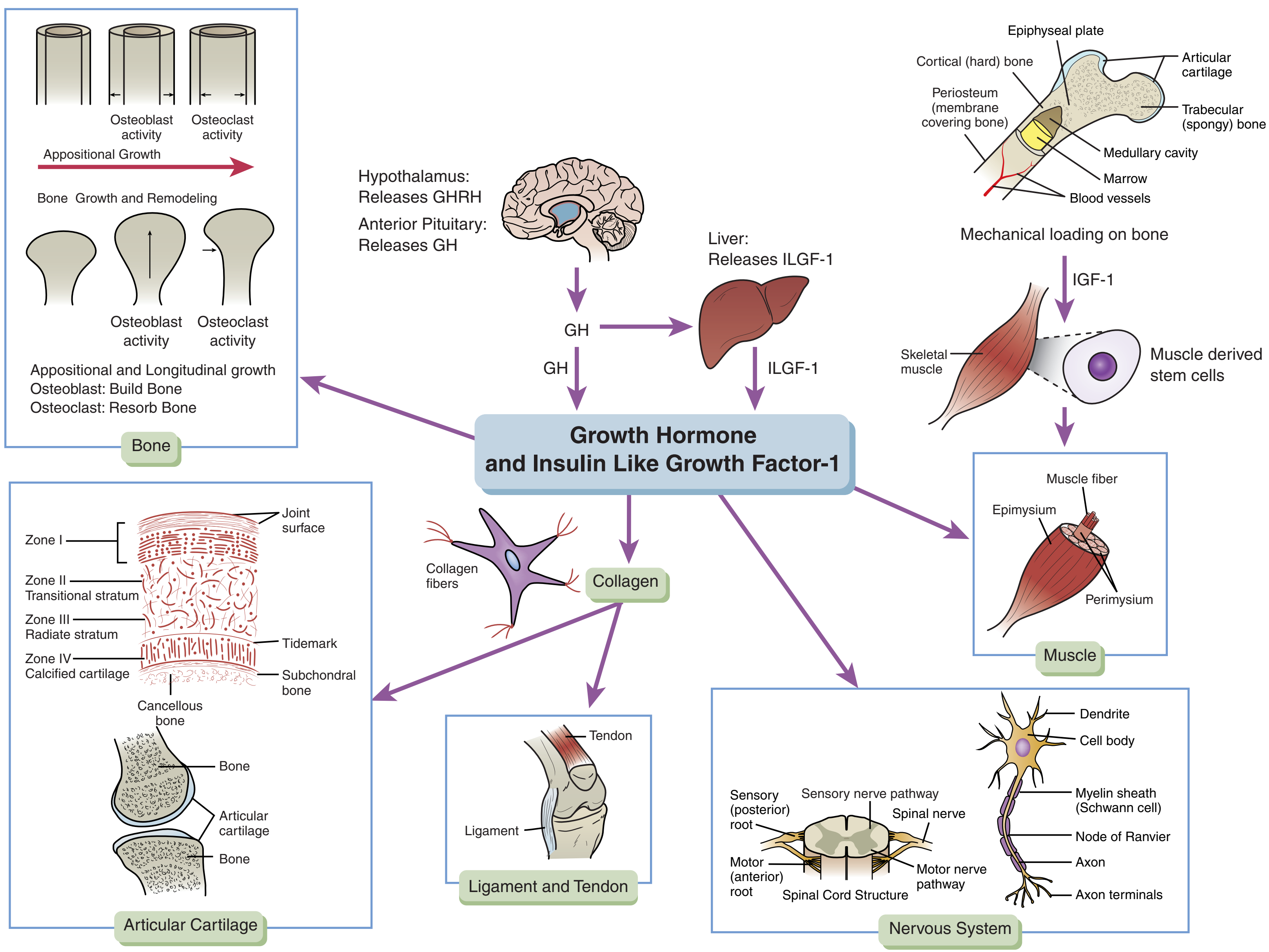

FIGURE 1.5: Growth hormone and IGF-1 in the neuromusculoskeletal system.

GH, growth hormone; IGF-1/ILGF-1, insulin like growth factor 1.

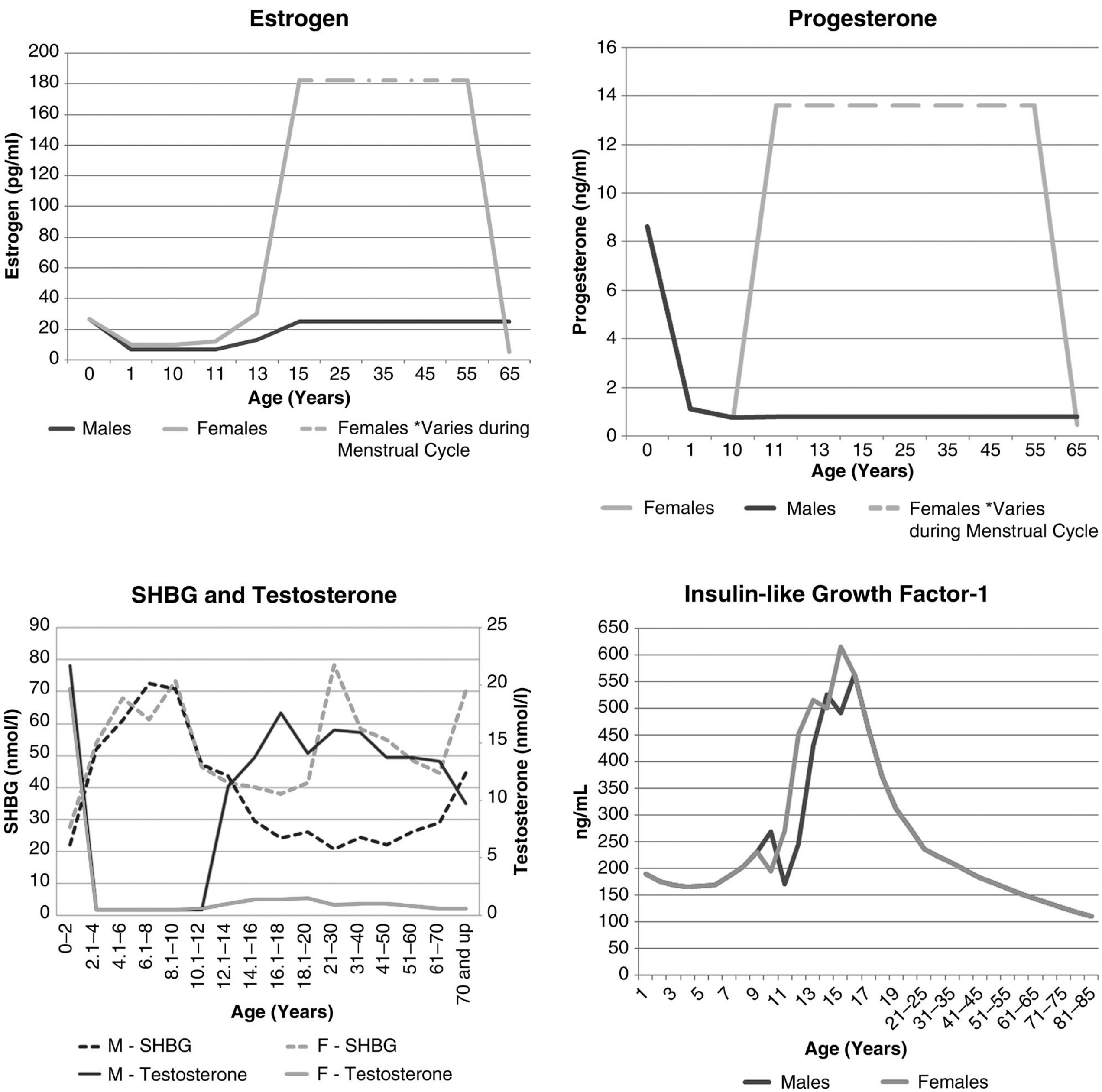

FIGURE 1.6: Sex differences in hormonal concentrations throughout the life span. This figure is derived from multiple sources in order to compile a master life span perspective. Estrogen values for the perinatal period are estimated from work by Thompson et al. (25) while other time points are estimated from the NIH Clinical Center Lab references (cclnprod.cc.nih.gov/dlm/testguide.nsf/Index?OpenForm). The data points for testosterone and SHGB are derived from Elmlinger et al. (26). The data points for progesterone and IGF-1 are estimated from NIH Clinical Center Lab. Testosterone and SHGB are derived from Elmlinger et al. (26).

SHBG, sex hormone-binding globulin.

Perinatal

At birth, many of the sex hormone levels are similar in males and females due to fetal exposure from the mother. Progesterone (27) and estrogen levels (25) are high at first, but decline rapidly during the first few weeks to months of life (25,27). Similarly, testosterone concentrations nearly reach adult values in the perinatal period, thought to be secondary to maternal human chorionic gonadotropin (HCG) presence in the neonate bloodstream. When HCG clears, androgen concentrations decline rapidly (26). In both males and females SHBG is low at birth since androgens are high (26). GH is released in spurts and is difficult to test during the life span, therefore IGF-1 levels are typically measured and are low during this time period (28).

Prepuberty

During childhood, gamma-aminobutyric acid (GABA) inhibits the neurons in the hypothalamus that release GnRH causing low, relatively constant, levels of estrogen, progesterone, and testosterone (29;8, ch. 15). Possibly due to ovarian production, girls generally have slightly higher levels of estrogen and progesterone than boys during childhood (8, ch. 15;30). SHBG levels nearly double in girls and boys between ages 2 and 4, likely since androgen levels are low during this time (26). Both spontaneous and stimulated GH secretion increase during childhood, as demonstrated by linear bone growth and height (31).

Puberty

Puberty occurs between 8 to 14 years of age in girls and 9 to 14 years of age in boys (32). Average onset of puberty is age 11 and 13 in girls and boys, respectively. Puberty is determined by an increase in growth rate and physical sexual characteristics, described by the Tanner stages (33). During puberty, higher levels of excitatory amino acids such as glutamate increase the amplitude of GnRH pulses (29,34). In turn, FSH and LH pulses increase, leading to increased sex steroid output by the gonads (35). In both girls and boys, the initial rise in estrogen levels leads to a growth spurt (36;8, ch. 15). In girls, there is only a minor increase in testosterone while in boys testosterone increases rapidly and leads to the more obvious changes of virilization seen in males during puberty (26,35). In both sexes there is a continued decline of SHBG during sexual maturation. Both spontaneous and stimulated GH secretion increases during puberty, slightly earlier in females than males (31). Young adolescents secrete GH at almost 1.5 times the rate of healthy adults, and levels peak during teenage years (37,38). Serum relaxin levels during pubertal growth have been poorly studied. One study found that the majority of young men and women have undetectable levels of relaxin, but when relaxin is detectable, levels are comparable for both sexes (39).

Females Postpuberty

After puberty and before menopause, females experience cyclic changes in estrogen, progesterone, and relaxin within their menstrual cycle (Figure 1.7) while GH/IGF-1 downtrends slowly over the female life span (37).

There is a large peak in estrogen just before ovulation and a smaller, relative peak during the mid-LP (8, ch. 13). Concentrations of progesterone are lowest during menstruation and highest during the LP (8). These hormonal variations also have considerable intra- and inter-person variability (42). Relaxin levels have been reported to be low in the follicular phase (FP) (43) and peak during the luteal phase (44) due to production by the corpus luteum (45,18). This remains controversial as Pehrsson et al. reported that women have stable levels of relaxin throughout the menstrual cycle (46). Since Pehrsson et al. was the only study to collect and compare concentrations of all the sex hormones during the menstrual cycle, this study is used as the basis for Figure 1.7. However, it is important to note that the women in the Pehrsson study were in their 30s and many of them had been pregnant at least once, so the concentrations may not be translatable to the younger, athletic female. Mild rhythmic changes also occur with testosterone and SHBG during the menstrual cycle, with small increases seen during ovulation (26,41).

Males Postpuberty

The large increase in testosterone seen during puberty in males is followed by a sustained elevation until a decline after age 70 (26). Estrogen and progesterone concentrations remain relatively constant and low after puberty in males, similar to concentrations seen in women after menopause (26). GH/IGF-1 downtrends slowly over the male life span similar to females (37).

Females Postmenopause

The average age of menopause is estimated to be 50 to 52 years of age, but this varies with race, ethnicity, and lifestyle factors (47). In postmenopausal women, levels of

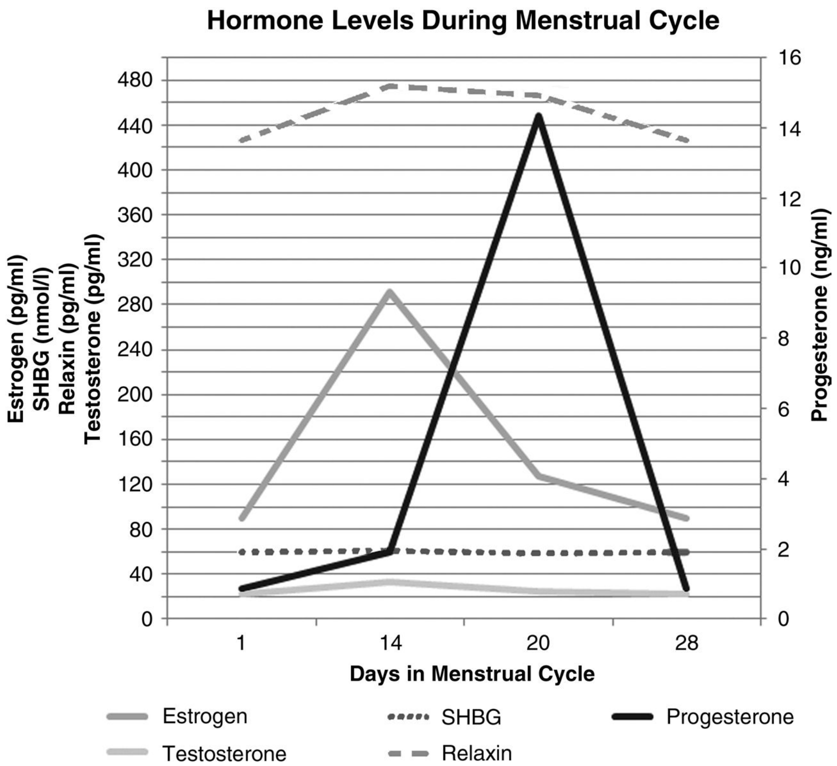

FIGURE 1.7: Fluctuations of hormones during the menstrual cycle. Estrogen and progesterone levels are derived from NIH Clinical Lab value references. The values used are the mean values, derived from the ranges given via the cited reference. Testosterone values are from Ahrens et al. (40). SHBG and relaxin concentrations are derived from Pehrsson et al. (41). Please refer to the text for further explanation of this graph and possible variations in the literature.

estrogen and progesterone drop and become comparable to levels in men, remaining relatively constant and declining only slightly with age (8, ch. 13). Female testosterone concentrations continue to remain constant and significantly lower than male levels after puberty and for the remainder of the female life span (26). In women, SHBG slowly decreases between ages 30 and 70 (likely with regard to lower estrogen), but then rises again after age 70, the mechanism and significance of which is unclear (26).

COLLAGEN METABOLISM AND FUNCTION IN THE MUSCULOSKELETAL SYSTEM

Collagen is a basic building block of ligaments, tendons, cartilage, and bone. Collagen synthesis occurs in several steps and involves several cell types, including fibroblasts, chondrocytes, and osteoblasts (48). Polypeptide chains are translated, hydroxylated, and glycosylated in the rough endoplasmic reticulum. Three of these chains combine to form a procollagen molecule, which exits the cell through vesicular transport. Once the procollagen has left the cell, the propeptide extensions are cleaved, resulting in a tropocollagen molecule, the smallest distinct unit of collagen. Tropocollagen molecules aggregate to form microfibrils held together through relatively weak hydrophobic interactions. Microfibrils comprise five radially packed tropocollagens that are vertically staggered and form long chains with micrometer lengths and 3.5 to 4 nm diameters. Microfibrils form crosslinks with one another, forming fibrils with micrometer lengths and diameters between 30 and 150 nm (49). Fibrils combine to form fibers that have diameters that range from 1 to 10 micrometers. When collagen is organized into a multiscale structure it facilitates tissue function (48) (see Figure 1.8).

Collagen clearance and degradation occur by distinct mechanisms. Cleaved or intact collagen molecules can be internalized by urokinase plasminogen activator receptor-associated protein (uPARAP) receptors (50), while matrix

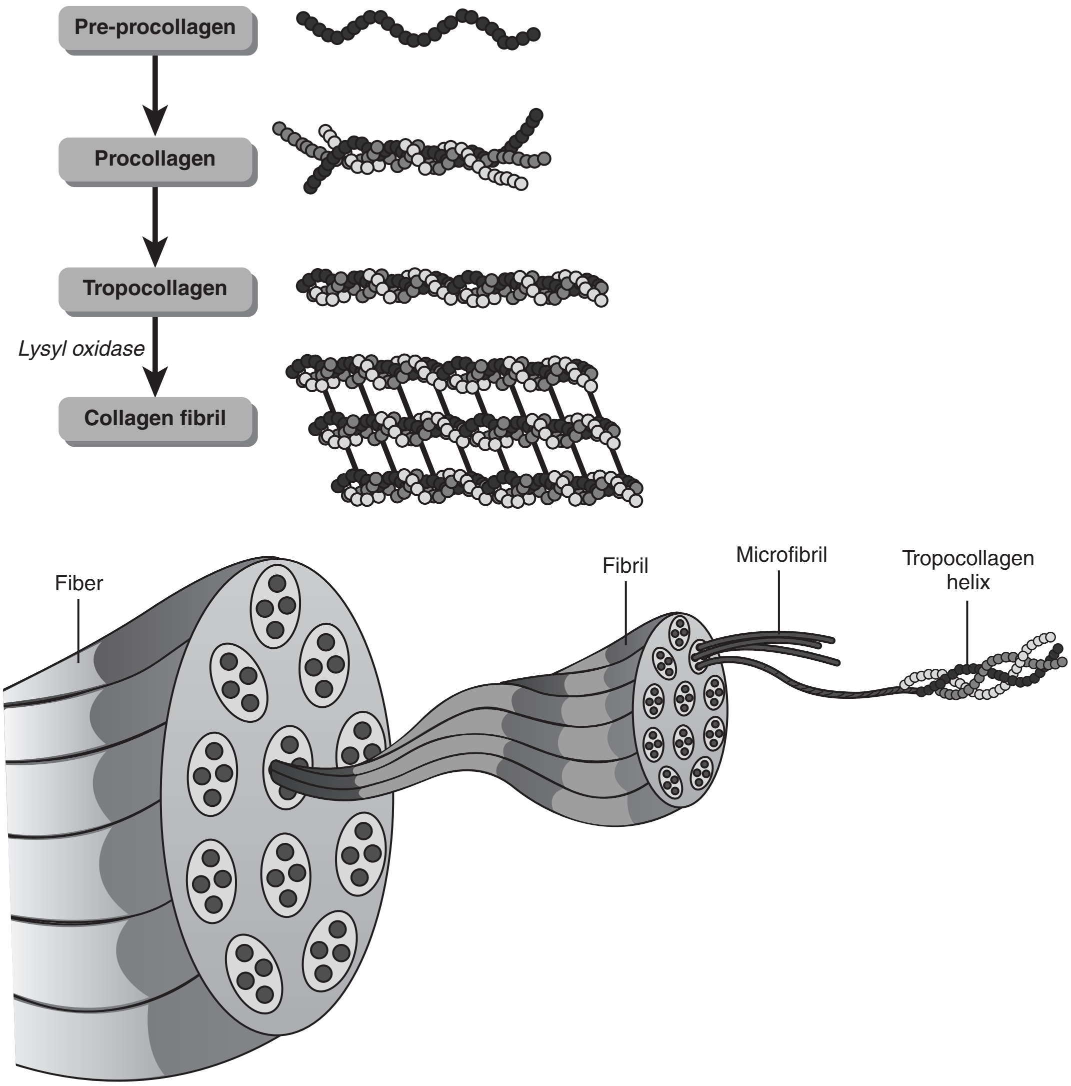

FIGURE 1.8: Key steps of collagen synthesis: Formation of the collagen fibril within the fibroblast cell and levels of collagen fiber organization.

metalloproteinases (MMPs) degrade fibrillar and nonfibrillar collagen, as well as the noncollagenous components of the extracellular matrix (ECM). More than 20 types of collagen have been identified. Collagen types I, II, and III are common types of fibrillar collagen (51). Type I collagen is the primary structural protein found in ligament, tendon, and bone. There are also nonfibrillar collagens found in basement membrane and ECM, including collagen IX, which is found in cartilage (48). Other collagen types of interest in sports medicine include type V, a fibrillar type that works with type I, and type XII, a fibril-associated collagen. Both are thought to provide structural support to ligaments (239). Variations in collagen genes may alter the structure of collagen types I, V, and XII, and this structural change might influence how ligaments respond to external load and risk of ACL injury (92,236,237).

Collagen can function as compressive or tensile tissue, and these different functions require different structural arrangements. Bone is a compressive tissue that requires strength and some flexibility provided by a composite material of collagen and minerals (48). The collagen in articular cartilage is made of chondrocytes and is tightly packed to allow absorption of cyclic stresses that occur at the articular surface (48). The collagen in tendon and ligament is aligned parallel to the axis of tension to enable these structures to withstand tensile loading (52).

Collagen and the balance between collagen production and degradation are critical to musculoskeletal structure and function. Hormonal influences on collagen metabolism occur at a microscopic level, yet there is emerging evidence that these changes can have important macroscopic and functional implications.

HORMONAL EFFECTS ON TISSUES

Hormonal effects on tissues, including ligament, tendon, muscle, bone, and cartilage will now be reviewed in detail; it is summarized as a quick reference in Table 1.1.

Ligament

Receptors for estrogen (53), progesterone (53), testosterone (54), and relaxin (55–57) have been identified on human ligaments, and these hormones affect both synthesis and breakdown of collagen. An in vitro model employed by Yu et al. showed estrogen-dependent suppression of fibroblast proliferation, whereas progesterone seemed to attenuate estrogen's effect on fibroblasts (58). Interestingly, estrogen's effect on collagen may vary even within a specific ligament. Yoshida et al. showed that estrogen increased collagen III synthesis in the middle section of the ACL, but decreased collagen I synthesis in the proximal portion (59). DHT enhances the expression of androgen receptors and collagen synthesis through fibroblast proliferation in canine ACLs (60). Relaxin promotes collagen degradation by increasing MMPs, including collagenases, gelatinases, and stromelysins (61–65). Relaxin's effect on MMPs is enhanced by estrogen (63), but attenuated by progesterone (63,66,67).

From the perspective of ligament function, high concentrations of estrogen have been shown to result in decreased stiffness of the human ACL (68) and decreased load to failure in rabbit ACLs (69). Prior work supports that relaxin also increases ligament and joint laxity (70–73) by reducing the density and organization of collagen bundles (74). The direct effect on human ligaments is unclear, but in guinea pigs, relaxin led to a 30% to 50% reduction in the strength the ACL (75). In addition, several studies have shown that markers of collagen metabolism (76), anterior knee laxity (77–79), and multiplanar knee laxity (80–82) fluctuate across the menstrual cycle.

However, there are several variables that limit our ability to understand how and which hormone(s) are driving these ligamentous changes. For example, there is a large intersubject variability in the timing and magnitude of sex hormonal fluctuations across the menstrual cycle (83). Furthermore, there may be a time lag of 3 to 5 days between the hormonal shifts and changes in ligamentous laxity (77). Finally, as described previously, sex hormones demonstrate a complex interaction, with estrogen enhancing the effect of relaxin and with progesterone modulating the effect of both estrogen and relaxin (54,58,84). Additionally, a lack of consistent methodology regarding how the hormone was administered, timing of measurements, and whether physiologic or supraphysiologic concentrations were administered further complicate our interpretation of the existing literature.

Tendon

Human tendons have been shown to have receptors for estrogen, relaxin, and testosterone (85–87). Estrogen increases tendon collagen synthesis by fibroblast-like cells called tenocytes (88,89) and has been shown to reduce stiffness of the hamstring tendon and the entire lower limb (90–93). However, other work has not demonstrated any change in patellar tendon stiffness across the menstrual cycle (94). Relaxin decreases the stiffness of patellar tendon in isolation (87), but this effect is attenuated by testosterone and enhanced by estrogen and progesterone (95). GH stimulates collagen accretion in dense fibrous tissue, with reduced collagen maturation (96). In addition, when GH was absent or in excess, there was decreased collagen fibril diameters (97). IGF-1 has anabolic effects on rat tendon fibroblast production of collagen, leading to tensile load-induced collagen formation and structural rearrangement (98–100). Furthermore, when IGF-1 is injected into injured rat tendons, there is acceleration of tendon repair (101). This information has some clinical applications that need further exploration. For example, when administering platelet rich plasma (PRP) as a treatment for tendinopathy or partial tears, platelets release IGF-1, which theoretically helps promote healing in ligaments and tendons, based on the literature (102). Another example that needs to be further explored is that males demonstrate an exercise-induced increase in aromatase and estrogen synthesis (12) and patellar tendon hypertrophy that is not seen in females (103). The mechanism of why patellar hypertrophy in exercise occurs only in males is unclear, but the study's authors postulated a hormonally driven mechanism.

Muscle

Recall that steroidogenesis occurs in muscle in both sexes (12). Human skeletal muscle expresses receptors for estrogen and testosterone (104). DHT and testosterone increase muscle weight and mass independently from other hormones

TABLE 1.1: Hormonal Effects on Tissues

	Ligament	Tendon	Bone	Articular Cartilage	Muscle	Nervous System
Estrogen	Dose-dependent fibroblast suppression (may vary at different locations within the ACL). Increased laxity and decreased load to failure.	Increases collagen synthesis by stimulating tenocytes. Reduces stiffness.	Linear growth of bone during puberty and the high levels in late puberty are required for growth plate closure in both males and females.	In females only, estrogen suppresses MMPs (enzymes that degrade the collagen of the cartilage) in articular chondrocytes.	Men: Increases of aromatase and estrogen synthesis only occur in men in response to acute exercise. Women: Unclear relation to muscle mass and strength.	Excitatory effect on neurons, possibly a role in gross motor control and muscle activation depending on phase of menstrual cycle.
Progesterone	Attenuates estrogen suppression of fibroblasts.	Indirectly increases collagen degradation by upregulating relaxin receptors.	Bone formation accelerates when progesterone is produced during the LP and bone resorption increases when progesterone is absent in the FH.	Prevents degradation of cartilage by suppressing MMP production and activity, as well as cytokines.	Effects have not been observed in premenopausal women; in postmenopausal women, it may enhance muscle growth.	Inhibitory effect on neurons; has been explored as an antiepileptic.
Testosterone	Stimulates fibroblast proliferation and enhances the expression of androgen receptors.	Increases collagen maturation; attenuates effect of relaxin.	Increases calcium absorption and retention in bone while determining bone width and bone mass. May influence GH secretion and therefore bone length.	Male effects only. Short term: Achieves a greater amount of cartilage. Long term: Higher free testosterone associated with higher rate of cartilage loss.	Increases muscle mass and protein synthesis.	Increases excitability of the motor system, attenuates atrophic changes, and improves regenerative capacity of motor neurons.
Relaxin	Promotes collagen degradation; increases ligament and joint laxity (both in pregnancy and across menstrual cycle). Relaxin ≥ 6.0 pg/ml may be a risk factor for ACL injury in collegiate female athletes.	Decreases patellar tendon stiffness throughout menstrual cycle.	Unclear effects. In vitro, relaxin stimulates osteoclastogenesis. In vivo it stimulates osteoblast differentiation.	Leads to cartilage degradation by inducing MMPs. Enhanced by estrogen and attenuated by progesterone.	Can enhance muscle healing after injury when in supraphysiological doses, such as increasing the number of regenerating myofibrils and decreasing fibrosis.	Affects spatial memory, stress response, energy balance, and reproductive signaling.
Growth Hormone (GH)		New collagen accretion with reduced collagen maturation.	GH/IGF-1: Determines bone length, bone mass, and mechanical bone strength.	GH/IGF-1: Stimulates the division and multiplication of chondrocytes, helping to determine cartilage thickness.	GH/IGF-1: Increases muscle mass through sarcomere hypertrophy and increases protein synthesis.	Critical for neurogenesis, myelin synthesis, and dendritic branching. Can activate neural stem cells.
Insulin-Like Growth Factor 1 (IGF-1)		Promotes collagen building and tendon repair.	GH/IGF-1: Determines bone length, bone mass, and mechanical bone strength.	GH/IGF-1: Stimulates the division and multiplic-ation of chondrocytes.	Independently stimulates muscle stem cells to differentiate into myotubes.	Improves regenerative capacity of motor neurons.

ACL, anterior cruciate ligament; FP, follicular phase; LP, luteal phase; MMP, matrix metalloproteinase.

(105). GH/IGF-1 increases muscle mass by promoting sarcomere hypertrophy, increasing protein synthesis, and inhibiting protein degradation (3,106,107). IGF-1 also independently stimulates muscle stem cells (in response to mechanical loading on bone) to differentiate into myotubes (3) and induces muscle glycogen synthesis (20). Relaxin treatment in the muscles of mice increases MMP activation, increases satellite cell activation, increases angiogenesis, and decreases inflammation compared to untreated controls (108). Relaxin can also enhance muscle healing after injury in vivo. Supraphysiological doses of relaxin cause an increase in the number of regenerating myofibrils and decrease the area of fibrosis in damaged muscle (109). Direct effects of endogenous progesterone on muscle have not been observed in premenopausal women (92,94,110).

The clinical applications of hormones on muscle in athletes are numerous. Concentrations of intramuscular steroid hormones are independent predictors of muscle strength in premenopausal and postmenopausal women (111). With regard to athletes building muscle mass, exercise increases endogenous GH levels to achieve sarcomere hypertrophy and increase protein synthesis in both sexes (112). Intramuscular steroidogenic enzymes, testosterone, DHT, and DHEA are also upregulated in skeletal muscle (113) with acute and chronic exercise stimulation leading to increased muscle mass (114). It has therefore been suggested that when in excess, a hyperandrogenic state could lead to performance enhancement (115,116). In fact, up to 11.1% of males report using performance-enhancing agents in their lifting routine (117). In women, Hagmar et al. reported overrepresentation of polycystic ovaries (higher free androgen index) in female Olympic athletes (37%) versus the general population (20%) (118). To recognize a hypoandgrogenic or hyperandrogenic state in women, the clinician must look beyond menstrual history alone. For instance, Rickenlund et al. (116) found that athletes with oligomenorrhea or amenorrhea did not always have associated hyperandrogenism. Those with hyperandrogenism (with or without menstrual abnormalities) did, however, have a higher anabolic body composition, higher total bone mineral density (BMD), higher maximal oxygen uptake, and higher performance values compared to those without hyperandrogenism (116). On the opposite end of the spectrum, reductions in testosterone in men can trigger a decline in muscle mass (119).

Given the importance of androgen effects on muscle and possibly performance, serial serum androgens concentrations, including SHBG, are being explored as a way to evaluate performance and establish normal values for elite athletes (120). For example, these profiles have shown lower testosterone concentrations and higher SHBG levels in athletes taking exogenous hormones such as oral contraceptives (118,120,121). The significance of this is very important for clinicians treating athletes, as almost 47% of Olympic athletes in 2009 were hormonal contraceptive users and, based on the literature, may be at an athletic disadvantage (118). Oral contraceptives are further discussed in this chapter in the section on effects of hormonal contraceptives on the musculoskeletal system, injuries, and performance. In treating hypogonadal states, hormone replacement therapy (HRT) has been demonstrated to be useful. Selective ligands and selective androgen receptor modulators (SARMs) have been shown to maintain the positive effects on muscle repair (122). Postmenopausal women on HRT also demonstrated greater muscle strength and mass than their untreated twins (122).

Another important clinical application of hormonal influence on muscle is demonstrated by studying muscle function during the menstrual cycle. There are discrepancies in the literature on whether changes in muscle strength and function occur in the quadriceps and hamstrings with regard to the menstrual cycle, likely again with regard to how hormones were measured and how each phase of the menstrual cycle was determined (123). Sarwar et al. found that muscle strength varies throughout the menstrual cycle, with a peak in quadriceps isometric torque at mid-cycle when estrogen levels are highest. These authors also found increased fatigability and longer relaxation time at mid-cycle (124). Bell et al. also showed that estrogen is negatively correlated with the rate of force production in women during the early FP (92). Bambaeichi et al. found that peak knee extensor torque occurred on a day near ovulation while peak knee-flexor torques occurred on a day in the ovulatory phase (125). However, Kubo et al. showed stable levels of muscle strength, peak torque, and relaxation time despite fluctuations in progesterone and estrogen levels across the menstrual cycle (94). Gur also found no change in concentric or eccentric muscle torques of the quadriceps and hamstrings throughout the menstrual cycle (126).

Clinically, the effects of GH on muscle are better understood by examining GH-deficient patients. GH-deficient patients demonstrate reduced muscle mass and reduced BMD, but with exogenous GH supplementation, skeletal muscle mass increases in the first 12 months of therapy (127). Athletes are aware of the effects seen with growth hormone administration in deficient children and adults. Therefore, healthy power athletes often seek GH supplementation to enhance performance. However, it has not been definitively shown that healthy athletes will benefit from GH treatment like deficient patients. For example, in experienced weightlifters, amino acid incorporation into skeletal muscle protein was not increased and the rate of whole body protein breakdown was not decreased with GH administration. In another study of exogenous GH in power athletes, GH did not increase maximal strength in the biceps or quadriceps (128). Contradictory to this finding, when exogenous GH was given to a portion of healthy men over 50 years of age, there was a significant increase in leg press in the GH group (129). Another study showed that with supraphysiologic doses of GH to athletes, there was reduced oxidative protein loss during exercise (130).

Bone

Bone development and maintenance is a multihormonal phenomenon. Bone growth increases during childhood through puberty, with puberty being the final stage in bone growth (131). During puberty there is a rapid and significant growth rate increase called the acceleration phase. During this phase, there is an increase in standing height velocity of greater than 6 centimeters/year in girls and more than 7 centimeters/year in boys; this acceleration phase typically last about 2 years and is followed by a deceleration phase (33). The hormone estrogen has a critical role in this bone development and also in bone maintenance. The initial rise of estrogen in early puberty is needed for linear growth of bone during puberty, and the high levels of estrogen in late puberty are required for growth plate closure in both males and females (8, ch. 6;36). Free estrogen is a positive predictor of cortical volumetric bone marrow density (132). For bone maintenance, estrogen triggers apoptosis of osteoclasts, leading to reduced degradation of the bone (133). Furthermore, when estrogen decreases and osteoclast activity increases, the net result is degradation and resorption of the bone (134). Meanwhile, androgens increase calcium absorption and retention and help determine bone width and cortical bone growth (34,132,135). This is further supported by bone length being unaltered in the absence of androgen receptors (135). Progesterone helps stimulate bone growth and maintain established bone mass in concert with other hormones (238). GH/IGF-1 is largely responsible for enhancing cortical bone mass via estrogen and mechanical bone strength (136). During puberty, boys acquire more bone mass at the periosteum than girls (137), a process which relies on GH/IGF-1 regulation of estrogen (138). GH also contributes to bone length, as deficiency leads to short bone length (139). The influence of relaxin on human bone is unclear, but in vitro and in vivo animal experiments have provided clues about its possible effects. In vitro experiments have shown that relaxin stimulates osteoclastogenesis from hematopoietic precursors (140,141). Relaxin may also help stimulate osteoblast differentiation and bone formation through bone morphogenic protein (BMP)-2 in vitro (142).

Clinically, the amount of estrogen in males and females and the timing of puberty are very important in both sexes in determining lifelong bone health and fracture risk. For example, excessively high levels of estrogen during puberty can lead to premature hardening of the epiphyseal cartilage and short stature (8, ch. 6;36). Furthermore, in men with estrogen resistance, there is continued linear growth of the bone and the density and strength of the bone are compromised (36). Women who achieve menarche at age 15 or older are at an increased risk of fracture due to reduced bone strength after menopause (143). Low serum estrogen can predict incident fractures, and this risk increases with low testosterone and high SHBG (144). Female athletes have been shown to have a higher incidence of stress fractures compared to male athletes (145). This increased fracture risk associated with late menarche, or primary amenorrhea, may result from disturbances in estrogen levels seen with energy deficiency associated with the female athlete triad (FAT), which may lead to a decrease in bone cortical thickness, an increase in trabecular area, and a deterioration in bone microarchitecture (143,146). Chapter 12 on bone health has further details regarding the FAT and stress fractures.

Over the past decade, there has also been a statistically significant increase in the incidence of radial and carpal fractures seen in girls and boys age 10 to 14 as compared to children age 5 to 9 and adolescents age 15 to 19 (147). The study extrapolates that this increase is due to increased participation in sports. While this may certainly be the case, one must also consider that the varying factor for that age group compared to the others may be the hormonal changes occurring during peak growth phases, like that seen in puberty with high bone turnover and growth (147). Ongoing research is needed to determine the clinical utility of serum sex steroids for fracture prediction (144).

Cartilage

Sex hormone receptors have been found on animal and human chondrocytes, and many studies have focused on their role in cartilage protection (148). Interestingly, the hormonal implications on cartilage appear to be sex specific (149). Claassen and others demonstrated that estrogen protects chondrocytes by providing an antioxidative effect (150,151). Kenny et al. demonstrated that only female rat chondrocytes respond to estradiol supplementation, despite both males and females having estrogen receptors (152).

Similar to estrogen in females, testosterone appears to only affect male chondrocytes (153). Higher serum testosterone is associated with achieving a greater amount of knee cartilage over short periods of time. Longitudinally, however, higher free testosterone correlates to an increased rate of cartilage loss (148). Estrogen also suppresses matrix metalloproteinases (MMPs) in articular chondrocytes from female patients but not in male patients (150). Relaxin leads to degradation of cartilage by inducing MMPs (62,64). The degenerative effect of relaxin on MMPs may contribute to the progression of osteoarthritis (OA). One study found that the intensity of immunostaining for RFXP1 correlated to the severity of OA (154). The effects of relaxin on MMPs can be enhanced by estrogen and attenuated by progesterone (62,63). GH also has direct effects on chondrocytes, stimulating division and multiplication of chondrocytes in cartilage (155). In a study with human articular cartilage pretreated with a cytokine (that stimulates cartilage degradation and chondrocyte apoptosis), there was rescued matrix biosynthesis when treated with IGF-1 (156).

Clinical studies examining the relationship between endogenous hormones and OA in humans suggest there may be association between endogenous estrogen and cartilage protection, but the evidence is inconsistent (157). A large cohort study focused on the relationship between endogenous sex hormones, laboratory levels, and radiographic OA. The study examined radiographs and determined that subjects with low estradiol levels had increased risk of OA incidence (158). Those with low 2-hydroxyestrone (a breakdown product of estradiol catabolism with weak estrogenic activity) were at greater risk for both incidence and prevalence of knee OA. The study proposed that higher levels of 2-hydroxyestrone may delay the development of knee OA by inhibiting leukotrine synthesis (158). Another study that measured serum estrone, estradiol, testosterone, and androstenedione determined concentrations of hormones do not affect OA severity (159).

There do not appear to be any studies examining the effect of sex hormones and other cartilage lesions such as osteochondritis dessicans or chondromalacia patellae.

Nervous System

The role of hormones on the central and peripheral nervous system is less understood when compared to joints, ligaments, muscle, and tendon. GH and IGF-1 are both critical for neural development. They regulate the size, morphology, and function of cells of the central nervous system (CNS). GH treatment affects neurogenesis, myelin synthesis, and dendritic branching and can activate a subpopulation of neural stem cells (160). IGF-1 can improve regenerative capacity of motor neurons in both the central and peripheral nervous systems (156). Nuclear and membrane receptors for progesterone, estrogen, and testosterone also exist in the nervous system (161–163). Estrogen has an excitatory effect on neural substrates in the brain and spinal cord (164,165). Meanwhile, progesterone likely plays an inhibitory role in the CNS (166). In addition, nuclear progesterone receptor expression increases with estrogen exposure, indicating potential interactions between these hormones in the brain (161). Although the mechanism is unclear, progesterone may influence the perception of pain. Locally synthesized progesterone can help reduce the perception of pain in the CNS by upregulating endorphins and opioid receptors (167). In the nervous system, progesterone also seems to have an anti-anxiety effect through the gamma-aminobutyric acid (GABA) receptor, specifically GABA-A (6). Testosterone has been shown to increase cell excitability, attenuate atrophic changes, and improve the regenerative capacity of motor neurons (163). In the brain, relaxin acts as a novel neurotransmitter with numerous functions, affecting spatial memory, stress response, food intake, the sleep-wake cycle, and arousal (168). Relaxin may also be involved in energy balance in the CNS and reproductive signaling (169).

More clinically focused studies have examined different measures of motor control across the menstrual cycle, but differences in methodology and lack of daily testing have resulted in several studies demonstrating changes (170–173) while others have not (174–176). Two recent studies that focused on more basic measures of neuromuscular control demonstrated changes across the menstrual cycle: Casey et al. detected a decrement in the muscle stretch reflex measured at the rectus femoris during the time around ovulation (177), while Tenan et al. demonstrated changes in vastus medialis firing and control during the menstrual cycle (178). Finally, Bonifazi et al. observed increased corticospinal excitability in the setting of supraphysiologic levels of estrogen in males (179). The findings in these studies warrant future investigation regarding the underlying mechanisms of change as well as the origin along the neuromechanical axis.

EFFECTS OF HORMONAL CONTRACEPTIVES ON THE MUSCULOSKELETAL SYSTEM, INJURIES, AND PERFORMANCE

Exposure to exogenous estrogen and progesterone in the form of hormonal contraceptives is common in active females. Approximately 100 million women worldwide and up to 70% of collegiate athletes in the United States report using hormonal contraceptives (180,181). Given such a high prevalence of hormonal contraceptive use in athletes, it is imperative that the musculoskeletal and physiological effects are well understood so that clinicians and athletes can consider the impact of these medications on injury and performance. This section reviews the current state of knowledge and will pose critical questions for future investigation.

The menstrual cycle is controlled by the hypothalamic-pituitary-ovarian axis. Hormonal contraceptives prevent ovulation through negative feedback at the level of the hypothalamus through exposure to exogenous estrogen and progesterone. Hormonal contraceptives can be administered through oral, transdermal, or vaginal routes. The pharmacokinetics vary by administration type with the vaginal route resulting in the lowest and most precise doses of serum hormonal concentrations (182). Oral contraceptives are the most commonly used hormonal contraceptive and are available in monophasic and triphasic formulations. Monophasic pills have consistent doses of exogenous hormones for 21 days and then 7 days of a placebo, whereas triphasic pills have varying concentrations of estrogen and progesterone to mimic a eumenorrheic cycle for 21 days and placebo for 7 days (183). In addition, many women have adopted a regimen of taking consecutive active pills and foregoing the placebo pills to avoid having any breakthrough bleeding. Over the past 30 years, the formulations of oral contraceptives have shifted to lower dosages of estrogen and progesterone with varying degrees of progestin androgenicity (Table 1.2)(184).

TABLE 1.2: Progestogen Potency and Androgenicity Values

Trade name	Ehinylestradiol dose (mg)	Progestogen			
		Type	Dose (mg)	Potency[a]	Androgenicity[a]
Alesse® 21 or 28	0.020	Levonorgestrel	0.10	0.53	0.83
Brevinor®-1	0.035	Norethindrone	1.0	1.0	1.0[b]
Cilest®	0.035	Norgestimate	0.25	0.33	0.48
Demulen® 1/35–28	0.035	Etynodiol	1.0	1.4	1.6[b]
Demulen® 1/50	0.050	Etynodiol	1.0	1.0	1.0[b]
Diane® 35 (Dianette®[c])	0.035	Cyproterone	0.20	NA[d]	NA[d]
Femodene®	0.030	Levonorgestrel	0.15	0.8	1.25[b]
Femodette®	0.020	Gestodene	0.075	0.68	0.26
Loestrin® 1/20	0.020	Norethindrone	1.0–1.5	1.0	1.0[b]
Loestrin® 1.5/30	0.030	Norethindrone	1.5	1.5	1.5[b]
Marvelon®	0.030	Desogestrel	0.15	1.35	0.51
Mercilon®	0.020	Levonorgestrel	0.15	0.80	1.25[b]
Microdiol®	0.030	Desogestrel	0.15	1.35	0.51
Microgynon® 30	0.030	Levonorgestrel	0.15	0.8	1.25[b]
Min-Ovral®	0.030	Levonorgestrel	0.15	0.8	1.25[b]
Minulet®	0.030	Gestodene	0.075	0.68	0.26

(*continued*)

TABLE 1.2: Progestogen Potency and Androgenicity Values (*continued*)

Trade name	Ehinylestradiol dose (mg)	Progestogen			
		Type	Dose (mg)	Potency[a]	Androgenicity[a]
NeoGentrol® 30/150	0.030	Levonorgestrel	0.15	0.8	1.25[b]
Norimin-1®	0.035	Norethindrone	0.50	0.5	0.5
Norinyl-1®	0.050	Norethindrone	1.0	1.0	0.34
Norlestrin® 21	0.050	Norethindrone	1.0	1.0	1.0[b]
Ortho-Novum®	0.050	Norethindrone	1.0	1.0	1.0[b]
Ortho-Novum® 1/35	0.035	Norethindrone	1.0	1.0	1.0[b]
Ortho-Novum® 1/50	0.050	Norethindrone	1.0	1.0	1.0[b]
Ovcon 35®	0.035	Norethindrone	0.40	0.4	0.4
Ovral®	0.030	Norgestrel	0.30	0.78	1.26[b]
Ovran® 50	0.050	Levonorgestrel	0.25	1.33	2.1[b]
Ovranette®	0.030	Levonorgestrel	0.15	0.8	1.25[b]
Sterdinil-m®	0.030	Levonorgestrel	0.15	0.8	1.25[b]

Calculated using the method found in Ref. (184). Greer JB, Modugno F, Allen GO, Ness RB. Androgenic progestins in oral contraceptives and the risk of epithelial ovarian cancer. *Obstet Gynecol.* 2005;105(4):731–740. doi: 10.1097/01.AOG.0000154152.12088.48. PMID: 15802398.

[a]The oral contraceptive pill (OCP) progestogen dose is multiplied by its progestational activity (for potency) or by its androgenic activity (for androgenicity). Progestational and androgenic activity are calculated relative to a 1 mg dose of norethindrone.

[b]OCPs that may have the potential to alter performance, based on androgenicity cut-off value of ≥1.0.

[c]Alternative name for OCP.

[d]Antiandrogen, so no potency or androgenicity values.

This variety in medication delivery, hormonal type, and concentration represents only some of the challenges facing researchers when attempting to explore the effect of exogenous hormones on nonreproductive tissues. Additional challenges include the large intersubject variation in the serum levels of endogenous estrogen and progesterone (177) and almost no information regarding the bioavailability of the exogenous hormones in women taking oral contraceptives (185). Finally, hormonal contraceptives have been shown to alter the concentrations of other hormones, such as relaxin, testosterone, and IGF-1 (43,120,121,186), yet the relationship between exogenous estrogen and progesterone with other hormones is rarely explored. Given these obstacles, it is clear that the current approach of measuring a specific variable, such as ligament laxity, tendon stiffness, landing mechanics, or injury, will be fraught with confounding variables. A more optimal approach to determine the effect of exogenous hormones is to nonsteroidally inhibit the hypothalamic-pituitary-ovarian axis with medication (such as leuprorelin, a GnRH receptor antagonist). This would enable researchers to examine measures of musculoskeletal structure and function in a placebo group as well as those exposed to varying concentrations of estradiol and progesterone (187). While this method is optimal from a reproductive endocrinology standpoint, there are clear disadvantages limiting recruiting, and this approach is not feasible for a prospective study looking at risk of injury across a competitive season.

Despite the challenges, some clinically relevant information regarding the effects of hormonal contraceptives on specific musculoskeletal tissues does exist.

Ligament

Controversy exists regarding the effect of hormonal contraceptives on ligamentous laxity with Martineau et al. demonstrating reduced anterior knee laxity in women taking oral contraceptives compared to eumenorrheic women (188). Yet Lee et al. did not find a difference in laxity between these two groups (189). Furthermore, Pokorny et al. did not find a difference in peripheral joint laxity and oral contraceptive use (190). However, Shultz et al. demonstrated differences in markers of collagen metabolism and IGF-1 in women taking oral contraceptives compared to eumenorrheic women, with higher levels of collagen production markers in the contraceptive group (76).

Tendon

Bryant et al. observed a reduced strain of the triceps surae aponeurosis during maximal isometric plantar flexion in oral contraceptive users (191), but Lee et al. showed that oral contraceptives do not affect knee tendon flexibility (189). Initial research by Hansen et al. demonstrated a lower collagen fractional synthesis rate in the patellar tendon of oral contraceptive users, both at rest and after exercise (192,193). However, more recent work by the same group failed to show any significant influence of use of oral contraceptives on tendon morphology, strength of collagen, or tendon biomechanical properties in female athletes (194).

Muscle

Muscle strength of hand and leg muscles appears to be unaffected by oral contraceptives (124,195,196). However, oral contraceptives may result in decreased handgrip endurance times (197). In addition, oral contraceptives do not affect muscle stiffness (198). Hansen et al. (199) demonstrated decreased postexertional rate of muscle protein synthesis in women who used oral contraceptives compared to controls. Interestingly, this difference was only observed in women taking third-generation oral contraceptives (pills with lower androgenic progestins) and women taking second-generation pills (higher androgenic progestins) were not different from controls (199).

Bone

Our understanding of the effect of oral contraceptives on bone accretion and metabolism has shifted over the past few years. Historically, oral contraceptives were thought to be protective for bone, especially in females with hypothalamic amenorrhea due to low energy availability (female athlete triad) (200–202). In a multicenter, double-blind, placebo-controlled, randomized trial, Grinspoon (202) evaluated bone metabolism markers in two groups of women with hypothalamic amenorrhea and osteopenia. The experimental group was administered a triphasic oral contraceptive pill (OCP) with 35 mcg of ethinyl estradiol and the control group received a placebo pill. The experimental group demonstrated decreased bone turnover. Other work has shown that exercise, including a 3-week jumping protocol, was equally stimulating to bone metabolism regardless of whether or not women were taking oral contraceptives (203). However, more recent studies demonstrate that oral contraceptives interfere with peak bone mass accrual in females in their teens and 20s. Almstedt Shoepe and Snow found that 18- to 24-year-olds using oral contraceptives had significantly lower BMD than controls in the spine, femoral neck, greater trochanter, total hip, and whole body (204). Two studies have shown detrimental effects of oral contraceptives on achieving peak of bone mass in young women (205,206). Cibula et al. (206) conducted a prospective study with 56 females (ages 15 to 20) randomized to either 30 or 15 mcg of ethinyl estradiol in a crossover design of 9-month intervention each in reverse order. During the 18-month study, the average lumbar spine (LS) BMD increase in healthy controls reached 2%, while the oral contraceptive users did not demonstrate a significant increase in BMD. Furthermore, during the time women were taking the lower dose estrogen pill, they had significantly more pronounced BMD growth reduction than the higher dose and control groups (206). Finally, Cooper et al. has shown an increased risk of subsequent fracture in women who reported taking oral contraceptives compared to women who had never taken oral contraceptives (relative risk 1.20, 95% confidence intervals 1.08 to 1.34)(207). This information is critical for physicians who advise the young female athlete, and hopefully practice patterns will be adjusted to avoid the low dose estrogen pills in those at risk for stress fractures.

Cartilage

There are very limited data regarding the effect of hormonal contraceptives on articular cartilage. Wei et al. showed that prior exposure to oral contraceptives was not associated with cartilage volume, cartilage defects, or radiographic change in the knee joint (208). Clinical studies on exogenous hormones and the development of OA suggest that exogenous estrogen may have a protective effect on cartilage and bone turnover. For example, one randomized control trial found there were decreased urinary carboxy-terminal collagen crosslinks (CTX), specifically CTX-1 and CTX-II, after 1 year of treatment with either oral or transdermal estradiol therapy, suggesting decreased cartilage breakdown (209). However, it remains unclear if exogenous estrogen in turn affects radiographic OA, cartilage volume, or joint replacement (157). For example, Erb et al. used data from the Ulm Osteoarthritis Study (a study that enrolled consecutive female patients who were hospitalized for hip or knee joint replacement because of advanced OA) and found no change in radiographic hip, knee, and hand OA in 475 women on HRT (210). Another study found that in women taking estrogen for at least 10 years, there was a greater reduction in the risk of OA of the hip, as well as the development of moderate to severe OA on radiographs, compared to those taking HRT of less than 10 years duration (211).

Nervous System

Only a few papers have investigated the effect of oral contraceptives on neural function and motor control. Bryant et al. demonstrated consistent foot center of pressure during hopping in monophasic oral contraceptive users, whereas eumenorrheic controls had acute increases in foot center of pressure length and velocity around ovulation compared to menses (172). Casey et al. showed a larger periovulatory decrease in the muscle stretch reflex at the knee in eumenorrheic women compared to oral contraceptive users (177). Rechichi and Dawson showed that reactive strength measured from a drop-jump changed throughout the OCP cycle (212). Collectively, these studies suggest that oral contraceptives influence neuromuscular control, but more research is needed, including the differential effect of endogenous and exogenous hormones as well as which types or modes of delivery of oral contraceptives might result in decreased injury.

Injury

It has been proposed that oral contraceptives might reduce the risk of injury in female athletes because they minimize the magnitude of fluctuations of endogenous estradiol and progesterone compared to those experienced by eumenorrheic women (213). However, oral contraceptives have not been included in most menstrual cycle injury epidemiology research, so the influence of exogenous estradiol and progesterone on neuromuscular function, performance, and injury of athletes is not well understood (115,214).

Moller-Nielsen and Hammar reported lower rates of traumatic injuries in soccer players on oral contraceptives compared to controls (215), but there was no difference in the prevalence of low back pain (LBP) in soccer, volleyball, and basketball players taking oral contraceptives compared to controls (216). Two studies did not find a difference in risk of ACL injury related to hormonal contraceptive use (180,217), whereas a more recent retrospective review indicates a protective association of oral contraceptive use for ACL injury, but further investigation is need to clarify the causal association between oral contraceptive use and the likelihood of sustaining an ACL injury (218).

To our knowledge, only one study has investigated tendon injuries and oral contraceptives and demonstrated that there is an association between Achilles tendinopathy and oral contraceptive use (219).

Performance and Exercise Physiology

Although this is one of the more extensively studied areas regarding oral contraceptive use and sports, many questions remain. This uncertainty is, in part, due to the fact that most studies lump various types of oral contraceptives together, rather than focus on pills with similar hormonal concentrations and progestins with higher androgenicity. This is particularly problematic because hormonal contraceptives containing progestins with higher androgenicity would likely have a greater impact on sports performance (220). One study demonstrated improved running economy in women taking oral contraceptives (221). Lebrun et al. demonstrated that in highly trained women taking a triphasic oral contraceptive, maximum oxygen consumption (VO_{2max}) had decreased 4.7% compared to an increase of 1.5% in controls (222). However, there was no difference in maximum ventilation, heart rate, respiratory exchange ratio, anaerobic speed test, aerobic endurance, or isokinetic strength between the groups (222). In contrast, Vaiksaar et al. did not find any difference in endurance performance in rowers with or without exposure to oral contraceptives (223).

Pain

The use of oral contraceptives has been associated with a greater risk of persistent pelvic pain (224), LBP (225), and increased muscle pain after heavy resistance exercise (91).

CLINICAL CORRELATION: SEX HORMONES AND ANTERIOR CRUCIATE LIGAMENT INJURY

One of the most widely studied injuries in sports medicine is noncontact tears of the ACL. One intriguing feature of this injury is that females are two to five times more likely to tear their ACL compared to males who participate in similar sports (226,227). It is clear that the underlying mechanism of injury and the sex disparity are multifactorial with anatomical, biomechanical, genetic, and hormonal factors playing a role (228). Support for the role of sex hormones as a risk factor stems from the fact that sex differences in movement patterns and risk of injury emerge at puberty (229,230) and injuries occur more often in the follicular and preovulatory phases of the menstrual cycle (231,232). More recently, the hormone relaxin has been implicated in ACL injury, as female athletes had a fourfold increased risk of ACL injury if they had relaxin concentrations greater than or equal to 6.0 pg/ml (233). In this study, some of the female athletes did not have detectable levels of relaxin while others had significantly elevated levels. At this point, it is unclear if there are truly two groups of women with and without fluctuations in relaxin or if this is due to a limitation in the relaxin assays that were used or the timing in which the single hormone samples were taken.

Receptors for estrogen (53,72), progesterone (53), testosterone (54), and relaxin (57) have been found in multiple locations of the musculoskeletal system involved in ACL injury, including ligaments, tendon, muscle, and the nervous system. There is mounting evidence that these hormones alter the structure and function of ligaments, tendon, and muscle through modulation of collagen synthesis (76,77,80,92,93). Furthermore, sex hormones have receptors in the CNS (234) and may have the capacity to adjust corticospinal excitability (179), which could lead to changing motor controls strategies employed by female athletes across the menstrual cycle. A few studies suggest that lower limb neuromechanics change across the menstrual cycle (173,177), but whether this a direct effect of changes in connective tissue mechanics, neural excitability, or a combination of the two has yet to be determined.

A complete understanding of how and to what extent fluctuations of sex hormones influence risk of noncontact ACL injury in female athletes is limited by several factors, including (a) heavy reliance on animal and in vitro studies, (b) the large variation in the magnitude and timing of hormonal fluctuations across the menstrual cycle, (c) the lack of consistency in the timing of testing and poorly validated ways to determine menstrual cycle phase, (d) the high prevalence of several types of menstrual dysfunction in female athletes (235), and (e) the large variety in the type, hormonal concentration, and mode of delivery of hormonal contraceptives being used by athletes. Future investigations should address these issues to allow us to understand if the hormonal milieu can be modulated to reduce the risk of ACL injury, and if there are optimal times during maturation or the menstrual cycle where the neuromechanical axis is primed to adopt less risky movement patterns related to ACL injury. Knowledge of how all forms of sex hormones affect the neuromusculoskeletal system is critical to our understanding of the sex disparity in ACL injury, as well as other forms of sports-related injury and performance in both males and females.

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2

SHOULDER

Chi-Tsai Tang and Scott Simpson

EPIDEMIOLOGY

Shoulder injuries are one of the most common injuries in sports. The incidence of shoulder injury naturally depends on the sport being played. Age of the athlete, level of competition, and gender seem to play a role as well. In epidemiologic studies of high school athletes, significant shoulder injuries accounted for 8.3% to 10.9% of all injuries. Shoulder injuries were more common in boys (11.1% to 14.4%) as compared to girls (1.6% to 3.4%), and this relationship held true even when they participated in the same sport, such as soccer and basketball (1,2). Looking at different sports, the sports with highest injuries to shoulders included boys' wrestling, boys' baseball, boys' football, and girls' softball (2). Another way to look at injury incidence is to assess injuries per athlete exposure (AE). One study looking at several high school sports found an overall shoulder injury rate of 2.15 per 10,000 AEs. Rates of injury were higher in competition compared to practice. Boys were more likely than girls to sustain their injuries after contact with another person or with the playing surface. Common injuries included shoulder sprain/strain and shoulder dislocation/separation (3). A separate study, one looking at high school baseball and softball only, found an injury rate of 1.72 per 10,000 AEs for baseball and 1.0 per 10,000 AEs for softball (4). It can be assumed that the baseball players were predominantly if not all boys, and softball players were predominantly if not all girls.

Data on whether there is a sex-based bias in shoulder injuries for collegiate and more competitive athletes is a little less clear. In a study comparing seven collegiate sports (including basketball, cross-country running, track, swimming, soccer, tennis, and water polo) from one school, the data overall suggest little difference in the pattern of injury between men and women competing in comparable sports. There was an increased rate of shoulder injuries among female swimmers and water polo players, but the study's authors suggest this probably resulted from the more rigorous training philosophy of a particular coach at the school (5). One study of elite overhead athletes in sports that included swimming, rowing, wrestling, basketball, volleyball, and handball found males had higher lifetime prevalence of shoulder pain than females (6). However, a separate study of elite male and female badminton players showed no difference in prevalence of shoulder pain (7). In a study of female competitive swimmers of varying ages, it was found that 21.4% of swimmers age 8 to 11, 18.6% of swimmers age 12 to 14, 22.6% of high school swimmers, and 19.4% of masters swimmers had shoulder pain and disability. Greater swimming exposure, higher incidence of previous traumatic injury, patient-rated shoulder instability, and reduced participation in another sport were found to be statistically significantly correlated with shoulder pain and disability (8).

In a population that holds particular interest to physiatrists, those with physical disabilities, the shoulder was the most commonly injured body part in athletes participating in the 2012 Paralympic games, representing 17.7% of all injuries. This should come as no surprise given the stress placed on shoulders from wheelchair use. Rates of shoulder injury were similar in male and female athletes (9).

Looking at the general population of people presenting to primary care, physical therapy, or physical medicine outpatient clinics for shoulder pain, it appears that more patients tend to be female, with percentages ranging from 55% to 74.3% (10–12). The painful shoulder is more likely the dominant shoulder (10). The mean age ranged from 47 to 50 years in these studies (10–12). Moderate intensity pain predominated in males, while severe intensity pain was more frequent in females. Limitations of movements were present mainly in women, likely presenting a female predilection to frozen shoulder. Concurrent cervicalgia was reported in 7.7% of women and 2.9% of men (10). Pain medication consumption was significantly higher among men than women (11). The most common diagnoses included subacromial pain, myalgia, and adhesive capsulitis (12). In a study looking at men and women with neck/shoulder disorders, the highest improvements in pain and disability in both men and women were seen after 3 months. After 5 years, both men and women had significant improvements, but men more than women (13).

ANATOMY

There are several studies looking at differences in shoulder anatomy between the sexes. Overall, males have larger bony structures compared to females. This includes larger humeral head height and width, larger coracoid process, and larger and rounder glenoid (14–16). For the glenoid, the presence and location of the anterior notch varied between genders. See Figure 2.1 for a depiction of a mean male and female glenoid (15). Differences in glenoid anatomy may have implications in shoulder surgeries, such as planning for the glenoid component in shoulder arthroplasties. The anatomic relationship of the humeral head inclination was not found to be different between the sexes (16). One study showed a difference in humeral head and glenoid version, with males having more retroversion than females, but other studies found no differences in the glenoid version (15,17,18). See Figure 2.2 for a depiction of how to calculate humeral head retroversion and glenoid retroversion. Both the humeral head and glenoid are thought to be retroverted in higher demand shoulders, and the dominant shoulder typically has higher retroversion. Greater humeral head retroversion increases external rotation and decreases internal rotation. Humeral head retroversion is known to be high in the fetus and infant and to become smaller with growth (17).

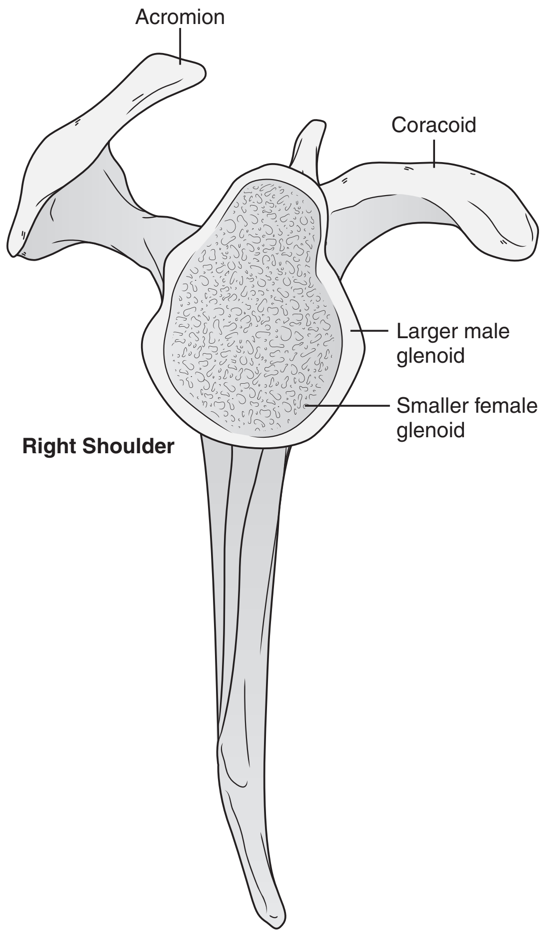
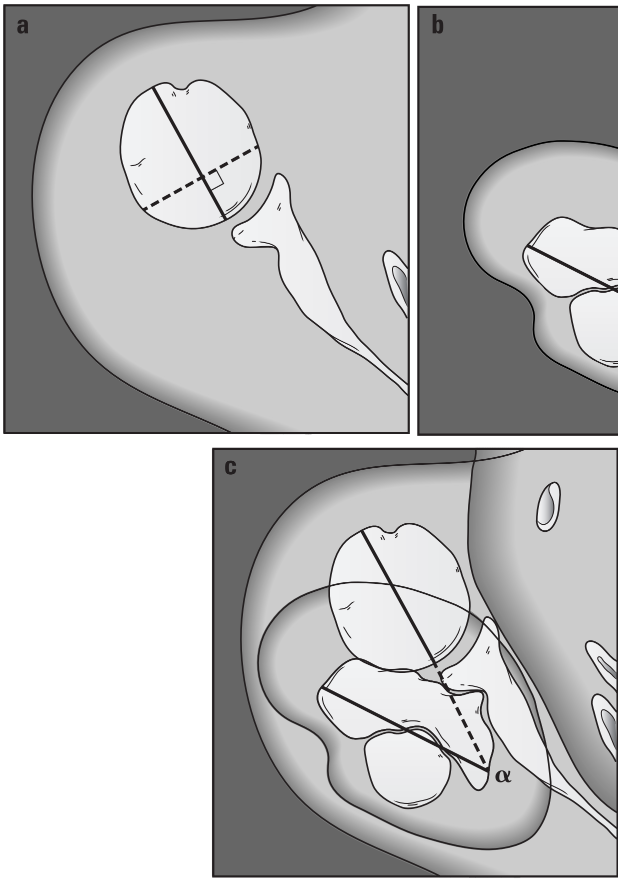


FIGURE 2.1: Depiction of lateral scapula "Y view" of the right shoulder, illustrating mean differences between male and female glenoids (15)

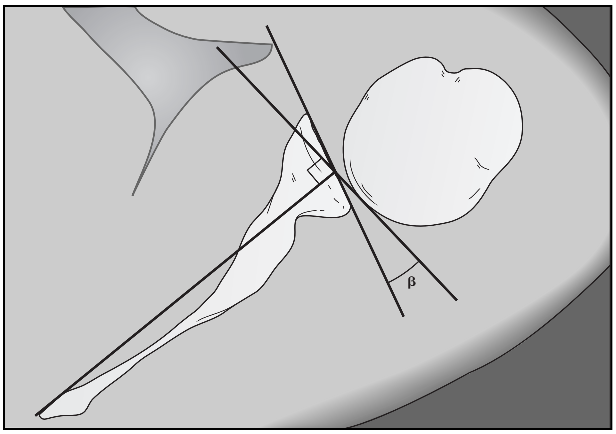
One of the main differences between male and female bony structure is the size of the scapula (18). Scapular breadth was found to have a high degree of sexual dimorphism (19). In fact, many people have proposed looking at the scapula as a way to differentiate male and female skeletons. The longitudinal scapular length and transverse scapular length were found to be larger in males than females (20). Looking at the morphology of the acromion, there appears to be a predominance of type III (hooked) acromions in men (56.2% versus 43.7%) and type I (flat) in women (56.5% versus 43.4%). Enthesophytes and a rough inferior surface were most frequently found in type III acromions (21).

An interesting difference in bony anatomy between genders that has clinical implications is the shape of the suprascapular notch. Males are approximately three to four times more likely to suffer from suprascapular nerve entrapment than females. A study of the suprascapular notch found that the frequency of type I (maximal depth greater than superior transverse diameter) and type IV (scapulae with bony foramen) was higher in males than females. Type III (superior transverse diameter was greater than the maximal depth) was more common in females than males. Therefore, notches that are "narrow and deep" as opposed to "wide and shallow" and also notches that are a bony foramen may predispose the nerve to injury because of tethering of the nerve within the notch (22).

Looking at differences in soft tissue structures in the shoulder, it is found that the size of the subscapularis insertion onto the humerus is larger in men (23). Looking at ultrasound dimensions of the rotator cuff in young healthy adults, the mean maximum width of the supraspinatus footprint was significantly larger in men than women (14.9 mm versus 13.5 mm). The mean thickness of the supraspinatus tendon (5.6 mm versus 4.9 mm), subscapularis tendon (4.4 mm versus 3.8 mm), and infraspinatus (4.9 mm versus



A



B

FIGURE 2.2: (A) shows how to calculate humeral head retroversion. (a) The humeral head axis (solid line) is the line perpendicular to the cord of the articular surface of the humeral head (dotted line) at the slice with the maximum humeral head diameter. (b) The elbow epicondylar axis is the line drawn between the medial and lateral epicondyles (line) at the slice with the most prominent epicondyles. (c) Humeral head retroversion (alpha) is defined as the angle between the humeral head axis and the elbow epicondylar axis of the humerus. The humeral head is retroverted because the humeral axis is pointing posterior (17). (B) shows how to calculate glenoid retroversion. Glenoid retroversion (beta) is defined as the angle between the glenoid line and a line perpendicular to the scapular axis. The glenoid line is the line connecting the anterior and posterior rims of the glenoid. The scapular axis is the line connecting the tip of the medial pole of the scapula and the center of the glenoid line. The glenoid is considered retroverted because the face of the glenoid is pointing posterior (17).

4.4 mm) tendon were all larger for men, but differences did not reach statistical significance. There was no correlation between height and weight with any tendon measurement (24). Differences in rotator cuff thickness have clinical relevance because increased thickness is one of the main criteria used to diagnose rotator cuff tendinopathy. Other criteria include inhomogeneity and hypoechoic appearance. In a separate study, average thickness of an intact rotator cuff was described to be 4.7 mm and was not found to be related to age, sex, or symptoms (25). The common practice at our institution is to use 5 mm as the cutoff value for normal cuff thickness, though perhaps men should have a slightly higher cutoff. Typically, to make the diagnosis of tendinopathy, other features of tendinopathy need to be seen, and there may oftentimes be a focal area of thickening that is seen. The contralateral shoulder can also be scanned for comparison if it is asymptomatic. This highlights some of the challenges with using ultrasound to diagnosis rotator cuff pathology because there is not always standardized criteria.

There also appear to be differences in bone maturation and bone quality within the shoulder between sexes. This should be no surprise given what we know about sex differences in overall bone metabolism. Females had earlier epiphyseal union of the upper limb and scapular girdle by about 2 years compared to males, reflecting earlier skeletal maturation (26). Looking at bone quality within the greater tuberosity, males tend to have "denser" bone, with higher bone volume to total volume ratio, larger trabecular thickness, greater trabecular number, and greater connectivity density. Furthermore, there was a strong inverse correlation between age and bone volume to total volume ratio, which was more pronounced in females (27).

BIOMECHANICS

There is a difference in absolute shoulder strength between males and females, with males being stronger, which is not surprising. However, this difference is no longer present after normalization for segmental skeletal muscle mass (28). In a study of healthy subjects using surface electromyography (EMG) to look at two portions of the trapezius, deltoid, and infraspinatus through repetitive maximal isokinetic shoulder forward flexions, males were significantly stronger than females and, on average, females produced approximately 60% of the output of the males for peak torque; 76% after normalization for body mass (29). In a separate study testing strength in the shoulder using a dynamometer, no statistically significant differences in agonist/antagonist strength ratios were found between dominant and nondominant sides or between sexes (30). However, a separate study of badminton players showed males were generally stronger than females in all strength measurements except internal rotation on the dominant side. In females only, internal rotation strength of the dominant side was stronger than internal rotation strength of the nondominant side, and a higher internal rotation strength on the dominant side was not balanced by a higher external rotation strength (31). Different positioning of the shoulder for strength testing did uncover some differences in strength between sexes. For women only, the internal rotators demonstrated significantly greater strength in the seated neutral position than in the prone position with the shoulder abducted to the 90° position. Similarly, the external rotators demonstrated greater strength in the prone position with the shoulder abducted to the 90° position, compared to seated positions (32).

There appears to be a sex difference for endurance of shoulder girdle muscles, with women having better endurance than men. In one study, men had significantly lower endurance levels for the trapezius and infraspinatus, but significantly higher activation of the deltoid muscle than women, when performing shoulder flexion (29). A separate study showed that women have better endurance than men in upper body resistance exercises and can perform more repetitions with lower decrement in force output and faster recovery capacity when doing these exercises. Women are thought to have better endurance because of reduced adenosine triphosphate (ATP) depletion, faster ATP recovery, lower blood lactate levels, lower epinephrine levels, a lower respiratory exchange ratio, and lower glycogen breakdown in type I muscle fibers in response to maximal sprint and resistance exercises (33). Also, men and women appear to use different strategies to improve endurance during a repetitive shoulder task. Women increased variability in muscle activation to improve fatigue, whereas men decreased coactivation between muscles to increase endurance (34). There were no significant effects of gender or age on the ability to relax between repetitive contractions (29).

There appears to be some differences in muscle activation patterns between sexes when performing arm elevation in the scapular plane. Females demonstrated higher percent activation levels for three of the four divisions of the trapezius, but had slower onset of timing for activation of the descending trapezius. This just indicates there is a difference in muscle activation between the sexes, but the clinical implication is not clear (35). For isometric exercises with a loading of 50% maximum force, gender-specific differences in functional intermuscular coordination patterns were seen. Women showed less activation of muscles acting in the main force direction, and more activation in those muscles less necessary for the actual force production. This can be interpreted to mean that shoulder activation in men is more precise than in women (36).

Looking at static scapular resting position, there was a significant difference between males and females in nonswimmers but not in swimmers for the distance between the medial spine of the scapula and T3/4. Males had larger values with a mean difference of 11.3 mm (37).

A couple of studies looked at shoulder biomechanics in sports. Looking at propelling of the arm in males and females swimming the front crawl at submaximal speeds, the distance covered per stroke is similar before puberty, reaches its maximum at about 20 years of age, and then steadily declines. Shoulder-to-hand distance is significantly larger in males than in females, and this difference tended to offset the difference in distance covered per stroke so that efficiency of the arm stroke is almost the same in male and female swimmers of the same age group and swimming ability (38). Looking at rowing technique, males have greater upper body strength than females, and there is slight difference in rowing techniques adopted by each sex. Male rowers expended more total external energy per stroke and made a larger percentage contribution of angular shoulder energy to their total external energy expenditure. The overall percentage of work done was higher for male rowers, and this difference further increased at higher stroke rates (39).

PATHOLOGY

Frozen Shoulder

Frozen shoulder is a common condition characterized by limited passive shoulder range of motion (ROM) and pain. Typically, shoulder external rotation is particularly restricted because frozen shoulder usually includes scarring of the rotator interval—a triangular area in the anterior superior shoulder where the capsule is reinforced externally by the coracohumeral ligament and internally by the superior glenohumeral (GH) ligament; it is defined at its base by the coracoid process, superiorly by the anterior margin of the supraspinatus tendon, and inferiorly by the superior margin of the subscapularis tendon. Frozen shoulder can occur idiopathically, in which case it is also known as adhesive capsulitis; alternatively, secondary frozen shoulder can occur related to decreased use of the shoulder in the setting of another painful shoulder condition such as rotator cuff tear or tendinopathy.

The etiology of frozen shoulder remains unknown. Histopathological examination of GH capsular tissue in frozen shoulder demonstrates scattered inflammation and mast cell infiltration, suggesting an inflammatory component (40). This is also reinforced by the typically robust improvement of frozen shoulder following GH joint corticosteroid injection.

The incidence of frozen shoulder increases with age and is higher in women than in men. This preponderance of frozen shoulder in females is well known. Data from the United Kingdom published in 2011 demonstrated an incidence of adhesive capsulitis in women of 3.3 per 1,000 person-years versus 2.36 per 1,000 person-years in men. After adjusting for age, a 40% higher incidence was seen in women. The incidence for both men and women increases with age, although the increase plateaus for both sexes somewhat after age 60 (41). That the incidence increases with age may be particularly pertinent for sports medicine providers with the rising numbers of masters athletes (42,43). Data from the United Kingdom show a rising incidence of frozen shoulder among younger women, with no similar trend seen among men (41). The incidence of idiopathic frozen shoulder is higher among diabetics and among women with thyroid disease (44). Results following treatment for idiopathic frozen shoulder may also be somewhat worse among diabetics (45). In the UK study, the increasing incidence of frozen shoulder in younger women persisted despite adjustment for rising rates of diabetes (41).

In the absence of frozen shoulder, shoulder ROM has been demonstrated to remain relatively preserved throughout the aging process, confirming that decreased ROM represents a pathologic state across the age spectrum. Aging women have been demonstrated to have slightly greater range of shoulder flexion than men (46).

Many different treatments for frozen shoulder have been described, ranging from allowing the condition to run its course without intervention, to stretching programs, manipulation of the GH joint under anesthesia, and arthroscopic or open release of joint contracture. Few studies have demonstrated differences in outcomes with adhesive capsulitis between men and women. There are some data to suggest that women are able to achieve greater improvement in shoulder ROM than men with stretching programs for adhesive capsulitis (45), although other studies have found no gender difference in ROM following a stretching program (47). Functional outcomes have not been reliably demonstrated to be different between men and women.

Traumatic/Multidirectional Instability

Instability of the GH joint can be classified based on whether the onset of instability was traumatic or atraumatic and on the direction of instability. Instability is commonly referred to as unidirectional if instability is limited to one plane, or multidirectional if instability includes the anterior, posterior, and inferior directions. The term "instability" implies the presence of symptoms (apprehension or pain) associated with increased motion. "Laxity" refers to abnormal motion (the ability of the shoulder to sublux or dislocate in one or more directions) in the absence of symptoms. Thus, global laxity of the shoulder is not equivalent to multidirectional instability (MDI), although those with laxity are at increased risk for developing symptoms and thus progressing to MDI.

MDI was first described by Neer and Foster in 1980 (48). MDI is defined by the ability to sublux or dislocate the GH joint inferiorly as well as anteriorly and/or posteriorly, as well as the presence of symptoms during the midrange in a given plane of GH motion. Most authors describe inferior instability as a necessary component in the diagnosis of MDI (48–51). The anatomic findings in MDI include an enlarged inferior capsular pouch and a defect in the rotator interval capsule (the anterosuperior portion of the GH joint capsule in the region of the bicipital groove and the attachment of the coracohumeral and superior GH ligaments) (48,49,51).

In general, unidirectional instability is more likely to be related to a particular traumatic injury whereas MDI is more likely to have an atraumatic onset or to follow relatively minor trauma. The initial inciting event for MDI can, however, be more significant trauma (48,51). The repetitive stress from athletics, particularly gymnastics, weightlifting, and swimming the butterfly or backstroke, may be enough to cause the transition from laxity to instability in susceptible individuals (49–52). Female gymnasts are known to be at a particular risk for shoulder instability. In a survey of female NCAA gymnasts, 59% reported shoulder pain, more than 25% reported excess shoulder motion, and 11% met criteria for MDI (50,53).

Whether MDI is more common in females continues to be debated in the medical literature. While generalized laxity is more common in females, generalized laxity does not necessarily correlate with shoulder laxity specifically. Currently, the literature is inconclusive as to whether MDI of the shoulder is more common in females; however, it is our impression that instability is more of a problem in premenopausal females. This may be due to the fact that the sex hormones influence the structure and function of collagen (see Chapter 1 for more information on sex hormones). Studies looking at GH joint excursion in asymptomatic volunteers have demonstrated conflicting results. One study demonstrated more generalized GH hypermobility in women with increased anterior GH translation and decreased anterior GH stiffness compared to men with application of an anteriorly directed force (52), but a subsequent study by the same authors showed no gender difference in translation (54). A retrospective review of pediatric shoulder instability did not find MDI to be more common in girls than boys (53). In a study of shoulder instability at the U.S. Military Academy, MDI events associated with trauma were found to be more common in female cadets (55).

Estimates of the incidence of shoulder instability have focused on traumatic instability, which is more common in males (53,55). A study of shoulder dislocations presenting to the emergency department found an incidence of dislocation in men of 35 per 100,000 person-years and in women of 13 per 100,000 person-years. Dislocations in males occurred predominantly related to trauma from sports or recreation, whereas dislocations in females were more likely than in males to occur at home (56).

The trajectory of laxity during development is different in boys and girls. General joint laxity decreases consistently for boys as they age. In girls, general joint laxity decreases approximately from age 9 to 12 and then increases around the time of puberty (57). A study of young competitive swimmers demonstrated lower general joint laxity in 9-year-old girls but no change at age 12 compared to peer controls. Boys who were competitive swimmers demonstrated higher general joint laxity at both ages compared to peers. The authors postulated that the decrease in laxity in girls was due to increased muscle mass and that the higher laxity in boys was due to repetitive motion toward the extremes of ROM, counteracting the trend of boys generally becoming less lax as they age. They also commented that there is also likely an effect of sex hormone on laxity during and after puberty. They did not, however, find a difference between young swimmers and peer controls with regard to shoulder laxity specifically (58).

Other data on pediatric shoulder instability have shown that girls are more likely to have voluntary shoulder instability than boys and that girls with instability typically are younger at the time of their first instability episode (subluxation or dislocation). In a cohort in which some children with shoulder instability were managed operatively and some nonoperatively, boys demonstrated greater stability in long-term follow-up than girls. Girls also reported more limitation of sports participation due to instability. Boys, however, were more likely to have instability than girls, but the inciting event in boys was usually trauma. The group that did the worst in follow-up were older girls with voluntary instability, regardless of whether they were managed operatively or nonoperatively (53).

There are minimal data regarding outcomes in males versus females for shoulder MDI. In one study, males did slightly worse with nonoperative management than females

(59). In studies of operative management, females have a larger increase in GH capsular volume 1 year after capsular shift with Bankart repair. Being an elite athlete was also associated with larger capsular volume following surgery in that study (60). A study of patient satisfaction following surgery for MDI, however, found no sex difference in patient satisfaction following the procedure (61).

Minimal data are available regarding outcomes following surgery for traumatic dislocation that differentiate findings between men and women, but men have been shown to have a higher risk of redislocation following arthroscopic repair after a first anterior dislocation (62).

Rotator Cuff Pathology

Rotator cuff pathology, including partial- and full-thickness rotator cuff tears and rotator cuff tendinopathy, is a common source of shoulder pain and functional impairment. Some articles have also included subacromial impingement in the spectrum of rotator cuff pathology, but whether actual impingement underneath the acromion occurs has been questioned and remains unresolved. Evidence has demonstrated that subacromial spurs are associated with full-thickness rotator cuff tears, but that morphologic variants with a downsloping or hooked acromion (classically referred to as a type II and type III acromion, respectively) are not associated with tears (63). Subacromial impingement as a clinical entity, however, remains controversial. The incidence of rotator cuff tears increases with age (25,64,65). In a study using shoulder ultrasound in patients presenting with shoulder pain, the average age of patients with rotator cuff tears was 58.7 years old for unilateral tears and 67.8 years old for bilateral tears. Patients in whom no rotator cuff tear was demonstrated averaged 48.7 years old (25). Similar to shoulder instability, rotator cuff tears in men are more likely than those in women to be related to trauma or a direct blow to the shoulder (64,66).

There is likely a slightly increased prevalence of females with rotator cuff disease. Looking specifically at the incidence of rotator cuff pathology, it was found to be more common in women (90 per 100,000 person-years) compared to men (83 per 100,000 person-years), with the highest incidence (198 per 100,000 person-years) in those aged 50 to 59 (67). Another study demonstrated a higher prevalence of smaller rotator cuff tears specifically in young women compared with men, but no difference was seen between tear size in older women and men (64). A recent study elucidated that the mechanism behind this may be partly due to an association between a variant of estrogen-related receptor-beta and rotator cuff disease (68). However, not all studies support a gender difference, as there is a study that did not show increased prevalence of rotator cuff tears in young women (69). Focal osteoporosis of the proximal humerus in the setting of rotator cuff tears has been shown using quantitative computed tomography, with greater decrease in focal bone mineral density in women than in men (70).

A study of subjects electing nonoperative management for full-thickness rotator cuff tears demonstrated that women with full-thickness rotator cuff tears were less active with their shoulders compared to men. The authors hypothesized that the difference may be related to differences between men and women with regard to work, sports, and recreational activities (71). Women with full-thickness rotator cuff tears have also been shown to have decreased shoulder function compared to men with full-thickness tears (72,73).

In patients with planned rotator cuff surgery, concerns regarding surgery and postoperative recovery have been shown to be higher in women than in men (74), with concerns including the length of recovery and the postoperative course, as well as postoperative pain. Women have been shown to have different expectations for surgery than men with regard to interacting with and providing care for others, ROM, and return to work after surgery (66). Separately, patients with higher concerns going into surgery have been shown to have worse functional outcomes after rotator cuff repair (75). Women have been shown to report more emotional difficulty related to their shoulder injury preoperatively (64). Women with planned rotator cuff surgery also report a higher level of disability related to activities of daily living and sleep in comparison to men with a similar or lower level of pathology (66). Studies have also demonstrated that women report more interference in social functioning (66), lower activity levels (76), and worse scores for health-related quality of life than men prior to rotator cuff surgery (76).

Following rotator cuff repair, women have been shown to have less shoulder pain relief and more postoperative pain (65,77–79), as well as less recovery of shoulder activity (65,77), ROM (65,77), and strength (65,77,78) as compared to men. Women have also been demonstrated to be slower to return to work than men following rotator cuff repair (80). Younger women demonstrate more postoperative disability than older women after rotator cuff surgery (69); however, there are data that also show greater postoperative satisfaction in younger women than in older women (65). The level of postoperative disability may be more related to the degree of preoperative disability in women than men (69). Decreased outcomes with regard to function, pain, and stability have also been demonstrated in women compared to men following revision rotator cuff surgery (81,82). One study, however, showed greater improvement in pain and function in women than men following arthroscopic rotator cuff repair (83), while another demonstrated no difference in patient satisfaction between men and women following rotator cuff surgery (84).

Research has demonstrated baseline differences between men and women on the scores used to evaluate shoulder symptoms and function. The Constant Score, which measures pain, ROM, activity level, and strength (85), has in particular been shown to highlight baseline sex differences across all age groups in subjects without shoulder complaints, with higher scores seen in men (86,87). Some of the sex differences demonstrated in prior studies, particularly those using the Constant Score as an outcome measure, may thus overestimate sex differences in the setting of shoulder pathology. Due to the known baseline differences in shoulder functional scores, many studies now evaluate male and female subjects separately with no comparison between sexes.

Fractures

Fractures of the humerus are more common in women than in men when including all humeral fractures together, with an incidence nearly 1.5 times higher in women than in men (88). The incidence of proximal humeral fractures increases with age in both men and women, with a higher incidence of proximal humeral fractures in women. The incidence of proximal humeral fractures increases for both males and females in the 10- to 19-year-old age group, decreases in the following decade, and then slowly rises until age 50 with similar rates in both sexes. Following age 50, the incidence rises for both sexes but for women much more steeply than for men, with data from Rochester, MN, demonstrating a peak incidence of 439 fractures per 100,000 person-years in women aged 80 and over with a female-to-male ratio of proximal humeral fractures of approximately 4:1 after age 80. The proportion of proximal humeral fractures due to mild or moderate trauma as opposed to severe trauma also increases with age and is higher in women than men (88–90).

The complexity of proximal humeral fractures also increases with age. A study of patients hospitalized for humeral fractures in Germany found the majority of complicated, four-part proximal humeral fractures to be in women over age 60, with fractures in older women typically related to low-energy trauma such as ground level falls. Males under age 60 were more likely to have three- or four-part fractures than women in the same age group, with more than half of the fractures in men under age 60 from high-energy trauma (89). Isolated fractures of the greater tuberosity in particular are more common in men and are typically seen in younger patients than other proximal humeral fractures (91,92).

Although the scapula is uncommonly fractured (accounting for 1% to 3% of all fractures, including patients with polytrauma), data from motor vehicle collisions show a more than threefold higher rate of scapular fracture in men than women (93). Similarly, data from the military have shown the incidence of clavicular fractures to be more than twice as high in men than women (94).

Labral Tears

The glenoid labrum is a fibrous structure around the rim of the glenoid that deepens the cavity and adds support. The labrum can be torn from a single trauma or repeated microtrauma, and labral tears are oftentimes associated with shoulder instability. Tears of the glenoid labrum typically present as shoulder pain with mechanical symptoms that can include popping, locking, catching, or clicking.

Tears of the labrum have been described to occur at various locations. The most common location is the superior labral tear with extension from anterior to posterior (SLAP lesion). Repetitive overhead activities have been hypothesized as a mechanism for causing SLAP lesions. One theory of how this happens is that high eccentric activity of the biceps muscle creates tension on the long head of the biceps and its attachment onto the labrum during the deceleration and follow-through phase of throwing. Another theory is termed the "peel back" mechanism—when the shoulder is placed in a position of abduction and maximal external rotation, the rotation causes a torsional force at the base of the biceps and its attachment onto the labrum. SLAP lesions have also been associated with shoulder instability (108). Mechanical symptoms are present in approximately half of all patients with superior labral tears (95). In a single-institution retrospective review of all arthroscopic shoulder surgeries over an 8-year period, superior labral injuries were seen in 6% of cases with an average patient age of 38. In that study, 91% of superior labral injuries seen were in men with 9% of tears found in women (95). Management of glenoid labral tears, particularly SLAP tears, remains controversial. A retrospective study utilizing a national database to examine trends in labral repair surgery demonstrated that repair of SLAP tears was performed three times more often in men than women in the period from 2004 to 2009. One reason for the higher incidence and rate of repair in men may be the link between overhead throwing sports and SLAP tears. Additionally, orthopedic surgeons may be more likely to repair SLAP tears seen arthroscopically in men than women (96).

Labral tears can also occur antero-inferiorly and postero-inferiorly, and these are mainly due to shoulder instability. Postero-superior lesions have been described in overhead athletes, and this entity was first described as Walch's internal impingement, where repeated contact between the deep surface of the rotator cuff and the posterior superior labrum causes undersurface rotator cuff tears and degenerative labral tears (109). Internal impingement is associated with GH internal rotation deficit (GIRD) and scapular malposition, inferior medial scapular winging, coracoid tenderness, and scapular dyskinesis (SICK scapula syndrome). It has been suggested that internal impingement is most likely caused by fatigue of the muscles of the shoulder girdle resulting from lack of conditioning. As the shoulder girdle muscles become fatigued, the humerus drifts out of the scapular plane, which can lead to tensile stressing of the anterior aspect of the shoulder capsule. This can compromise the obligatory posterior rollback of the humeral head, leading to anterior translation and therefore causing the undersurface of the rotator cuff to abut the margin of the glenoid and labrum (110).

Myofascial Pain and Delayed Onset Muscle Soreness

Myofascial pain is characterized by pain related to sensitive trigger points in muscles. Myofascial trigger points can be either latent, where pain is present only with pressure over the trigger point, or active, with pain present constantly, including in the absence of overlying pressure. Trigger points prevent full lengthening and relaxation of the muscle (97) and produce a local muscle twitch response when stimulated. Trigger points can refer pain locally and even distally into an extremity (97).

Myofascial trigger points are commonly present in the shoulder musculature. The prevalence of myofascial trigger points in the shoulder region may be higher in women than in men (97). Although the prevalence of myofascial pain is unknown, a study of patients with chronic, atraumatic, unilateral shoulder pain presenting to a physical therapy clinic demonstrated active trigger points in shoulder girdle musculature in all 72 examined patients with a median of six involved muscles. The most common locations were the infraspinatus and upper trapezius. Myofascial trigger points were also commonly found in the middle trapezius, anterior deltoid, middle deltoid, and teres minor (97).

In asymptomatic subjects, women have been shown to have a lower pain threshold than men with pressure applied over the trapezius (98). A higher pain intensity has also been reported in women versus men following nociceptive stimulation with a noxious agent (hypertonic saline or glutamate) into the upper trapezius in subjects without pain at baseline (99–101). With repeated injections, a decrease in pain is seen in men but not in women, suggesting a gender difference in pain modulation (101). Additionally, motor control strategies during experimentally generated pain in the trapezius are different in women and men. Without experimentally induced pain, both genders show differential activation of different portions of the trapezius with sustained contraction (potentially to prevent overload of a specific muscle region during sustained contraction). That pattern has been shown to be maintained in men but not in women during experimentally induced pain in the trapezius, with women demonstrating no change in the recruitment pattern of the trapezius during experimentally induced pain (99). Men have also been shown to recruit more motor units of the trapezius during sustained contraction in the setting of experimentally induced pain with no similar increase in women (100).

Delayed onset muscle soreness following exercise has not been shown to be different between women and men when comparing pain pressure thresholds in shoulder girdle muscles up to 48 hours after resistance exercise (102) or when comparing pain with muscle contraction during delayed onset muscle soreness (103).

Osteoarthritis

Arthritis in general is more common in women than in men (46,104,105). GH osteoarthritis is associated with aging and is more common in elderly women than in elderly men (12). The prevalence of acromioclavicular osteoarthritis is more similar between the sexes (12), but may be more common in men than in women in the subset of patients with rotator cuff tears (66). A cross-sectional study of men and women living independently after age 65 showed decreased ROM with shoulder abduction in both men and women associated with aging, but a greater decrease was seen in women than in men. The prevalence of disability related to the shoulder was also higher in elderly women than men (105). In middle-aged and elderly individuals without shoulder pain, however, sex has been shown not to be predictive of degenerative changes on shoulder x-rays (106).

Management of severe GH osteoarthritis frequently includes total shoulder arthroplasty. There are minimal data to suggest postoperative differences between men and women; however, loosening of the glenoid component is more common in women than in men (107).

CONCLUSION

There are some definite differences between the sexes when looking at shoulder injuries, anatomy, biomechanics, and pathology. High school boys tend to have higher incidence of shoulder injuries than high school girls, and this includes injuries sustained from contact. However, this trend is not as clear for collegiate and elite athletes. When looking at the general population, shoulder pain tends to be more common in females than males. The anatomy of the shoulder is also different between the sexes. Males tend to have larger bony structures than females, including the humeral head, glenoid, and scapula. The rotator cuff insertions and thickness also appear to be slightly larger in males. Shoulder biomechanics between the sexes are also found to be different, with males having more strength but females having better endurance. There are differences in muscle activation patterns between the sexes. When looking at various diseases and pathology, suprascapular nerve entrapment, shoulder dislocations, isolated greater tuberosity fractures, scapula fractures, clavicle fractures, and SLAP tears tend to be more common in males, while frozen shoulder, MDI, rotator cuff disease, proximal humerus fractures, myofascial shoulder pain, and GH arthritis tend to be more common in females. Looking at postsurgical outcomes, males have a higher redislocation rate after arthroscopic stabilization surgery and tend to do less well with nonoperative treatment of MDI. Females tend to not do as well as males after rotator cuff repair or revision rotator cuff repair. All these differences between the sexes are interesting and not always intuitive. Practitioners can use this information to educate patients and also to be more aware of certain diagnoses based on a patient's sex.

Summary of Sex Differences With Regard to the Shoulder

Epidemiology	Sex With Higher Rate of Shoulder Injury/Pain
High school athletes	Boys (1,2)
Injuries after contact	Boys (3)
Collegiate and other athletes	Unclear, likely no difference (5–7)
Disabled/wheelchair athletes	No difference (9)
General population	Females (10–12)
Concurrent cervicalgia with shoulder pain	Females (10)
Biomechanics	**Sex With Greater Advantage**
Absolute shoulder strength	Males (28,29)
Endurance	Females (29,33)
Precision of muscle activation	Males (36)
Diagnoses/Conditions	**Sex With Higher Incidence/Prevalence**
Suprascapular nerve entrapment	Males (22)
Frozen shoulder	Females (41,44)
MDI	Possibly females, but inconclusive (52–55)
Shoulder dislocation	Males (53,55)

(*continued*)

Summary of Sex Differences With Regard to the Shoulder (*continued*)

Diagnoses/Conditions	Sex With Higher Incidence/Prevalence
Voluntary shoulder instability in pediatric patients	Girls (53)
Shoulder instability in pediatric patients (mostly related to trauma)	Boys (53)
Rotator cuff disease	Likely females (64,67,69)
Proximal humerus fractures	Females (88–90)
Isolated greater tuberosity fractures	Males (91,92)
Scapula fractures	Males (93)
Clavicle fractures	Males (94)
SLAP tears	Males (95)
Myofascial trigger points in shoulder	Females (97)
Delayed onset muscle soreness	No difference (102,103)
GH osteoarthritis	Females (12)
Acromioclavicular osteoarthritis	No difference (12)
Surgical Outcomes	**Sex That Does Worse/Has More Complications**
Nonoperative management of MDI	Males (59)
Patient satisfaction following surgery for MDI	No difference (61)
Shoulder redislocation after arthroscopic repair	Males (62)
Following rotator cuff repair	Likely females (65,77–80,83,84)
Following revision rotator cuff repair	Females (81,82)
Loosening of glenoid component after total shoulder arthroplasty	Females (105)

GH, glonohumeral; MDI, multidirectional instability.

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3

ELBOW, WRIST, AND HAND

Berdale Colorado

INTRODUCTION

Injuries of the elbow, wrist, and hand are common in the athletic population. Approximately 25% of all sports injuries involve injuries to the elbow, forearm, and wrist (1). Sex differences associated with the anatomy and biomechanics of elbow, wrist, and hand structures have been reported in the literature. These differences can have implications in various traumatic and overuse injuries seen in athletes. To understand and treat injuries of the musculoskeletal system, it is important to first understand the "normal" functioning of the involved body part among different populations, such as males and females. This can help providers identify risk factors for injury in order to optimize treatment and/or injury prevention. This chapter provides an overview of gender and sex differences in elbow, wrist, and hand anatomy and biomechanics and looks specifically at various injuries in which sex differences have been reported in the literature.

ANATOMY AND BIOMECHANICS

Elbow

The elbow joint involves three articulations: the proximal radioulnar joint, the ulnohumeral joint, and the radiocapitellar joint. It has two degrees of freedom: flexion-extension and pronation-supination. Stability of the elbow joint is accomplished primarily by the congruity of the articulations, the capsule, as well as the ligament complexes. Myotendinous units that cross the joint also provide dynamic stability.

Normal elbow range of motion (ROM) is approximately 0° to 150° of flexion and 80° of pronation and supination (2). Golden et al. evaluated 600 elbows (300 participants) of healthy children and adolescents and found females to have greater total ROM, greater flexion, and greater extension than males (3). Chapleau et al. demonstrated similar findings of greater elbow ROM in females compared with males in an adult population (4).

The elbow has a relative valgus alignment, formed between the long axis of the humerus and the long axis of the ulna when in full extension and supination, called the carrying angle. This angle is approximately 5° to 10° (2). Numerous studies have demonstrated an increased carrying angle in females (5–11). This difference has often been considered to be a secondary sex characteristic. Not all studies, however, have noted this difference. Beals conducted a radiographic study of the carrying angle in 422 patients and found no real differences in males and females (12). The author suggested that the clinical observation of an increased carrying angle in females may be explained by increased joint laxity, allowing for a greater degree of extension (Figure 3.1).

An increased carrying angle, when combined with the significant valgus and extension forces generated in overhead throwing motions, can lead to stress injuries of the elbow. Continued valgus stress can cause ligament damage, formation of olecranon tip osteophytes, loose bodies, articular damage, flexor-pronator tendonitis, ulnar neuritis, and medial epicondylitis or apophysitis (13).

Wrist

The wrist consists of the distal ulna, distal radius, eight carpal bones, and the bases of the metacarpals. It is divided into three primary joint regions: distal radioulnar, radiocarpal, and midcarpal. It has two primary degrees of freedom: flexion-extension and radial/ulnar deviation. Normal wrist palmar flexion is 75° to 80° and normal dorsal extension is 75° to 85° (2). Normal radial deviation is 20° to 25°; normal ulnar deviation is 35° to 40° (2). Allander et al. analyzed wrist joint ROM in 517 females and 203 males, all ranging in age from 33 to 70, and found

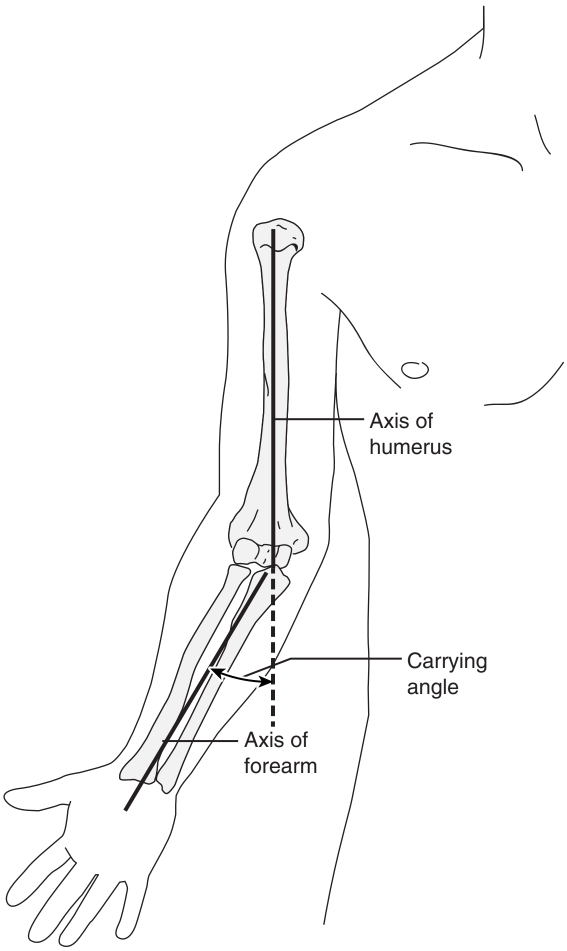

FIGURE 3.1: Carrying angle.

that females had significantly larger ROM in the wrist than males (14).

The relative length of the ulna in relation to the radius at the level of the wrist is called ulnar variance (Figure 3.2). Ulnar variance may be positive (ulnar projects distally), negative (ulnar projects more proximally), or neutral (both the ulnar and radial articular surfaces are the same length).

Ulnar variance has been associated with various pathological states. Positive ulnar variance has been associated with ulnar impaction syndromes and triangular fibrocartilage complex (TFCC) injury. Negative ulnar variance has been associated with Kienbock's disease, avascular necrosis of the scaphoid, and scapholunate dissociations.

Goldfarb et al. assessed ulnar variance in the adolescent population and found that young adolescent boys demonstrated a greater degree of negative ulnar variance compared with young adolescent girls (15). Nakamura et al. measured ulnar variance in 325 normal wrists, consisting of 203 males and 122 females ranging in age from 14 to 79 years (16). The study found that males had a lower mean value (i.e., greater degree of negative ulnar variance) in all age groups compared with females.

Hand/Fingers

The skeletal anatomy of the hand consists of phalanges, metacarpal bones, and carpal bones. These 27 bones serve as attachment and insertion sites for muscles and ligaments that can produce a vast array of movements and tasks through complex interactions (17).

Mallon et al. assessed the ROM of fingers in young healthy adults. The study found that females showed an increased amount of both active and passive extension at all joints on all digits (18).

Overarm Throwing Kinematics

The position of the hand, shoulder, and elbow during overarm throwing all play a role in the amount of stress experienced across the elbow. Van den Tillaar and Cabri investigated the throwing velocity and kinematics of overarm throwing in elite female and male handball players (19). The analysis consisted of maximal joint angles, angles at ball release, maximal angular velocities of the joint movements, and maximal linear velocities of the distal endpoints of segments and their timing during the throw. No major differences in kinematics were found, except for the maximal endpoint velocities of the hand and wrist segment (19). The authors conclude that male and female handball players throw with the same technique, and differences in throwing velocity are generally not the result of changes in kinematics in the joint movements.

The perception that sex alone causes suboptimal throwing mechanics appears false. "Throwing like a girl" may simply be an immature throwing mechanic and not a specific gender-related anatomic or physiologic finding (20). Multiple studies have reported that the pace of developing a mature throwing mechanic may be delayed in females compared with males (21,22). While gender has generally been a reasonable predictor when evaluating throwing velocity, if grouped by stages of development, gender explains no more than 2% additional variance (23). This finding is discussed in greater depth elsewhere in this textbook, in Chapter 4 on upper limb mechanics: throwing.

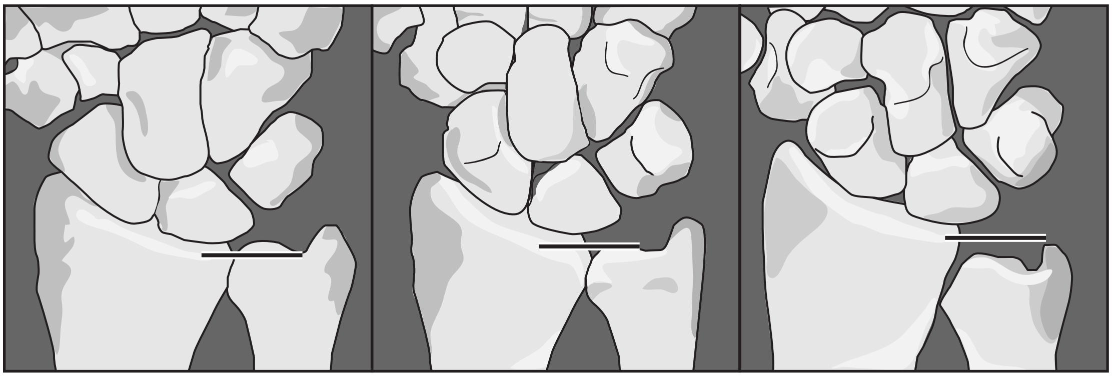

FIGURE 3.2: Ulnar variance.

Swing Kinematics

The golf swing is a complex movement utilizing the whole body in a coordinated fashion. Repeated motion can result in injury in both professional and amateur golfers. Female golfers have been found to have twice as many wrist injuries as males (24). Zheng et al. compared the golf swing kinematics between 25 female and 25 male professional golfers (25). Significant differences were found in the maximum angular velocity of both wrists, the maximum angular velocity of the right elbow extension, and the timing when the maximum left wrist angular velocity occurred. These velocity differences may account for the difference in wrist injury incidence.

SELECTED INJURIES/PATHOLOGY

Reported sex differences in specific injuries/pathology of the elbow, wrist, and hand are somewhat limited in the literature. However, the injuries described in the following sections have been found to have differing incidence in males and females.

Valgus Extension Overload

Valgus extension overload (VEO) is a constellation of symptoms and pathology seen with overarm throwing athletes as a result of high repetitive stresses generated by overarm throwing motions. There is increased incidence of VEO in males, given the high association with baseball pitchers. With each pitch, the elbow joint is subject to a valgus torque reaching an average of 64 Nm, of which approximately 50% is taken up by the ulnar collateral ligament (UCL) (26). Overhead sports requiring similar motions, such as a tennis serve, football pass, or volleyball spike, can also produce tensile forces to the medial elbow. The valgus carrying angle of the elbow, which can be increased in females, may predispose the medial elbow to overuse injuries.

A valgus torque of 45 Nm is generated at the elbow during underhand softball pitching (27). Although a smaller magnitude of force is exerted on the softball pitcher's elbow compared with a baseball pitcher, Barrentine et al. suggest that the underhand throwing motion in softball may not be as safe from overuse injuries as previously thought (27).

Ulnar Neuropathy

Compression at the Elbow/Cubital Tunnel

At the level of the elbow, the ulnar nerve enters the ulnar groove formed between the medial epicondyle of the humerus and the olecranon process of the ulna. Distal to this groove, the ulnar nerve travels under the two heads of the flexor carpi ulnaris muscle, known as the cubital tunnel (Figure 3.3). Ulnar neuropathy at the elbow may be caused by compression at the ulnar groove or at the cubital tunnel.

Ulnar neuropathy at the elbow is the second most common entrapment neuropathy of the upper extremity. Richardson et al. compared characteristics of patients with and without ulnar neuropathy at the elbow and found that men were more likely to have an ulnar neuropathy at the elbow than women (28). The study also found that more women with a body mass index (BMI) of less than or equal to 22.0 had ulnar neuropathy at the elbow when compared to women with a BMI greater than 22.0, suggesting that thin women are at increased risk for ulnar neuropathy

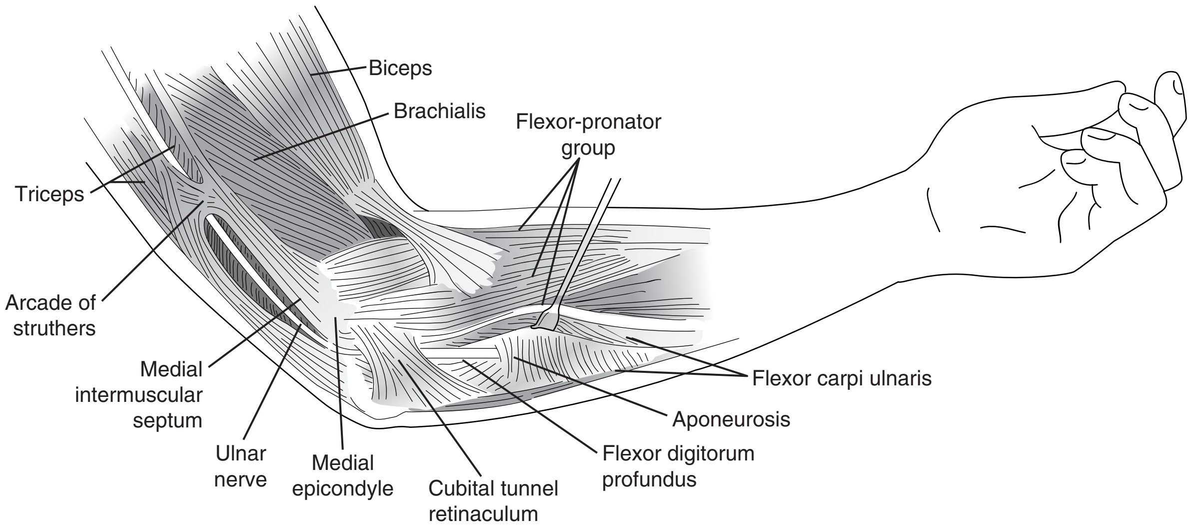

FIGURE 3.3: Cubital tunnel.

at the elbow, presumably due to susceptibility to external compression. This trend was not seen among men. The authors suggested that any mechanical protective effect of an increased BMI in males may be offset by increased forearm muscle mass and grip strength that produce greater pressures over the ulnar nerve (28).

Contreras et al. also looked at sex differences and their relationship to ulnar neuropathy at the elbow (29). They found significantly larger (2 to 19 times greater) fat content on the medial aspect of the elbow in women compared to men. In addition, the tubercle of the coronoid process was approximately 1.5 times larger in men. These two anatomical findings suggest two mechanisms by which the ulnar nerve may be predisposed to increased risk of compression in males compared to females.

There has been increased use of ultrasound in the evaluation of nerves, including the ulnar nerve. Multiple studies have demonstrated increased cross-sectional areas and increased cross-sectional diameters in healthy males when compared with healthy females (30,31).

Compression at the Wrist/Guyon's Canal

At the level of the wrist, the ulnar nerve enters a canal formed proximally/medially by the pisiform bone and distally/laterally by the hook of the hamate, called Guyon's canal. In the canal, the nerve divides into the superficial sensory and deep palmar motor branches.

Ulnar neuropathy at the wrist/Guyon's canal is much less common than ulnar neuropathy at the elbow. It is most commonly due to a ganglion cyst within Guyon's canal that compresses the ulnar nerve. Women are three times more likely to be affected by hand and wrist ganglions than men (32). Ulnar neuropathy at the wrist/Guyon's canal can also be associated with trauma and fractures.

Olecranon Bursitis

Olecranon bursitis is inflammation of the subcutaneous synovial-lined sac of the bursa overlying the olecranon process of the ulna. Annual incidence is approximately 10/100,000 and predominantly affects male patients (80%) aged 40 to 60 years (33). Most cases of nonseptic bursitis seen in athletes are posttraumatic or due to overuse.

Lateral and Medial Epicondylosis

Lateral epicondylosis, often referred to as tennis elbow, is a common cause of lateral elbow pain. It is an overuse syndrome affecting the wrist extensors, particularly the extensor carpi radialis brevis tendon. The literature is mixed regarding incidence of lateral epicondylosis between males and females. Several studies note an increased incidence in females (34–36). Other studies note equal incidence in males and females (37–39).

Medial epicondylosis, often referred to as golfer's elbow, is a common cause of medial elbow pain. It is less common than lateral epicondylosis. It is an overuse syndrome affecting the wrist flexors. There appears to be equal incidence in males and females (38–40).

Triangular Fibrocartilage Complex

TFCC consists of the articular disc, the meniscus homologue, the dorsal and palmar radioulnar ligaments, the ulnolunate and ulnotriquetral ligaments, and the extensor carpi ulnaris tendon sheath. The TFCC plays a key role in stabilization, rotation, translation, and loading transmission to the wrist and acts as an essential pivot point (41). It is prone to injuries because of its anatomical location and involvement in rotation and load bearing. Positive ulnar variance is associated with degeneration of the TFCC, while negative ulnar variance is associated with less degenerative wear (41).

Mallet Finger

Mallet finger, also known as baseball finger, is a deformity caused by rupture of the extensor tendon after sudden passive flexion of the distal interphalangeal joint when the finger is extended. Peak incidence has been found to vary between sexes, occurring in young to middle-age men and in older women (42).

Boxer's Fracture

Boxer's fracture is a fracture of the metacarpal neck/shaft that may be seen after a person strikes a wall or another person with poor technique. It may occur at any digit but is commonly seen in the fifth digit. Gudmundsen and Borgen reviewed 271 fifth metacarpal fractures and found 48% were related to aggression, with males comprising 93.1% of the aggression group as well as 70.2% of the nonaggression-related group (43).

CONCLUSION

Significant sex differences exist in the anatomy and biomechanics of the elbow, wrist, and hand. In addition, various injuries have higher incidence in males or females. Knowledge of these differences can provide greater understanding of the musculoskeletal system and can help providers optimize their treatment of elbow, wrist, and hand injuries in athletes.

Summary of Sex Differences in the Elbow, Wrist, and Hand

Anatomy/Biomechanics	Sex Difference
Elbow ROM	Increased in females (3–4)
Wrist ROM	Increased in females (14)
Finger ROM	Increased in females (18)
Carrying angle	Increased in females (5–11) No difference (12)
Negative ulnar variance	Increased in males (16)
Musculoskeletal Complaint	**Sex Difference in Prevalence**
VEO	Increased in males (26)
Ulnar neuropathy at the elbow	Increased in males (28)
Ulnar neuropathy at the wrist	Increased in females (32)

(*continued*)

Summary of Sex Differences in the Elbow, Wrist, and Hand (*continued*)

Musculoskeletal Complaint	Sex Difference in Prevalence
Olecranon bursitis	Increased in males (33)
Lateral epicondylosis	Increased in females (34–36) No difference (37–39)
Medial epicondylosis	No difference (38–40)
TFCC injury	Possibly increased in females due to association with positive ulnar variance
Boxer's fracture	Increased in males (43)

ROM, range of motion; TFCC, triangular fibrocartilage complex; VEO, valgus extension overload.

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4

THROWING

Ashwin N. Babu and Gary P. Chimes

INTRODUCTION—WHY IS THROWING IMPORTANT?

Throwing has long been an important part of American culture. Evidence of this can be found in the presence of throwing sports such as baseball and softball. Over 5.6 million youth age 6 to 18 participated in baseball in 2012 (1). According to the National Federation of State High School Associations, in 2013/2014, softball was the fourth most popular high school sports activity for girls and baseball was the third most popular sport for boys (2). National Collegiate Athletic Association (NCAA) baseball and softball participation has increased every year for the past decade, and as of 2014, over 33,000 baseball and 19,000 softball athletes took the field (3). On the professional level, the 2014 World Series drew an average of 13.9 million viewers according to an article in *Forbes* (4). Furthermore, participation in throwing sports is not limited to the United States. The World Baseball Classic is an international baseball tournament that drew teams from 15 countries around the globe in 2013. According to a Major League Baseball (MLB) press release, over 850,000 people attended the tournament, and television viewership records were set in several countries including the Dominican Republic, Japan, and Puerto Rico (5).

While these figures are impressive, viewership and participation in baseball has declined in recent years, particularly in youth programs such as Little League Baseball (6). Despite this, throwing is still important due to its role as a gateway to understanding human biomechanics and evolution. Several researchers propose that throwing may have been a core component of early human hunter-gatherer societies (7–9). In fact, while several primate species are able to throw, humans can do so with significantly higher velocity and accuracy (10). This was likely an important mode of early hunting and defense. As an example, in a model proposed by Bingham in 1999, throwing was *the* pivotal element that helped define humans as a unique species (11). Early human societies needed to enforce cooperative behavior among non-kin. Bingham proposed that this was accomplished in part by throwing, which allowed early humans to deliver punishment at a distance. This spread the cost of enforcing cooperation across all those who were throwing, while still carrying significant cost to the punished individual. Given the potential role throwing played in human evolution, both as an early hunting method and as a form of community justice, it is unsurprising that certain forms of throwing are still present in the modern age.

The importance of sex differences in throwing can be seen in the prevalence of the phrase “throw like a girl.” These four words are more than an observation of throwing technique; rather, they carry strong emotional undertones. As a result, they appear in books (12,13), newspapers (14), websites (15), TV commercials (16), and research articles (17,18). The sex differences in throwing have clearly captured the public’s attention and warrant further investigation.

THE BIOMECHANICS OF THROWING

Before investigating the sex differences present in overhead throwing motions, it is important to have a firm grasp of the intricate biomechanical processes present in this activity. This section discusses both the kinetics and kinematics of throwing. Kinetics is the study of the forces responsible for movement, while kinematics is the description of movement independent of the forces producing that movement (i.e., displacement, velocity, acceleration) (19). In order to study the throwing motion, investigators have used technology such as electromyography (EMG) to analyze muscle activation patterns, as well as more sophisticated three-dimensional motion analysis equipment (20,21).

While there are several ways to classify throwing motions, it would be prudent to use the terms most often cited in the baseball overhand pitching literature. A "mature" movement pattern was defined by Wickstrom in 1975 (22) as a basic motor pattern used by skilled adults for that activity. For the purposes of this chapter a "mature throwing pattern" is defined as one used by skilled adults. Later, it will be necessary to investigate how the mature patterns differ between men and women.

It is also important to define and discuss the six phases of the mature throwing pattern. The description that follows is partly based on the model outlined by Fleisig in 1996 (23). Similar accounts have been seen in more recent literature, for instance by Weber et al. in 2014 (24). The six phases are wind-up, stride, arm-cocking, arm acceleration, arm deceleration, and follow-through. An in-depth discussion of each follows, and a visual representation can be seen in Figure 4.1.

The Wind-Up Phase

The wind-up phase begins the throwing motion (Figure 4.1A–C). The thrower lifts the lead leg, which is defined as the leg contralateral to the throwing arm. By doing this, all the weight is placed on the stance (ipsilateral) leg. It should be noted that in baseball pitching, there are two main variants of the wind-up phase (21). One form is termed "from the wind-up," in which the pitcher stands initially with feet, hips, and shoulders all facing the batter. In this instance the first motion is typically a small step with the lead leg moving backward (away from the batter) and laterally. Next, the ipsilateral leg is repositioned so the foot abuts the pitching rubber with toes facing perpendicular to the batter. In a right-handed pitcher, the toes are facing third base. The lead leg is then lifted. The other wind-up form is called pitching "from the stretch" and is the more basic throwing pattern described in the literature. In this case, the pitcher stands facing perpendicular to the batter, with the stance leg (ipsilateral to the throwing arm) abutting the pitching rubber. Regardless of which variant is used, at the end of the wind-up phase, the lead leg is raised with hip and knee flexion, while the stance leg remains planted.

The Stride Phase

Next is the stride phase of throwing (Figure 4.1C–F). This phase is characterized by the forward motion of the lead foot toward the target until it contacts the ground (23,24). While moving forward, the lead hip abducts and externally rotates, resulting in the lead foot contacting the ground with the toes facing the target and the hips beginning their rotation. In addition, the hands begin to separate, allowing the lead hand to mimic the lead leg's position pointing toward the target. Simultaneously, the throwing arm begins to abduct at the shoulder in the horizontal plane and externally rotate, beginning the arm-cocking motion (24). The stride contributes to the velocity of the projectile in two important ways. First, it involves stretching the body, which stores the kinetic energy that will be used later on in the throw. Second, the stride provides forward linear velocity directly contributing to the projectile's release velocity.

The Arm-Cocking Phase

The next phase is the arm-cocking phase (Figure 4.1F–G). After the lead foot hits the ground, the quadriceps activate

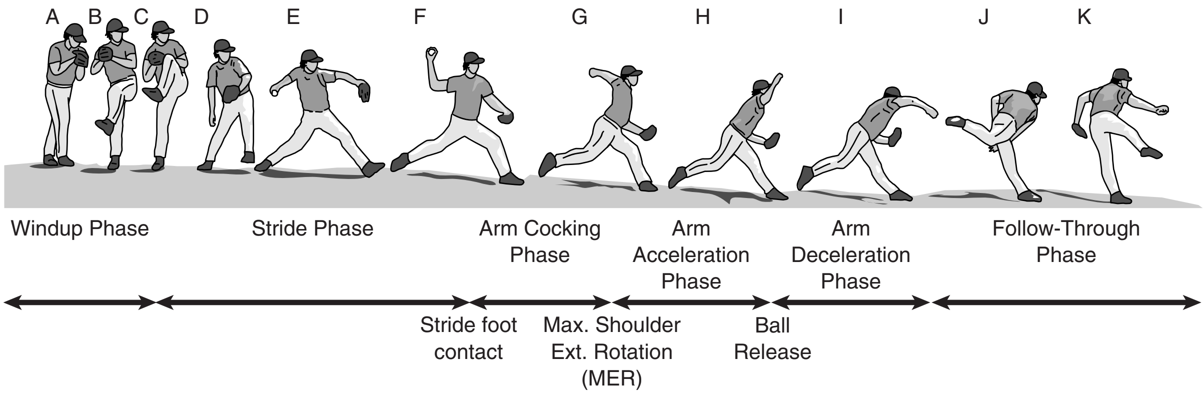

FIGURE 4.1: The phases of the baseball pitching motion.

Source: Adapted from Ref. (31). Chu Y, Fleisig GS, Simpson KJ, et al. Biomechanical comparison between elite female and male baseball pitchers. *J Appl Biomech.* 2009;25(1):22–31.

eccentrically to slow knee flexion and then isometrically to stabilize the leg. This creates a stable platform, which allows the pelvis to begin its rotation followed by the trunk and upper torso. At the same time, in the throwing arm the elbow begins to flex toward 90° while the shoulder begins to externally rotate. The arm-cocking phase ends once the throwing shoulder reaches maximal external rotation (MER). At this stage, the legs, hips, and trunk have all completed their acceleration and the throwing arm is poised to begin its rapid acceleration toward the target. Many researchers and clinicians consider the instant when the throwing shoulder is at MER to be a critical moment regarding pathologic and adaptive changes seen in the elbow and shoulder (24). At this time, there are tremendous forces acting at the glenohumeral (GH) joint. The rotator cuff muscles are crucial at this juncture to maintain GH stability. Some individuals who frequently partake in high-velocity throwing motions develop adaptive or pathologic changes to their range of motion (ROM) at the throwing shoulder (24,25). Specifically, experienced throwers gain external rotation and lose internal rotation in the throwing shoulder, although the total ROM typically remains the same (24).

The Arm Acceleration Phase

Following MER, the thrower enters the arm acceleration phase (Figure 4.1G-H). This is when the majority of the stored kinetic energy from the previous phases is translated into projectile velocity. The stride leg begins to extend, correlating with the trunk moving from an extended to flexed position. In the throwing arm, the shoulder begins to internally rotate while the elbow begins to extend. This is accomplished by concentric activation of the triceps, pectoralis major, latissimus dorsi, and serratus anterior muscles. The elbow extension is controlled by eccentric firing of the elbow flexors. Elbow extension lags behind shoulder internal rotation. This decreases the amount of internal rotation resistance at the shoulder, allowing for greater shoulder rotational velocity. These coordinated movements of the kinetic chain culminate at ball release, which ends the acceleration phase. During this phase, the humero-thoracic rotational velocities can reach up to 6,000 degrees to 8,000 degrees per second at ball release (24).

The Arm Deceleration Phase

Arm deceleration is the next phase (Figure 4.1H-I). It begins with ball release and ends when the shoulder reaches maximal internal rotation. Immediately after ball release, there is a large distraction force on the throwing arm, which is counterbalanced by the rotator cuff muscles. Also, during this phase, the arm begins to adduct across the body in the horizontal plane and large eccentric loads are required to slow down the arm's internal rotation and anterior translation in the GH joint. This is accomplished by firing of the infraspinatous and teres minor muscles, as well as by the mechanical constraints of the posterior capsule of the shoulder. Eccentric firing of the elbow flexors slows elbow extension (24).

The Follow-Through Phase

The follow-through (Figure 4.1J-K) is an important phase where the extreme forces generated by the throwing motion must be dissipated safely. This phase begins after maximal internal rotation and extends until the thrower regains balance. Here, the body weight and momentum are transferred to the stride leg. The trunk continues to decelerate and the stance leg is brought forward with the hip and knee flexed. The arm and scapula continue decelerating, an action modulated by the eccentric contraction of the deltoid, rotator cuff muscles, serratus anterior, trapezius, and rhomboids. Elbow extension continues to slow as well, controlled by eccentric elbow flexor contraction (24).

THE SEX DIFFERENCES IN THROWING OUTCOMES

Once one has a firm understanding of the biomechanical principles behind the mature throwing motion, an investigation of the differences present between male and female throwers can begin. There are several ways one could distinguish throwing characteristics between two groups, and they fall into two categories. The first category involves looking at the outcomes of a throw. For example, one could compare the throwing velocity, throwing accuracy, or throwing distance between the groups. The second category involves an examination of the throwing action itself. One could compare the biomechanical characteristics of an individual's throwing motion to the model of the mature throwing motion described previously. These two categories are certainly interrelated since the mature throwing motion was described by analyzing individuals who were able to throw with the most desirable outcomes. Therefore, one would expect that individuals with biomechanics most closely related to the mature throwing pattern may also be the individuals who are able to throw with the greatest velocity, highest accuracy, and greatest distance.

Sex Differences in Throwing Velocity

The first outcome that will be used to determine the differences in throwing ability between males and females is velocity. Variation in throwing velocity is considered to be the result of variation in throwing biomechanics and force production. The landmark studies examining sex differences in throwing velocity were conducted by Thomas and French in 1985 (26). Their work initially was not intended to examine the sex differences in throwing; rather, the intention was a literature review examining how boys and girls differed in their performance of various motor tasks. The authors performed a meta-analysis, and it became clear that throwing was uniquely suited to show sex differences compared with other tasks. They used standard deviation scores (also referred to as effect size) to summarize the magnitude of sex differences. For the majority of motor tasks tested, there were small or negligible differences in performance until puberty, at which point males began to outperform females. This trend was seen for balance, tracking tasks, tapping, sprinting, sit-ups, long jump, grip strength, and shuttle running. Generally speaking, after puberty these effect sizes were in the range of 1.0 to 2.0.

Fascinatingly, the data for throwing velocity were markedly different. Even at the earliest ages studied (as young as 5 years of age), the average effect size between boys and girls was found to be 1.5. This was a larger effect size at age 5 than some tasks demonstrated even after puberty. Furthermore, this difference increased at older ages. Just *prior* to the onset of puberty (age 11), males outperformed females with an effect size of 3.5 standard deviation units (26). This indicates that the overwhelming majority of boys threw with higher velocity than girls, and this change is likely not accounted for by pubertal changes such as a growth spurt.

Other studies have shown similar results. Hyde reviewed 46 meta-analyses examining gender differences in various categories including cognitive, social, psychological, and motor domains and found the largest gender differences in overhand throwing for velocity and distance (27). Halverson et al. (28) investigated how children developed skill with overarm throwing longitudinally. Again, boys outperformed girls with the gap between the two groups growing with age. Of note, at the seventh-grade level, the highest-performing boy only marginally outperformed the highest-performing girl. The main difference between the two groups was that the slower throwing boys as a group outperformed the slower throwing girls. Runion et al. repeated this experiment 20 years later in 13-year-olds and found that throwing velocities of boys and girls were very similar to the original study and that boys still significantly outperformed girls (29). This trend is mirrored in more elite athletes as well, based on studies performed in handball (30) and baseball (31) athletes. Interestingly, a study by Lorson et al. found a sex difference in throwing form and velocity for adolescents and young adults but not for older adults (mean age 44.9 years), suggesting the sex difference decreases into middle age (32). Further study examining throwing throughout the life span is certainly warranted. In summary, this body of work showed that females displayed a significantly higher variation in throwing velocity than their male counterparts overall. While a small number of high-performing female athletes threw with velocities similar to high-performing males, the vast majority of average and lower-performing boys outperformed the average and lower-performing girls. A visual representation of this effect is seen in Figure 4.2.

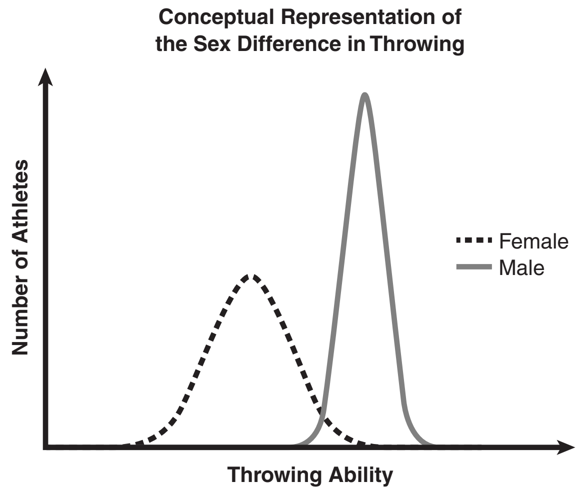

FIGURE 4.2: Conceptual representation of the sex difference in throwing.

Sex Differences in Throwing Distance

The next outcome that is examined is throwing distance. Like throwing velocity, maximal throwing distance is largely a factor of throwing mechanics and force production. As might be expected, the sex difference in throwing distance mimics that of throwing velocity. Again, the work by Thomas and French (26) was instrumental. They found that by age 3, boys threw farther than girls with an effect size of 1.5. By the onset of puberty, this effect size was over 2.0. At age 17, this effect size reached an enormous 3.5

standard deviation units. In a literature review, Alexander summarized that the average 17-year-old male throws farther than 99% of 17-year-old females (33). These findings were substantiated by other similar studies, such as those done by Nelson et al. (43) who studied kindergarten-aged boys and girls and found an effect size of 1.8 standard deviation units. Katzmarzyk et al. studied both African American and Caucasian boys and girls performing various motor tasks, including throwing for distance. At ages 7 to 8 (the youngest ages tested), throwing distance best differentiated boys from girls irrespective of race (34). This, combined with the other studies described previously, provides ample support that a large sex difference in throwing distance exists between males and females, and this difference is present at a young age.

Sex Differences in Throwing Accuracy

The next outcome to examine is throwing accuracy. A reasonable critique of using throwing velocity or throwing distance as a metric for throwing skill is that both are in part dependent on the force the thrower is able to produce. Since it is generally accepted that, on average, males are stronger and able to generate larger forces than females, it would be helpful to use an outcome that is not force dependent. Throwing accuracy, therefore, would be a useful outcome measure since force production is less relevant.

Studies thus far have shown that males throw with greater accuracy than females at any age (26,35). This has been shown to be true regardless of the subjects' history of sports participation, throwing style (over versus underhand) or object thrown (balls versus darts) (36). Furthermore, this sex difference does not appear to be related to improvements in accuracy with repeated practice, since men and women adapt to incorrect throws at a similar rate in the short term (36). However, unlike throwing velocity and distance, the sex difference seen in throwing accuracy does not change with age (26). It is worth noting that highly skilled females performed close to high-performing males, but overall the less-skilled males performed much better than the less-skilled females. This mimics the trend seen in throwing velocity and distance, with the major contributor to sex differences in throwing accuracy being the relatively larger number of females performing at a lower level.

In summary, it has been seen that males typically outperform females in throwing for velocity, distance, and accuracy (26–36). These findings are present very early in development, and the magnitude of this difference is far greater than that seen with other physical activities. The gulf between males and females in throwing velocity and distance grows significantly with age, while the difference is throwing accuracy stays consistent.

Sex Differences in Throwing Form

After examining the large body of literature describing the sex differences in throwing outcomes, one may be interested in critically appraising the throwing motion itself. In 1938, Wild developed a descriptive way to analyze throwing mechanics (37). A more detailed scale was put forth by Roberton et al., and this has been used extensively in the recent literature (28,32,38–40). Roberton and Halverson used a body component approach and described developmental changes in different body sections during the throwing motion (41). In the 1980s and 1990s, several investigators performed studies showing that boys progress toward a mature throwing pattern faster than girls (28,42–44). For instance, Halverson et al. noted that by the seventh grade, only 29% of girls had developed a mature throwing pattern of the humerus compared to 82% of the boys in the study. Similar results were found for throwing patterns of the trunk and forearm. Halverson concluded that boys and girls go through the same pattern of development in throwing, but girls tended to lag behind boys by 5 or 6 years (28). Similar results were found by Runion et al. (29). Earlier it was noted that a large component of the sex difference between boys and girls in throwing velocity, distance, and accuracy was due to the large variability in the female population, (i.e., a few girls were very high performing, but a large number were very low performing). This trend was mirrored when investigating throwing biomechanics. A study performed by Rippee et al. demonstrated that girls were much more variable than boys in throwing mechanics (44).

WHY SEX DIFFERENCES IN THROWING EXIST

The body of literature supporting the notion that males outperform their female counterparts in throwing activities is quite convincing (see table in Conclusion section). The next logical question is *why*? Investigators have proposed several theories to explain this sex difference, and the majority fall into the two most familiar categories in behavioral science: nature versus nurture. More specifically, one category of theories cites reasons that are tied to the inherent sex differences in anthropomorphic, strength, or hormonal variables (i.e., nature). The other category focuses on sex differences in societal pressures and gender role expectations (i.e., nurture).

Sex Differences in Anatomy

The first of the "nature" theories attempting to explain why men throw with better outcomes than women is perhaps the most obvious: the sex differences in physique. There are well-documented sex differences in height, weight, body shape, and alignment of extremities (45). One may expect several of these parameters to correlate with maximal throwing velocity and distance. From a biomechanical perspective, having shorter limb segment lengths may be a factor for decreased velocity (31,46). In fact, in a study comparing professional and amateur female handball athletes, the professionals were found to be taller and have a higher fat-free body mass (FFBM). These were also the athletes who threw with the greatest velocity (47). Similar findings were seen in elite female water polo players (48). In another study by Van den Tillaar (30), males threw with faster velocities than females, but the differences between the two groups could be explained by size differences when expressed as FFBM, as opposed to height and weight. While this may appear to contradict the body of work described earlier, it should be noted that Van den Tillaar's study was performed in a small number of *elite* handball players; therefore, a smaller gap in throwing velocity between men and women would be less surprising. The conflicting available studies make it difficult to quantify the impact that sex differences in physique have on throwing outcomes, although being taller and having higher FFBM appears to be correlated with increased throwing velocity.

Sex Differences in Strength

Perhaps an even more intuitive explanation for throwing differences between men and women would be differences in strength. In order to execute a forceful throw, the athlete must be strong enough to manipulate the object being thrown. This line of thinking led several researchers to investigate the effect of strength relative to ball weight on throwing velocity. To test this idea, one could vary the weight of the ball or vary the strength of the thrower. Fleisig et al. reasoned that if the ball is too heavy for the athlete, he or she may attempt to decrease the torque required to throw the ball by keeping the ball closer to the head. This is referred to by pitching coaches as "pushing the ball" or "leading with the elbow." This motion is similar to that adopted by quarterbacks throwing a football, which weighs roughly three times that of a baseball (20). These authors conducted a study comparing the throwing velocities and throwing kinetics of male youth pitchers using regulation (5 ounce) and lighter (4 ounce) baseballs. They then compared the findings to those of college and professional pitchers, collected from another study. Throwing a lighter ball did not change the joint angles used during the throw, although the pitchers were able to generate higher arm and ball velocities than when throwing the regulation baseballs (20). This would imply that increased velocities are possible with lighter balls to a degree. These results were corroborated by work done by Van den Tillaar and Ettema, who found that accomplished female handball athletes were able to throw lighter balls faster than heavier balls. This study also found kinematic differences in shoulder internal rotation and elbow extension (49), both of which are prime determinants of ball velocity. It should be noted that several studies were done investigating the use of slightly heavier or slightly lighter balls during training to improve throwing velocity. This work has its roots in Soviet research from the 1970s and 1980s, which was summarized by Escamilla et al. in 2000, who concluded that training with overweight or underweight baseballs can improve throwing velocity of typically weighted implements (50). Given that training with *either* heavier or lighter balls improved throwing velocity, it is unlikely that strength gains alone are responsible for this improvement.

As mentioned previously, another way to investigate the role of strength on throwing velocity is to vary the strength of the thrower. Several studies have investigated the role of strength training on throwing velocity with the assumption that the only major difference between athletes before and after training would be their strength. Van den Tillaar reviewed several training strategies aimed at improving throwing outcomes, including some involving resistance training. While many of the studies reviewed lacked proper control groups, he summarized that resistance training for the upper body incorporated at least three times a week for 5 weeks can increase throwing velocity (51). Several studies have since looked at ballistic resistance training programs with the rationale that throwing is a ballistic motion and thus strength gains need to be made in this context. This was partly the rationale behind a study performed by Escamilla et al. in 2012 (65), where the group investigated three different resistance training programs and the effect on pitching velocity, among other metrics. Two of the training programs used ballistic movements, while the third focused on slower, more deliberate exercises. They hypothesized that the ballistic training programs would result in greater performance gains. They found that while all three programs did improve throwing velocity by roughly 1.2% to 2% compared to a control group, there was no statistical difference between training groups. The authors pointed out that these training programs were fairly short in duration (6 weeks) and the study was carried out in a very specific population (high school athletes aged 14–17). It may be that more of a difference in throwing outcomes could be seen with a longer training duration or with more or less experienced athletes. Overall, the available literature supports the notion that increasing strength relative to the object thrown does improve throwing velocity. These differences are fairly incremental, however, and likely do not fully explain the large gap in throwing velocity between men and women on average.

Sex Differences in Motor Control and Spatial Perception

While size and strength factors marginally contribute to the sex difference in throwing velocity and distance, the same cannot be said for throwing accuracy. As mentioned already, size and strength are likely not the most important factors in accurate throwing. It is essential to remember that an accurate throw involves not only a skillful throwing motion, but precise spatial perception of the target as well. First one must investigate the throwing motion itself as it relates to throwing accuracy. After comparing the mechanics and accuracy of athletes throwing with their nondominant hand (52) and patients with cerebellar dysfunction (53), investigators generally agree that throwing accuracy requires very precise timing of finger extension or "opening" (54,55). One possible mechanism is that in experienced throwers, cerebellar calculations of finger stiffness and hand acceleration are involved to control timing of finger extension (55). At this time, there is little literature describing sex differences in accuracy as it pertains to specific biomechanical characteristics such as finger extension timing.

The other important aspect in the accurate throw is precise spatial perception. When one looks at the literature investigating sex differences in spatial perception, large and well-documented differences can be found. For instance, in a study of 40 college-age students, Davis (35) asked subjects to throw a ball at a plain circular target 11 meters away, instructing them to "try and hit the center of the target." Overall, men performed significantly better than women. When a small red dot was placed in the center of the target, the accuracy of the female subjects improved significantly, while the males continued to perform well. One interpretation of these results is that women prefer specific, "landmark" cues, whereas men can perform well utilizing geometric cues.

Further support for this notion comes from several studies, including work by Sandstrom et al. (56), who reported similar findings in men and women navigating a virtual water maze. It does appear that this difference in spatial ability is correlated to throwing accuracy based on work by Kolakowski and Malina (9) and Jardine and Martin (8). These two studies examined the relationship between throwing accuracy and tests of spatial ability. Regardless of the outcomes used, men outperformed women, and a strong correlation between throwing accuracy and spatial ability was found.

It should be noted that measuring female spatial skills may not be as straightforward as one might assume. There is strong evidence that spatial skills may be related in part to sex hormone levels, which vary in the menstrual cycle (57,58). Specifically, spatial abilities appear to decrease with increasing estrogen levels (58). Therefore, studies investigating throwing accuracy in postpubertal females should take into consideration potential hormonal influences. In summary, the available literature suggests that sex differences in spatial ability may be partly responsible for variation in throwing accuracy, although further research is needed to clarify the sex differences present in the specific motor patterns near ball release. Future studies should account for hormonal variation and its impact on throwing outcomes.

Sex Differences in Societal and Cultural Factors

Despite the documented differences in size, strength, and spatial abilities between men and women, many believe that societal influences (i.e., "nurture" as opposed to "nature") also play a role in the sex differences in throwing ability. This is a reasonable argument since these differences can be seen in prepubescent children (26,42,44,59,60), prior to the onset of size, strength, and hormonal changes that are seen in adolescents and adults.

A popular theory emphasizes the role of training. This line of reasoning infers that females do not throw as well as their male counterparts because they do not practice throwing as much. Support for this view can be found in studies such as that conducted by Williams (61), who found no differences in throwing velocity between males and females (ages 7–12) when they threw with their nondominant hand. The author concluded that "non-biologic factors" are important in explaining the sex differences in throwing.

A unique opportunity to examine the effect of throwing practice for females was presented by the passing of Title IX of the Education Amendments in1972 (the implementing regulations were signed by President Gerald Ford in 1975). This legislation resulted in a large increase in sporting opportunities for females during that era, although the impact on female motor skills and fitness levels is debatable (29). Based on an examination of *Sports Illustrated*, the popular sports magazine, Kane found that post–Title IX (in 1988), women were being portrayed more often in an athletic context, although she did find that female coverage was more profound in "sex-appropriate" sports, such as swimming and gymnastics (62). Similarly, in a 2012 article, Cooky and Lavoi concluded that although formidable cultural, societal, and institutional barriers to gender equality exist, the concept of gender equality in sport does appear to have broad support in the United States (63).

This thinking led Runion et al. (29) to compare a cohort of 13-year-old athletes in 1999 to a cohort studied by Halverson et al. in 1979 (28). The authors expected to see an improvement in female throwing performance in the 1999 cohort, partially as a result of the implementation of Title IX. Instead, the authors found that males outperformed females to the same extent in 1999 as they did in 1979. The authors did provide several plausible explanations for this finding, including the possibility that the 1979 cohort did not fully represent a "pre–Title IX" effect. Another explanation would be that the gap in throwing performance is primarily a "nature" rather than "nurture" effect.

Another way to study societal impact would be to study a cohort from a society in which throwing is not as prevalent. For example, Ehl et al. studied German teenagers and compared their throwing motions and velocities to those of an American cohort. In Germany, the most popular sport is soccer, with 1.5 million youth participating. The only relevant throwing sport is the much less popular handball (often called "team handball" in the United States), with only 200,000 youth taking part. While the American boys and girls in this study did have more throwing practice and threw faster and with more mature mechanics than their German counterparts, a large sex difference was still present in both cohorts (40). In fact, the boys and girls in both German and American cohorts differed in throwing velocity by the same value (23 ft/sec), which is almost identical to the findings of Halverson's study in 1979 and Runion's in 1999.

Together, these studies show three different cohorts separated by time and culture all showing essentially the same difference in throwing velocity between boys and girls. This work was built upon by Petranek and Barton in 2011 (39), who studied a cohort of U-14 softball players who were similar in age to those reported in the Runion and Ehl papers. Overall, these softball players had much more throwing experience than the subjects from either of the previously mentioned studies. The authors found that the experienced softball players threw with higher velocities than the age-matched girls from both the previous studies but not as fast as the boys from either study. As the authors mentioned, if throwing experience alone could account for the massive sex difference in throwing velocity between men and women, the U-14 softball players should have shown higher throwing velocities than the German boys. The authors did note that since the U-14 softball players threw softballs instead of tennis balls as in the Runion and Ehl studies, a direct comparison of these cohorts is difficult. Based on work mentioned earlier by Fleisig et al. (20) and Van den Tillaar and Ettema (49), it is conceivable that these girls may have thrown tennis balls with higher velocities.

The rationale behind studying boys and girls from the German culture is that *neither* boys nor girls participate in throwing sports to a large extent, so there would presumably be less societal difference between the sexes. A corollary to this work would be to study subjects from a culture where *both* boys and girls are expected to participate in throwing activities equally. Thomas et al. studied a cohort of Australian Aborigines, a society of hunter-gatherers separated from Western and Asian cultures (38). Aboriginal girls are expected to participate in throwing activities similar to their male counterparts. The authors found that Aboriginal males still threw with a higher velocity than Aboriginal girls, although the effect size was smaller than the American cohort when comparing boys and girls age 6 (0.73 versus 1.25) and age 10 (1.81 versus 3.25). Another notable finding was that while previous studies found that the effect size for the throwing velocity difference between boys and girls reliably increased with age (28), the same was not true for the Aboriginal children. Also, while the Aboriginal boys threw with the same velocity seen in American boys of the same age, the Aboriginal girls threw with velocities much higher than those seen in their age-matched American counterparts.

In summary, several studies have investigated the impact of sociocultural factors on the sex differences seen in throwing; however, drawing conclusions from this body of work is challenging given the conflicting results and varied methodologies used. It may be that societal and cultural pressures are partly responsible for the observed sex difference in throwing; however, the magnitude of this contribution appears to be small.

SEX DIFFERENCES IN IDEAL THROWING MECHANICS

While investigating the throwing mechanics of younger boys and girls, Rippee et al. made an important observation. They noted that while many girls improved in throwing outcomes, they still displayed immature throwing mechanics (44). Another, albeit controversial, way of stating this is to say that the girls improved their proficiency at throwing despite "incorrect" biomechanics. This leads one to a very important question: Is the optimal throwing pattern for females different than the one for males? The generally accepted pattern of "correct" throwing mechanics was understandably determined by critically appraising the throwing motions of individuals who could throw with the best outcomes. As was proven earlier, these individuals are generally male. There are reasons to suspect that ideal female biomechanics differ from those seen in men. It is well accepted that women in general have more subcutaneous fat than men, located typically around the buttocks, posterior thighs, and posterior arms (64). This difference may result in a female preference for a slightly different throwing motion that maximizes outcomes given their specific anthropomorphic profile. For instance, the axial trunk rotation seen in the mature male throwing motion may not be as pronounced in the ideal female throwing motion due to sex differences in body mass distribution. If ideal biomechanics for females are, in fact, distinct from the male pattern, the best way to elicit these patterns would be to examine elite females who throw with the best outcomes.

As was discussed earlier, a relatively small percentage of females are able to throw with great skill. Chu et al. analyzed a groups of 11 elite, amateur male and female baseball pitchers throwing fastballs (31). As may be expected, the males outperformed females in throwing velocity. Intriguingly, the rotational velocity of the shoulder (the most rapid part of the pitching motion) was found to be similar between male and female groups. However, the elbow extension angular velocity was significantly faster in men, which likely contributed to the higher velocities seen. Another major difference was the angle of separation between the pelvis and upper torso. The females in this study demonstrated significantly less separation, which may have translated into lower velocities. Further research examining highly performing female throwers is needed to determine if the most ideal throwing motion for females differs from those observed in males.

CONCLUSION

The overhand throw is a remarkable human movement pattern. The ability to launch a projectile with force and accuracy has its roots in early human evolution and is still an important part of many modern cultures. Throwing is also fascinating in that it is an action that displays a tremendous sex difference. In general, males outperform females in throwing velocity, distance, and accuracy. More specifically, there is a much wider variation in throwing outcomes for females than males. While a small percentage of women throw with great skill, a large number of females perform far worse than their male counterparts. The reasons for this difference are unclear and include primarily anthropomorphic, strength, hormonal, and to a lesser extent cultural and societal factors. Future research should focus on defining optimal biomechanics within sex and gender, to capitalize on the unique skills sets available to males and females.

Summary of Sex Differences With Regard to Throwing

Throwing Outcome	Findings
Maximal velocity	In general, males throw with higher maximal velocity than females (26–31).
Maximal distance	In general, males throw for longer distances than females (26,33,34).
Maximal accuracy	In general, males throw with more accuracy than females (26,35,36).
Maturity of biomechanics	In general, males throw with more mature biomechanics than females (28,29,42–44).

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5

SPINE

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INTRODUCTION

Low back pain (LBP) is a widely prevalent condition, with documented lifetime prevalence rate as high as 90% (1). Most cases of acute LBP are self-limiting, although recurrence may occur in 60% to 73% of people (2). Not only is LBP problematic for the general population, it can be debilitating or even career ending for a professional athlete. During sports, athletes have considerable loads placed on their spines throughout a dynamic range of motion (ROM), which may predispose them to spine injuries. Therefore, it is not surprising that LBP is the most common reason that athletes miss a game (3), with up to 20% of all sports-related injuries involving the spine (4). Sports with high prevalence of LBP include gymnastics, weightlifting, swimming, tennis, volleyball, and football (5–7).

Studies on sex differences as related to the spine remain largely inconclusive. Frequently it is difficult to separate the sex influences on spine pathology from the influences of specific sports or activities that have a gender preference. An example would be gymnastics, in which males and females compete in different activities. Therefore, the results of studies evaluating rates of spine pathology associated with specific sporting events could be due to the event or the sex differences. This example epitomizes how determining the exact contribution of gender differences in injury rates can be challenging. However, there are many other sports such as basketball that are played by both sexes and help facilitate comparisons between genders.

Despite these difficulties, some studies have found distinctions between the sexes. Female athletes are more likely to suffer from LBP as compared to males (4,5,7). According to NCAA Injury Surveillance Data from 1997 to 1998, female athletes were twice as likely to sustain low back injuries compared to males (7). Low back injury was the most common injury in women's volleyball and gymnastics, second most common in women's soccer, and third most common in women's basketball (7). This chapter reviews supported data on sex differences as they relate to anatomical and pathological conditions and offers potential insights where data are limited. We start by reviewing anatomic and alignment differences between the sexes, then offer insights and data on gender differences in spine pathology among several common spine disorders.

SPINE ANATOMY

The spinal column has multiple functions. It must offer osseous protection of the contained spinal cord and nerve roots. It must also offer significant stability to allow load transfer between the upper and lower limbs. In addition to these stabilizing features, the spine has a segmental multiplanar motion that is crucial for mobility. This combination of stability and segmental mobility results in unique demands on the spinal column. As such, the spine, especially the lumbar spine, is predisposed to great stress, putting it at risk of acute injury and repetitive overuse injuries. In assessing pathology in the spine, it is important to note that distinct gender differences exist in the spine anatomy secondary to sexual dimorphism. These differences are likely due to the load-bearing adaptations necessary for the accommodation of bipedal pregnancy.

Bony Anatomy

Although some minor variations in numbering exist, the vertebral column typically consists of 7 cervical vertebrae, 12 thoracic vertebrae, and 5 lumbar vertebrae along with the fused sacrum and coccyx. Vertebrates consist of a vertebral body anteriorly and laminae, spinous process and transverse processes posteriorly connected by two pedicles. The superior articular process (SAP) and inferior articular

FIGURE 5.1: Lumbar zygapophyseal joint.

IAP, inferior articular process; SAP, superior articular process.

Source: Adapted and modified from Ref. (8). Peh W. Image-guided facet joint injection. *Biomed Imaging Interv J.* 2011;7(1):e4.

process (IAP) arise from the junction of the pedicle and lamina to join with the vertebrae above and below in the form of zygapophyseal joints (z-joints) as shown in Figure 5.1.

There are regional differences in the vertebrae. The cervical vertebrae have foramen in each transverse process to house the vertebral artery. The first two cervical vertebrae are further specialized to allow rotation with the first level (C1 or atlas) supporting the head and the second (C2 or axis) forming a tooth-like dens that serves as a pivot to allow lateral rotation. The C0-1 joint provides the most amount of flexion extension at approximately 25° while the C1-2 joint is responsible for 80° of axial rotation (9). The thoracic vertebrae have costal facets on the antero-lateral ends of the transverse processes for articulation with the ribs. The lumbar vertebrae are broader and heavier to help facilitate load transfers from the lower limbs through the pelvis to the upper body (10).

Studies have shown that vertebral width and disc-facet depth of male cervical vertebrates are greater, yielding more stable intervertebral coupling (11). Such differences in stability may partially explain the higher susceptibility to trauma-related neck pain that is found in females (12,13). Lumbar vertebral bodies in females also have reduced cross-sectional areas (CSA) and volumes (14). This is true even when matched for age, weight, vertebral bone density, and vertebral body height (14). This difference confers an additional risk for vertebral fractures in females, as the smaller female vertebrates confer a 30% to 40% higher mechanical stress for equivalent applied loads even in the setting of comparable vertebral bone densities (15).

Alignment

Besides inherent differences in bony structure, there are also gender differences in alignment. Janssen and colleagues showed that the T1-L5 segments of the female spine are more dorsally inclined in the sagittal plane (16). Based on animal models, this dorsally directed shear load could predispose the female spine to reduced rotational stability (17). A comparative study of men and women with chronic LBP demonstrated that men exhibited earlier and greater lumbopelvic rotation ROM during hip medial rotation (18). Additionally, the study found a greater proportion of men reported an increase in LBP symptoms with hip medial rotation compared to women, suggesting that movement of the hip medial rotation may be more problematic for men than women with LBP. This could potentially increase risk of developing LBP in men who participate in rotational sports such as golf or tennis.

Pelvic incidence, defined as the angle between the line joining the hip axis and the center of the S1 end plate and the line orthogonal to the S1 end plate, is also higher in women. It has been shown that an abnormally high pelvic incidence upsets the spinal balance and is associated with higher rates of spondylolisthesis and increased likelihood of disease progression (19,20) and severity of scoliosis in the elderly population (21).

Lumbar lordosis is an important adaption for bipedalism. However, since pregnancy shifts the center of mass anteriorly, the female spine must have increased lumbar curvature and reinforcement to compensate for the increased bipedal obstetric load (22), as shown in Figure 5.2. Additionally breasts have been theorized to affect spinal alignment. Radiographic studies suggest that breast size can affect the thoracic kyphosis and lumbar lordosis angles (23), with larger breast sizes being associated with both increased thoracic kyphosis and lumbar lordosis, as shown by the difference in lordosis when comparing male to female vertebral columns in Figure 5.3. However, a study has shown that reduction mammoplasty does not seem to change the measurable thoracic kyphosis and lumbar lordosis angles (24).

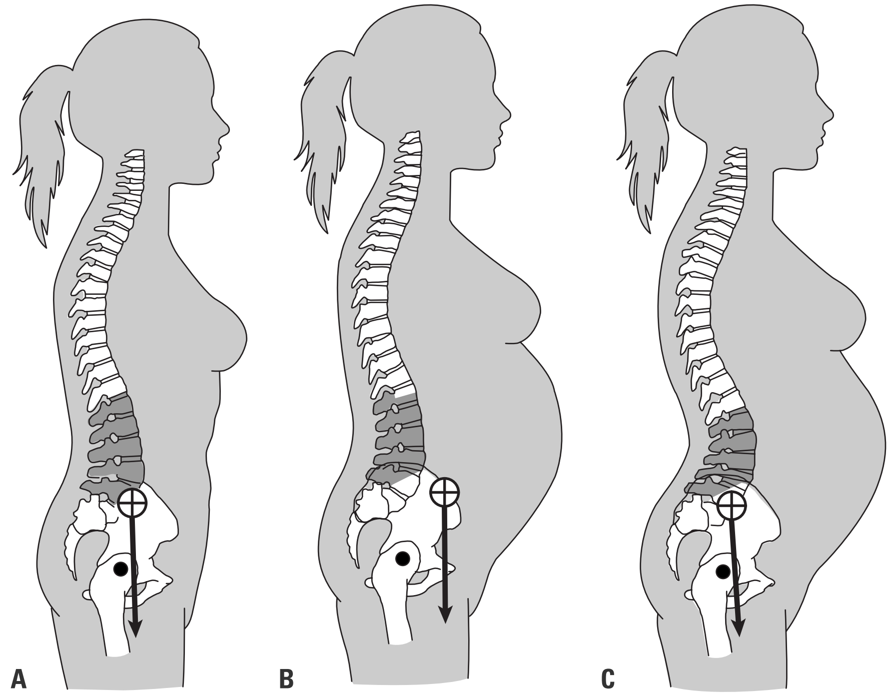


FIGURE 5.2: With pregnancy, human females have to adapt with increased lumbar lordosis to accommodate the anterior-translated center of mass. (A) Nongravidad female. (B) Gravidad female without lumbar lordotic compensation. (C) Gravidad female with lumbar lordotic compensation.

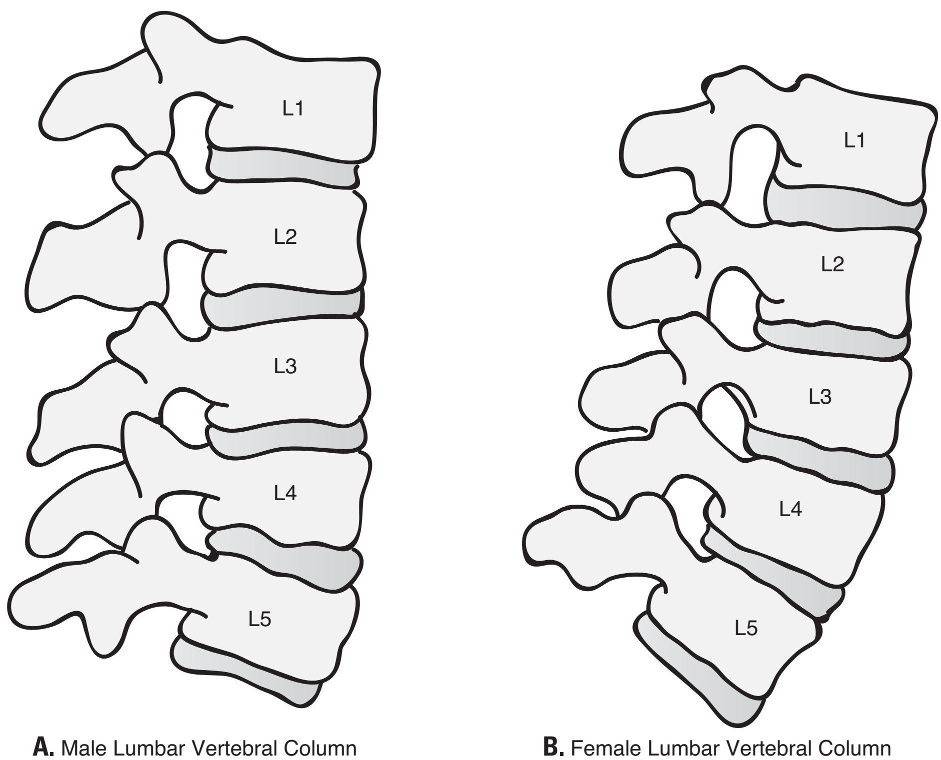


FIGURE 5.3: Male vs. female lumbar spine.

Joints, Ligaments, and Musculature

Spine mobility is maintained through the segmental intervertebral discs and a gliding movement of the paired synovial zygapophyseal joints. The cartilaginous nature of these joints may also provide shock absorption throughout the spine. Studies have shown that z-joint cartilage thickness is lower in females and the gap in the dorsal region is greater (25). Cervical z-joint shear and distraction motions in females were higher than that of males, providing a mechanism to explain why women may be more susceptible to whiplash injury (26). Studies have shown that disc height in women is higher than in men (27). Disc space narrowing is more frequent in women than men (28) while degenerative changes were observed more frequently in males (29).

Although spinous ligaments provide stability, the musculature is felt to be the primary stabilizer of the spine. In fact, it has been demonstrated that a cadaver with bones and ligaments intact but muscles removed will buckle under about 20 pounds (30). The anterior longitudinal and posterior longitudinal ligaments help to support the intervertebral discs. The intrinsic muscles of the back act primarily as extensors and rotators and help stabilize the spine. While gender variations in ligament and muscle activation have been documented in other joints and parts of the body (31–33), few available studies have described gender differences in spine ligament and musculature.

PATHOLOGY-SPECIFIC GENDER DIFFERENCES

Scoliosis

Scoliosis denotes pathological lateral curvature of the spine in the coronal plane. The four major types include congenital, neuromuscular, degenerative, and idiopathic scoliosis. Congenital scoliosis is associated with vertebral malformations; neuromuscular scoliosis is found in patients with trunk weakness associated with spina bifida, cerebral palsy, or neuromuscular disorders; and degenerative scoliosis results from traumatic or degenerative bone collapse secondary to osteoporosis. The prevalence of congenital, neuromuscular, and degenerative scoliosis shows little gender predilection apart from that associated with the primary condition.

Idiopathic scoliosis is however the most common etiology, accounting for 65% of structural scoliosis, and it affects adolescents during the growth spurt years (34). The exact pathophysiology is uncertain but it has been hypothesized that there is a complex interplay of defect in central control of growth as well as the spine's inherent susceptibility to deformation. Researchers are looking into genetic, hormonal, collagen, and platelet-related causes (35). Interestingly, some studies report that athletes of certain sports have a higher incidence of scoliosis, most noticeably among female rhythmic gymnastic trainees (36,37), though it is not clear whether this is because of the demands of the sport or the particular gender predilections of the participants.

Regardless of exact pathophysiology, idiopathic scoliosis is much more common in females. The female-to-male ratio ranges from 1.5:1 to 3:1, with a 7.2:1 predilection in curves greater than 40° (38). While the reasons are still unclear, females may be more predisposed given that they go through relatively shorter and more rapid adolescent growth of the spine. Thus, they may be more predisposed to any defect in control of growth affecting the spine.

Timing of screening for scoliosis depends on age of adolescence. The American Academy of Orthopaedic Surgeons (AAOS), the Scoliosis Research Society (SRS), the Pediatric Orthopaedic Society of North America (POSNA), and the American Academy of Pediatrics (AAP) recommend that girls should be screened twice, at age 10 and 12, and boys once, at age 13 or 14, by the Adam's forward bending test. The Adam's test is a visual scoliosis screening tool performed with the patient bending forward at the waist with feet together, knees straight, and arms hanging freely. The examiner observes the patient from behind to look for asymmetric rise of one side of the rib cage next to the vertebral column. The peak rise of the convex side can be measured more objectively using a scoliometer, a specialized tool with a bubble level and angle measure to help determine the degree of curvature, as demonstrated in Figure 5.4 (39).

Given the predisposition of scoliosis in females, research from Norway has demonstrated that screening is cost saving when performed in girls only (40). Referral to a spinal deformity expert and x-rays should be considered if the Adam's test is positive. Bracing should be initiated in patients with curves above 20 ± 5° Cobb who are still growing or demonstrating progression of deformity (41). Interestingly, males are less likely to respond to brace treatment and have been theorized to have more rigid spines (42).

Surgical intervention is usually considered when curves exceed 50°, are causing loss of pulmonary function, or are progressive (43). Fortunately, despite males having possibly more rigid spines, sex does not seem to affect outcomes of surgery for adolescent idiopathic scoliosis (44). Most experts advise a return to physical activity at the same level after surgery (36). A small study also showed that sports activity is not more restricted after surgical intervention than after nonoperative treatment; however, surgical and nonsurgical groups with scoliosis had reduced sport activity

FIGURE 5.4: Scoliometer.

Source: From Ref. (39). Izatt MT, Bateman GR, Adam CJ. Evaluation of the iPhone with an acrylic sleeve versus the scoliometer for rib hump measurement in scoliosis. *Scoliosis.* 2012;7(1):14.

secondary to back pain as compared to matched controls without spinal disorder (45).

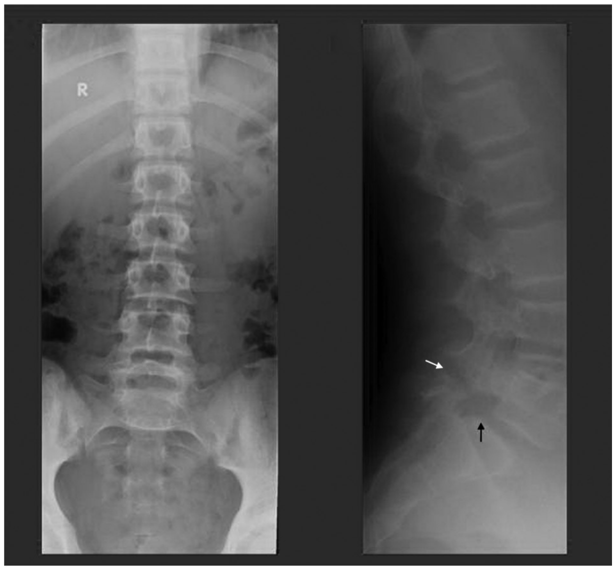
Kyphosis

The sagittal alignment of the thoracic spine displays a dynamic range and usually kyphosis naturally increases throughout life. Females exhibit significantly higher kyphosis after the age of 40 (46). This is often accompanied by decreased lumbar lordosis, and together the syndrome is termed lumbar degenerative kyphosis (47). In Takemitsu's epidemiological study, 90% of subjects with the syndrome report significant LBP. There have been studies associating increases in thoracic kyphosis with higher spinal loads and trunk muscle forces (48). The resultant flat back has been associated with anomalous pelvic tilt (49). Higher thoracic kyphosis, as determined by occiput wall distance, has also been associated with shoulder pain and subacromial impingement (50). Treatment of excessive thoracic kyphosis includes physical therapy focusing on posterior kinetic chain strengthening and even surgical fixation in some cases (51).

A distinct entity of thoracic kyphosis is Scheuermann's kyphosis, which is defined as the basis of anterior wedging of 5° or more of at least three adjacent vertebral bodies and typically occurs during adolescence (52). The prevalence of Scheuermann's kyphosis ranges from 0.4% to 8.3% (53). While historically it was thought to be more prevalent in males (54), more recent studies have shown no gender predilection (35,55,56). Mild cases are treated symptomatically for back pain with exercise and anti-inflammatory medications while kyphosis greater than 45° requires bracing before progressing to surgery for curves greater than 75° (52). In regard to sports, some experts recommend more extension-biased sports such as gymnastics, swimming, and basketball while avoiding sports associated with repetitive flexion and heavy loading (57). Most authors recommend a rehabilitation program focusing on maintaining flexibility, strengthening the extensor muscles of the spine, and correcting any postural component of kyphosis (58).

Spondylolysis and Spondylolisthesis

Spondylolysis is a unilateral or bilateral defect in the pars interarticularis of the vertebra, most commonly found at the L5 level (59), as illustrated in Figure 5.5. The exact pathogenesis of lumbar spondylolysis remains controversial and is likely multifactorial. The most accepted mechanism



A **B**

FIGURE 5.5: Radiographic findings in a patient with L5 pars interarticularis fracture and mild L5 on S1 spondylolisthesis: anteroposterior (A) and lateral (B) images. (White arrow points to the fracture and black arrow points to spondylolisthesis of L5 on S1.)

LBP, low back pain.

Source: From Ref. (68). Zukotynski K, Curtis C, Grant FD, et al. The value of SPECT in the detection of stress injury to the pars interarticularis in patients with low back pain. *J Orthop Surg Res.* 2010;5:13.

is biomechanical stresses due to chronic low-grade trauma from repetitive flexion, extension, or rotation of the lumbar spine on a congenitally weak or dysplastic pars interarticularis (60,61). There are two main mechanisms of how the stress fracture occurs. The first is the “nutcracker” mechanism in which there is direct compression of the IAP of the cranial vertebra on the pars interarticularis of the caudal vertebra when the lumbar spine is in extension (62–65). The second mechanism is when the pars interarticularis fails in tension through a traction mechanism (62,63,66,67).

The incidence of asymptomatic spondylolysis has been estimated to be approximately 6% of the general population (59,66,69). Some studies have shown the positive association between spondylolysis and other diseases including spina bifida occulta (66,69–71), Scheuermann’s disease (72,73), and scoliosis (74). Numerous studies have reported a high incidence of lumbar spondylolysis among family members (up to 69%), which suggests a genetic predisposition to this condition (69,75–77).

The incidence is higher in athletes than in the nonathletic population (78–80). Most studies report 10% to 15% of adolescent athletes have been reported to have spondylolysis (59,81,82), especially those involved in sports with repetitive flexion/extension such as gymnastics, weight lifting, diving, and rowing (59). Most cases of spondylolysis are asymptomatic. In children and adolescent athletes, however, it is the most identifiable cause of back pain (59,67), usually manifesting as axial LBP that is exacerbated with lumbar hyperextension.

Spondylolysis is also more frequently found in males, with an incidence ratio of 2:1 (66,67,69), although spondylolisthesis affects females two to three times more frequently (59,67,83). Some have suggested that the increased incidence of males compared to females, as previously reported, might be a result of a time when females were not as active in sports as males. Fredrickson et al. refutes this claim; he reported an incidence of 2:1 ratio of boys to girls at age 6, at which activity levels of both sexes are similar (69). The etiology of this difference between males and females remains unknown, although the progression to spondylolisthesis may be due to differences in pelvic incidence between males and females.

Bilateral pars defects can result in the development of spondylolisthesis. Patients with known spondylolisthesis, bilateral pars defects, or possibly those presenting with unilateral pars defects at a young age, should be screened for the development or progression of a spondylolisthesis by intermittent standing spine films from a lateral view. This is especially critical during the adolescent growth spurt, as this condition can develop without any changes in symptomology.

Adolescent athletes with extension-biased pain and high suspicion of stress fracture of the pars interarticularis should be treated presumptively as spondylolysis. Treatment includes relative rest until pain free, with a gradual return to sports after correction of biomechanical abnormalities through physical therapy. These injuries typically require several months of rest and therapy before a full return to activities. Nonsteroidal anti-inflammatory medications are typically avoided as these medications may delay bone healing. Bracing is controversial; while it may limit activity it may also increase movement through the affected segment. Practitioners may also consider screening for vitamin D deficiency as a contributor to the pathology. However, there are no studies supporting sex-specific workup or management algorithm of spondylolysis in athletes.

Intervertebral Disc Pathology

Lumbar intervertebral discs degenerate not only with normal aging but also as a consequence of intrinsic and extrinsic factors. Although the exact cause and mechanism of disc degeneration is still under investigation, genetic link (84–86), obesity (87,88), smoking (89,90), and physical loading related to occupation and sports are associated with disc degeneration (91–94). Clinical manifestation of discogenic pain includes LBP typically associated with activities that increase intradiscal pressures, such as sitting, bending forward, coughing, and sneezing.

Some studies report sex differences in disc degeneration. Miller et al. analyzed 600 intervertebral discs excised from 273 cadavers and found male discs degenerated earlier than female discs and to a greater extent, most significantly in the second decade (95). In this study, nearly 40% of males had evidence of Grade II degeneration, as compared to no degeneration found in females. While the exact mechanism explaining the gender difference remains unclear, the author proposes several contributory factors including increased mechanical load on the male lumbar spine, greater CSA of male discs resulting in longer nutrient pathways, and differences in biochemical composition of the discs between males and females.

Kjaer et al. performed a cross-sectional cohort study on 439 thirteen-year-olds and found patterns of differences when results were stratified by gender (96). In boys, there was a statistically significant association in upper lumbar disc findings as compared to girls, with association found in the lowest lumbar spine segments. Additionally, there was a strong association between “seeking care” and disc protrusion/high intensity zone in girls, but not in boys. Despite this literature on gender differences, there are no known implications for participation in sports.

Ankylosing Spondylitis

Ankylosing spondylitis (AS) is a progressive chronic inflammatory disease that affects the axial skeleton, with variable involvement of entheses, peripheral joints, and, rarely, internal organs. Clinical features of AS include low back or buttock pain, peripheral joint pain, enthesitis, dactylitis, and/or progressively limited spinal mobility. Extra-articular comorbidities include acute anterior uveitis, psoriasis, inflammatory bowel disease, cardiovascular disease, and pulmonary disease.

Historically, it was thought that AS was found predominantly in males with sex ratios quoted as 10:1 (97). Recent studies, however, indicate the male-to-female ratio is closer to 2:1 (98). A suggested explanation for underestimation of female prevalence includes milder and less extensive clinical manifestations with less disabling symptomatology among females (99–101). Other possible explanations include slower development of radiographic findings in women, more peripheral arthritis in women leading to alternative diagnoses, and traditional regard of AS being a disease of men (101). Clinically, women with AS tend to have more neck and peripheral joint pain (98).

Radiographic differences between men and women have been studied, although no conclusive findings have been found. Some studies have found higher frequency of cervical spine involvement in females (102,103) and higher lumbar spine involvement in males. Other studies refute this claim showing no sex differences in cervical involvement despite higher frequency of cervical pain (104). Radiographic progression is more severe in males with AS than females (98,105). It has been suggested that radiographic severity was associated with males due to earlier diagnosis and therefore longer duration of disease. However, a study by Lee et al. correcting for age and duration of disease showed that males were still more likely than females to have increased levels of radiographic damage (98).

Special consideration should be given to athletes with AS. Over time, development of osteoporosis and ossification of the axial skeleton and ligamentous structures result in progressive rigidity, loss of lumbar and cervical lordosis, and altered biomechanical properties of the spine. Limitations in mobility and altered biomechanics may result in increased risk of spinal fractures, particularly in the cervical spine, even from low energy impact (106,107). While there are no set guidelines, Harper and Reveille recommend cautioning patients with AS to avoid sports at high risk of spinal injury, including football, ice hockey, wrestling, diving, skiing, snowboarding, rugby, cheerleading, or baseball (108).

CONCLUSION

Much remains to be learned about sex differences as related to the spine. While there are some studies that describe sex differences due to anatomical and pathological conditions, much of the evidence remains inconclusive. As described, there are anatomical differences in body anatomy and spinal alignment between males and females, although the exact implications of these differences remain unclear. There are more studies looking at gender differences in certain pathological conditions of the spine. There appears to be a gender predilection in spondylolysis, disc degeneration, and AS for males, and in scoliosis for females. While there may be a gender predisposition for certain pathological conditions, there is not a gender restriction based on anatomic or pathological cause as relates to sports. In general, more studies are needed to evaluate gender differences in relation to the spine.

Gender Predilection Based on Spine Pathology

Spine Pathology	Sex With Higher Prevalence
Scoliosis	Females (38)
Scheuermann's kyphosis	No gender predilection (35,55,56)
Spondylolysis	Males (66,67,69)
Spondylolisthesis	Females (59,67,83)
AS	Males (97,98)

AS, ankylosing spondylitis.

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6

PELVIS

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OVERVIEW

The lumbopelvic region is the bridge between the upper body and the lower extremities. Most sports involve coordination between the upper body and lower limbs and rely on the pelvis to translate and coordinate these motions. The pelvis plays a pivotal role in nearly all sports. Understanding the sex differences within the pelvis can lead us to better understand the sex differences of body mechanics and injury in sports medicine. Often, there are overlapping clinical syndromes involving the lumbopelvic hip region; however, other chapters focus on lumbar and hip pathology while this chapter focuses on the pelvis.

The pelvis is defined as the lower part of the trunk between the abdomen and the thighs (1). The pelvis is connected to the lumbar spine via the sacrum at the fifth lumbar and first sacral vertebral segment interface (L5-S1). The pelvic skeleton is a ring that is formed by the sacrum and coccyx posteriorly and the ilia posteriolaterally, which extends anteriorly to form the pubic rami connected by the symphysis and inferiorly to form the ischia. The pelvis translates the upper body forces and weight to the lower extremities through the hip joints, composed of the acetabula and femoral heads, along with the soft tissue and ligaments that support the hip joint. The pelvic cavity is enclosed by the pelvic floor with complex layers of muscles, fascia, and soft tissue. The shape and function of the pelvis varies between males and females. In both sexes, it functions in locomotion, posture, and visceral support. In females it also serves as a birth canal (2). The evolution of pelvic sexual dimorphism is thought to be driven by the development of bipedal locomotion (which favors a narrow pelvis) of *Homo sapiens* in both sexes while maintaining a birth canal wide enough for parturition in females (2).

Anatomical Differences

Little difference is found between the male and female pelvis in the immature state. Variance in anatomy is found to occur through puberty and pelvic maturation (3). The ultimate shape of the pelvis is directed by hormonal influences, nutrition, and environmental influences. Animal studies have shown that the female pelvis is the default shape that develops in the absence of testosterone. The presence of testosterone is associated with the development of a male-type pelvis while the presence or absence of estrogen does not influence the pelvic shape (4–7). Additionally, the quality of diet during growth and development also affects the shape of the pelvic inlet. Poor nutrition and suboptimal growth is associated with flattening of the pelvic inlet (7–9).

The mature female pelvic skeleton is larger and broader than the male pelvis, which is taller, narrower, and more compact. The female pelvic inlet (maximum distance between the linea terminals) is larger, oval in shape, and thought to allow easier passage of the fetal cranium during parturition. The male sacral promontory projects farther and the inlet is more heart-shaped (Figure 6.1). The lesser pelvis, also known as the true pelvis, is the space between the pelvic inlet and pelvic floor and is larger in females. Conversely, the greater pelvis, also known as the false pelvis, is the space enclosed by the pelvic girdle above and in front of the pelvic brim of the ilia and is larger in males (10). The subpubic angle (the angle between the inferior pubic rami) in men is about 70°; known as the pubic arch in women, it is obtuse, about 90° to 100°. Congruently, the greater sciatic notch is wider in females and their ischia bones are wider apart to create a larger outlet. The iliac crests are higher in males, which make the male pelvis deeper and more narrow than females. The sacrum tends to be longer, narrower, and straighter in males compared to females who

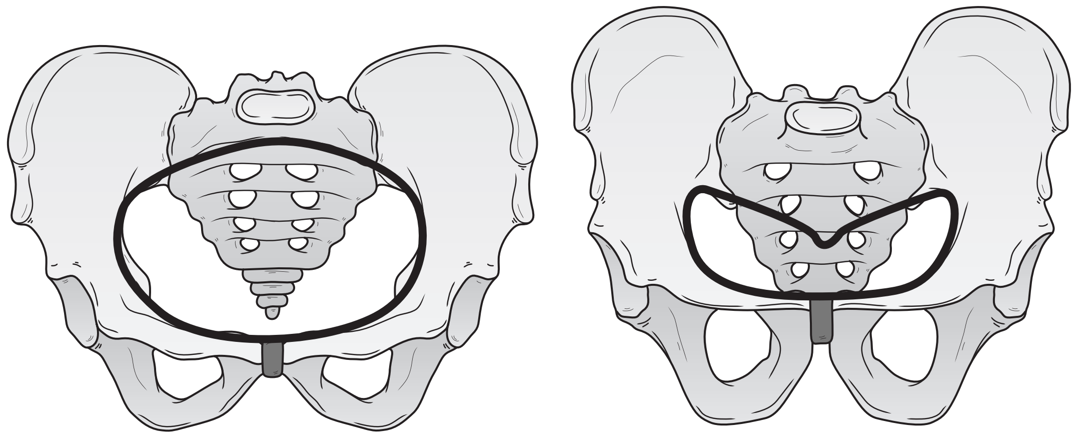

FIGURE 6.1: Male versus female pelvic inlet shapes: note that the male sacral promontory projects farther into the inlet and is more heart shaped while the female inlet is larger and oval in shape.

have a shorter, wider, and more posteriorly curved sacra. Finally, given the wider pelvis structure, the acetabula are wider apart in females than males. In males, the acetabula face more laterally while in females they face more anteriorly. The resulting gait is thus different in men and women: Men can move their legs forward and back in a single plane while in women, the leg must swing forward and inward with the change in femoral head angle, giving the female gait its characteristic "swinging of the hips" (11).

Given the pelvic anatomical differences between sexes, the resulting biomechanical functioning and injuries are consequently different. As women and men participate in sport, the injuries they suffer at times differ in type and frequency. In this chapter we highlight current findings in the literature about any sex differences found among pelvic injuries related to sport. We have divided the pelvis anatomically and comment on injuries relevant to each anatomic region. Any sex differences found in incidence, pathophysiology, clinical presentation, diagnosis, and treatments in pelvic sport injuries to date are addressed.

THE GROIN

Anatomy

The groin is a general term that typically refers to the anterior and medial junction of the leg with the trunk of the body. This region encompasses many of the major anterior pelvis stabilizing structures. The pubic rami, connected by the pubic symphysis, serve as the anchor to these anterior pelvis structures. The anterior edge of the inferior pubic ramus is noted to have some spiny projections that may rub against adductor muscles and potentially cause pain (12).

The main ligaments that help stabilize the anterior pelvis include the iliofemoral ligament, pubofemoral ligament, and iliotibial tract. Some of the muscles that traverse the groin include the rectus abdominis, iliopsoas, iliacus, and the group of adductor muscles along the inner thigh. The abdominal wall structures from superficial to deep include the external oblique fascia and muscle, internal oblique fascia and muscle, transversus abdominus muscle and fascia, and transversalis fascia. Of note, the rectus abdominis muscle is about three times wider at its insertion on the lower rib cage compared to its origin on the anterior pubic body (13). The pubic aponeurosis is formed by fibers of the rectus abdominis, conjoint tendon, and external oblique as they extend downward to merge together. The adductor and gracilis muscle origins are confluent with this pubic aponeurosis, also known as the rectus abdominis-adductor aponeurosis (14,15), as shown in Figure 6.2. The fibers of the internal oblique aponeurosis and transversus abdominis insert anterior to the rectus with only the transversalis fascia present posterior to the rectus in the lower one quarter of the abdomen. This anatomy renders this region of the abdominal wall vulnerable to injury (16). The inguinal canal passes obliquely through the abdominal wall spanning from the deep inguinal ring to the superficial inguinal ring within the transversalis fascia. It houses the spermaticord in males and the round ligament in females (14).

The adductor muscle group is composed of six muscles: pectineus, adductor longus, adductor brevis, adductor magnus, gracilis, and obturator externus muscles. The adductor longus is thought to be the most commonly injured muscle among the group. Each of the aforementioned adductor muscles originate in the groin at various points along the pubic rami and insert along the medial femur (except the

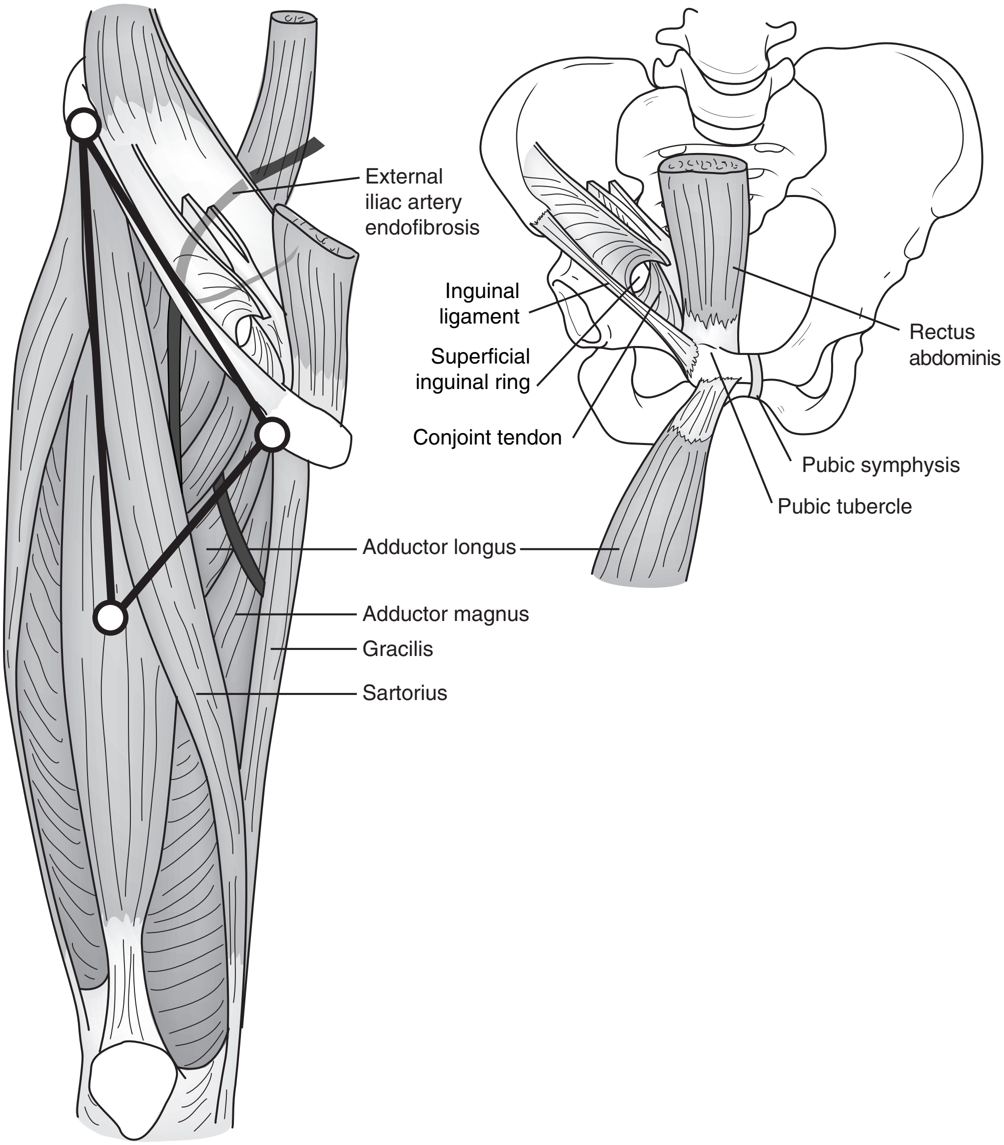

FIGURE 6.2: The rectus abdominis-adductor aponeurosis. The rectus abdominis, conjoint tendon, and external oblique merge to form the pubic aponeurosis and is confluent with the adductor and gracilis muscles.

gracilis, which inserts on the proximal medial tibia). The main function of the adductor muscles are to adduct the thigh when in the open kinetic chain and to stabilize the lower extremity when in the closed kinetic chain.

Biomechanics

Due to the complexity of the groin structures described, their overlapping nature, and the multitude of forces at play with movement, groin injuries are not well understood. Several theories exist that attempt to explain the underlying cause of painful groins. Some argue that because the origin of the rectus abdominis at the anterior pubic body is one third the width of its insertion at the lower rib, there is a concentrated force generated at the pubic symphysis with contraction and that may cause a greater frequency of rectus injuries near the pubic symphysis (17). There is thought that the rectus abdominis and adductor longus muscles generate antagonist forces on the pubic symphysis during rotation and extension from the waist (13). Imbalance of these muscular forces is thought to cause groin injuries. This complex is also theorized to impact other groin complexes:

MRI studies have shown an intimate relation between the lateral border of the rectus abdominis-adductor longus aponeurosis and the external ring of the inguinal canal, separated by only 2 to 5 mm (13). The close relation of these components illustrates the complex biomechanical chain reactions that occur with different movements and suggests that injury to one component would undoubtedly impact the surrounding structures and biomechanics of the pelvis.

There has been ongoing conflict regarding the terminology of groin injuries and their definitions are currently changing. According to the World Conference of Groin Pain in Athletes in November 2014, the suggested change in nomenclature groups groin injuries into the following categories:

1. Adductor-related groin pain
2. Inguinal-related groin pain
3. Pubic-related groin pain
4. Iliopsoas-related groin pain (18)

However, given that these recommendations are still undergoing consideration at this time, we will use the widely accepted nomenclatures—athletic pubalgia, adductor strains, and osteitis pubis—to discuss the pathophysiology of injury, guide specific treatment recommendations, and highlight the sex differences in sport.

Clinical Syndromes

Adductor Strains

Adductor-related groin pain in an athlete is typically considered secondary to a strain or tendinopathy of the adductor muscles. A strain can occur in the adductor muscles or myotendinous junctions. There can also be disruption of the tendons near or at the origin on the pubic ramus or at their insertion along the medial femur. Groin injuries make up 2% to 5% of all sport-induced injuries (19). Adductor strains are the most common injury among groin injuries and the adductor longus is the most commonly injured muscle among them (20). Adductor strains tend to occur in sports that involve rapid acceleration and sudden changes of direction and sports that involve cutting, pivoting, kicking, and sharp turns. They may also occur in sports that involve overstretching of the leg and thigh in abduction and external rotation. The most common sports associated with the injury include soccer, ice hockey, Australian Rules football, calisthenics, and cricket (21). Ice hockey is the leading sport that carries the diagnosis, with adductor strains comprising 10% of all injuries in elite Swedish ice hockey players (22).

Sex comparison studies are few and do not show strong evidence of sex differences (23), though some studies show a trend of higher rates of acute groin injuries in males compared to females. A study by Paajanen et al. showed that in soccer players, acute groin injuries tended to be more often associated with male than female soccer players. The authors did not propose any specific mechanisms responsible for the trend, but noted that predictor risk factors for groin strains include previous groin strains and decreased range of motion (ROM) in hip abduction (24). Hägglund, et al. also found groin injuries in elite soccer players to be more common in males than females, with adductor injury to be the second most common diagnosis for male players (hamstring injuries were the most common). Hägglund et al. propose that the sex disparities result partly due to abdominal wall deficiencies that may be more prevalent in males, as well as higher training and match load of male players (25).

The mechanism of adductor injury involves the disruption and damage of the muscle tissue and/or tendons of any of the six adductor muscles. These injuries can span from a low-grade muscle strain to complete disruption of the muscle/tendon. Additionally, chronic overuse can occur and lead to tendinopathy, which can be painful (26). An imbalance between propulsive muscles and stabilizing muscles of the groin and thigh is thought to be a mechanism for adductor muscle strains. Nonmodifiable risk factors associated with the injury include previous injury, age, sport experience, sport-specific preseason training, body mass index, and decreased dominant femur diameter. Modifiable risk factors include decreased hip abduction ROM, decreased levels of preseason sport-specific training, and abdominal muscle recruitment (27). A reduced hip ROM is associated with athletes with groin injury (28); however, critics argue that it is not yet possible to determine if this association is specific to adductor strains or other manifestations of pubic symphysis or groin pain. There may be confounding factors such as past injuries and other risk factors that affect hip flexibility in these studies (27).

Strength imbalance between the propulsive and stabilizing muscles of the hip and pelvis has been proposed as a mechanism for adductor strains in athletes (29). The inability to transfer load from the legs and/or torso to the pelvis has been suggested to cause a large percentage of groin pain (30–32). The eccentric force of adductors attempting to decelerate the leg during a stride is hypothesized to be the mechanism of injury in ice hockey players (33,34). Decreased muscle strength and/or muscle ratios have been found to be predictive of strain injury. It has been hypothesized that adductor strength throughout its length and adductor-to-abductor strength ratio are important factors for injury prevention (27). Tyler et al. demonstrated that intervention of strengthening the adductor muscle group can be an effective method for preventing adductor strains in professional ice hockey players identified to be "at risk" (having adduction-to-abduction strength ratio less than 80%). An intervention program consisting of strengthening and functional exercises to increase adductor strength was associated with a decreased incidence of adductor strain from 8% to 2% of all injuries (35). Eccentric training of the thigh muscles and abdominal muscular training is recommended, with the theory that this would allow more effective utilization of the muscles and lessen the onset of fatigue as the season progresses (27). Fatigue is also noted to be a contributing factor for muscle injury (36).

Athletic Pubalgia

Athletic pubalgia is another injury that may cause pain in the groin and lower abdomen. There are many versions of its definition and its cause has been debated. In the past, groin pain described as athletic pubalgia was thought to be due to weakness in the posterior wall of the inguinal canal with weakness or tearing of the transversalis fascia of the rectus abdominus (16). Others consider it to be an injury of the external oblique muscle aponeurosis and conjoined tendon (37). Through the years athletic pubalgia has accumulated a number of different names including sports hernia, athletic hernia, Gilmore's groin, pubic inguinal pain syndrome, footballers groin injury complex, and hockey player's syndrome (16,38). These terms may be used synonymously with athletic pubalgia; however, most of these syndromes encompass variable overlapping pathologic processes of the anterior groin structures. For ease and clarity, we will refer to athletic pubalgia as it is best understood today as "a group of musculoskeletal processes that occur in and around the pubic symphysis which share similar mechanisms of injury as well as clinical manifestations," as outlined by Omar et al. (13,31,39–41).

The incidence of athletic pubalgia among athletes has been reported to be between 2% and 5% in all sports (42–44). Sports that involve restriction of the lower abdomen and groin in combination with kicking and cutting actions more frequently cause groin and lower abdomen injuries, accounting for up to 10% to 13% of all soccer injures per year (45–47). Soccer and rugby are the most common sports plagued by athletic pubalgia injuries while sports such as ice hockey, Australian Rules football, tennis, running, and field hockey also have a high prevalence of the injury (48–52). Other studies have implicated that there is a clinical association between femoroacetabular impingement (FAI) and athletic pubalgia (53–55).

Athletic pubalgia has historically been more prevalent in males, but there have been an increasing number of female athletes suffering from this injury (15,56). Overall, it tends to be present among active males age 17 to 35 and among those participating the aforementioned sports and activities (57). There have been a few theories explaining possible reasons behind the difference in incidence between the sexes.

Although the etiology and cause of athletic pubalgia remains unclear, there are many postulations about the pathogenesis of the disease. There is common agreement that kicking, twisting, and rapid change-of-direction activities stress the groin components. It was originally thought that weakness in the posterior wall of the inguinal canal may result in a bulge in the posterior inguinal wall and deficiency in the transversalis fascia (16,31,47,58–60). Some extensions to this explanation include theories that a weakened posterior inguinal wall develops due to chronic hyperextension injury from imbalance between the adductors and lower abdominal musculature in athletes. More recent literature shows that patients with athletic pubalgia most commonly have injury along the lateral border of the rectus abdominis cephalad to its pubic attachment or at the origin of the adductor longus (13). It is proposed that after an injury to either the rectus abdominis or adductor muscle, repetitive unbalanced muscle contractions and lack of opposing forces lead to degeneration and microtearing of other nearby tendons (13,31). Consequently, the lesions may extend through the aponeurosis of the rectus abdominis and adductor longus and may disrupt their pubic attachment. In other cases, the injury may extend to the adjacent adductor tendon origins (pectineus and adductor brevis) or may extend along the anterior pubic symphysis to involve the contralateral abdominal and adductor aponeurosis or tendons (13).

Why there are such prominent differences in the incidence between males and females who develop athletic pubalgia is still not well understood. Two trains of thought exist: The first is that anatomic variation between the male and female pelvis causes biomechanical differences that put males at increased risk of developing the disease; the second is that there are fewer women participating in sports and activities associated with athletic pubalgia. In regard to the anatomic variation theory, it is thought that the male pelvis is thicker and heavier, which causes greater shifts in force. The narrower male pelvis and narrower subpubic angle may lead to a different distribution of forces that puts the muscles and aponeurosis at greater risk of injury. Also, the narrower pubic symphysis may cause decreased flexibility of the pelvis in males, which may increase their risk of muscular imbalances and injury. Meyers, Greenleaf, and Saad postulate that females, in contrast, may be at higher risk of developing lateral instead of anterior pelvic pain, involving the sartorius, psoas, or other lateral muscles. This may be due to inherent biomechanics in a wider pelvis that has “greater dependence on these ‘strap’ muscles for stability” (12). Omar et al. observed that female patients have larger and more robust caudal rectus abdominis attachments with aponeurotic fibers that cross midline along the anteroinferior pubic symphysis not seen in males. The authors suggest that this, as well as the wider female pelvis, may aid in the transfer of forces away from the pubic region to the lower extremity bony structures (13).

Though many argue that the anatomic and biomechanical differences may help stabilize the pubic region and decrease the risk of athletic pubalgia injuries in females, as discussed previously, the increasing incidence of the disease in females may argue in favor of the theory that the proportion of female:male participation in sports associated with the injury (e.g., soccer, ice hockey, running) may be a driving factor in the sex difference (15,56). In actuality, the sex differences seen in athletic pubalgia is most likely multifactorial.

MRI imaging is the modality of choice to detect the soft tissue defects in athletic pubalgia. In the past, MRI was mainly used to exclude other possible sources of groin pain. It is now recommended during the evaluation of persistent lower abdominal and groin pain because of the variable pathophysiologic processes that can potentially manifest with lower abdominal and groin pain. Fluid-sensitive sequences may reveal tears involving the rectus abdominis-adductor aponeurosis seen as irregular areas with signal intensity, as if fluid is undermining the aponeurosis. Abnormal marrow signal intensity isolated to the anterior-inferior aspect of the pubic body and deep to the rectus abdominis-adductor aponeurotic attachment, called a “secondary cleft sign” (an inferior extension of the central symphyseal fibrocartilaginous cleft along the anteroinferior margin of the pubic body) can be seen on MRI and may signify an aponeurotic lesion (13,15,39). This secondary cleft sign usually appears on the ipsilateral side of the injury and may reflect microtearing of the origin of the adductor longus and gracilis tendons (61). An edematous or atrophic appearance of the rectus abdominis near its pubic tendinous attachment on MRI may signify an aponeurotic lesion. If severe, there may be frank disruption of the tendon seen on MRI at the pubic attachment of its lateral head (13).

Though athletic pubalgia is less common in women, when present there is MRI evidence that aponeurotic injuries in females tend to be more severe than in males. Additionally, aponeurotic injuries in females tend to originate at the midline rectus abdominis-adductor aponeurotic plate and propagate bilaterally while in males such injuries tend to occur unilaterally (13,62). Because of the bilateral pathology tendency in females, findings on MRI may not be as apparent and make it more difficult to diagnose athletic pubalgia in women compared to men (13). Differences in internal pathologic processes in women may also confound their groin pain, which may make diagnosis more difficult. Common cofounding internal processes in women that should be considered and screened for include endometriosis, adnexal cysts, and uterine fibroids. Femoral hernias are also more frequently seen in women, thus the imaging approach in women suspected to have athletic pubalgia should be done carefully with these differentials and factors in mind (62).

More recently, dynamic ultrasound is also now used by some groups to aid in the diagnosis of athletic pubalgia. However, it is more difficult to visualize pathologic processes of athletic pubalgia using ultrasound and its accuracy is user dependent (16,47,63,64).

The treatment approach for athletic pubalgia is more straightforward than the etiology, pathophysiology, and diagnosis. Patients should first be treated with a trial of conservative treatment including rest, anti-inflammatory medications, and physical therapy. Clinical assessment of core stability, hip strength, and flexibility and identification of muscular imbalances are crucial. Targeted treatment should include strengthening and neuromuscular reeducation regarding timing and recruitment patterns during functional motion. Manual therapy techniques can be used to manage soft tissue and fascial restrictions. A comprehensive rehabilitation program to develop coordination and strength of the hip adductors, flexors, internal rotators, extensors, core stabilizers, and lumbopelvic spinal musculature is important for an effective recovery (65). One can consider steroid injections to the pubic symphysis or the adductor tendon origins for those having recurrent or refractory groin pain. This treatment, though it may provide temporary pain relief, is unlikely to be an effective treatment of the underlying injury over the long term. Surgery is usually reserved for those who fail conservative measures and usually is performed no earlier than 3 months from the onset of symptoms (16,47). Common surgical repair techniques to manage athletic pubalgia are directed at repairing the site of injury and stabilizing the anterior pelvis. There is no reported surgical outcome data comparing men with women; however, the majority of surgical outcome data studies mainly male subjects (16), probably because of the overall higher prevalence of athletic pubalgia among males.

THE PUBIC SYMPHYSIS

Anatomy

The pubic symphysis is a unique joint that joins the two pubic rami bones. The joint lacks synovium and consists of a fibrocartilaginous disc with supporting ligaments (66,67). Functionally it resists tension, shearing, and compression forces during weight bearing and motion yet is able to widen during pregnancy. The articular surfaces are covered with hyaline cartilage 1 to 3 millimeters in thickness (67,68). The fibrocartilage interpubic disc tends to be shorter and wider in females with a normal range of 3 to 10 millimeters in width (69). A retropubic eminence is sometimes prominent in multiparous females, which arises from a posterior bulge-like projection of the mid-region of the disc. This may be related to the presence of an interpubic cleft that is sometimes present: a narrow, slit-like, vertical oval-shaped cavity located within the interpubic disc itself (67,70–72).

The pubic symphysis is reinforced by four ligaments: superior pubic ligament, inferior pubic ligament, anterior pubic ligament, and posterior pubic ligament (though some anatomy texts only refer to the superior and inferior ligaments). The anterior pubic ligament is a thick and strong structure with several layers of collagen fibers that vary in orientation; this ligament connects the pubic bones anteriorly and plays a prominent role in maintaining stability of the pubic symphysis (73).

Biomechanics

From a biomechanical standpoint, everyday activities exert various forces: traction on the inferior and compression on the anterior region when standing, compression when sitting, and shearing and compression during single-leg stance. The symphysis usually allows 1 to 2 mm of mobility and 1° of rotation in males and allows about 2 to 3 mm more mobility in females in comparison (74). The ligaments have been shown to be strongest in withstanding mechanical forces in men, followed by nulliparous women and multiparous women, and are weakest in primigravide women in the third trimester of pregnancy (75). Generally in men, the upper and lower borders of the pubic symphysis are at the same horizontal level, however they may be uneven in women for reasons that have not been studied (76). It has also been shown that the subchondral bone is more compact anteriorly in males and posteriorly in females (CT study), the significance of which in injury is not yet known (77).

Clinical Syndromes

Osteitis Pubis

Osteitis pubis is defined as a self-limiting, noninfectious disease or inflammatory process of the pubic symphysis and the surrounding tendinous attachments. It was first described by Beer in 1924 as a complication of suprapubic surgery (78). Today it may be seen following surgery, after infections in the local region, postpregnancy, or with overuse injuries in athletes (79,80). In athletes, it has a propensity to affect men two to five times as frequently than women. It most commonly presents in the third and fourth decades of life with the typical history of gradual increasing discomfort or pain in the pubic areas, one or both groins, and in the area of the lower rectus abdominis and superior adductor muscles (81–83). Sports more commonly associated with osteitis pubis include soccer, Australian Rules football, American football, rugby, distance running, ice hockey, fencing, cricket, and road-walking. Potentially any sport or activity that involves kicking, running and pivoting, quick acceleration and deceleration movements, and cutting movements on one leg could induce the injury (80,81,84–87).

The exact mechanism of the injury is not fully understood. It is generally believed that shear forces produced by repetitive contraction of the adductor muscles of the groin may cause instability and movement of the symphysis, thereby causing inflammation and pain at the pubic symphysis (20,87). The pubic symphysis is the center point of multiple myotendinous attachments from the trunk and lower extremities that act together to dynamically stabilize the position of the anterior pelvis. The external and internal oblique muscles, transversus abdominis, rectus abdominis of the trunk muscles, and the pectineus, gracilis, adductor longus, adductor brevis, and adductor magnus of the thigh adductor muscles each attach to the pubic symphysis. Of these, the rectus abdominis and the adductor longus are the most robust and most critical for maintaining stability of the anterior pelvis (13). It is hypothesized that the rectus abdominis and adductor longus muscles create antagonizing vector forces on the pubic symphysis and injury to one predisposes the other to injury by altering the biomechanics, leading to instability of the pubic symphysis (13,31).

Given the lack of consensus about the mechanism of injury, the explanation for the propensity toward men remains a mystery. Some theories argue that the pelvic and hip anatomic variance between men and women puts men at a comparatively increased risk for pubic symphysis instability and injury. Arguments exist that the loss of internal rotation of the hip may be a predisposing factor for pubic instability, which subsequently may develop into osteitis pubis. Men tend to have decreased hip internal rotation relative to women with wider pelvic girdles and thus may be predisposed to developing osteitis pubis (28,84,88). Sacroiliac (SI) abnormalities have also been associated with athletic osteitis pubis. Several authors theorize that abnormal motion at either the SI joints or the pubic symphysis can cause instability due to the anatomy of the pelvic ring and lead to osteitis pubis as a secondary stress reaction (86,89). Additionally, FAI has been implicated as an underlying factor causing decreased hip ROM and subsequently causing osteitis pubis in male athletes; however, this theory has not been studied among the female population (90). Finally, some investigators reason that the higher incidence in men is related to higher participation in sports, which puts them at higher risk for the injury. They anticipate there may be an increase in incidence in women as their participation in competitive athletics grows (81).

Among those with osteitis pubis, most present with a gradual onset of groin pain that may or may not be associated with pain in the lower abdomen, hip, thigh, perineum, or testicles. The groin pain may be unilateral or bilateral and may be aggravated by sports involving running, kicking, quick acceleration or deceleration, and pivoting. Upon exam, the patient typically has pain with palpation over the pubic symphysis and pain with resisted hip adduction (20,80,81,87,89). The pubic spring test (pressing on the left and right pubic rami) may elicit pain at the pubic symphysis (81,91). In comparing male to female physical exam findings, males with osteitis pubis tend to have a higher rate of impairment with hip internal rotation (88). They also tend to have more variable findings with palpation over the pubic symphysis, which may not elicit pain as consistently as it does in women (87).

Despite the sex differences in anatomy and biomechanics of the pubic symphysis, the diagnosis and treatment of osteitis pubis is invariably the same among both sexes. Radiography, MRI, and radionuclide bone scans may be used to diagnose the condition, with MRI scans more capable of providing details regarding the chronicity and extent of the disease (81,89,92). Treatment options range from conservative treatment with rest from sport and reduction in weight-bearing activities with a progressive rehabilitation program, to injections with corticosteroids for temporary pain relief for severe pain, or even surgical arthrodesis, curettage, and plating to stabilize the joint in severe or chronic cases that have failed conservative treatment (81,89,92,93). Perhaps the most important role in understanding the sex differences in pubic symphysis pathology is the role in prevention of progression to osteitis pubis. There are few data supporting any preventive measures to the development of osteitis pubis, but understanding risk factors and biomechanical reasons that predispose a person to osteitis pubis is important.

Pubic Rami Fracture

Fractures of the pubic rami occur about one third as frequently as proximal femur fractures and are usually found in the elderly (94). When occurring alone they are typically classified as stable type A fractures (according to the Association for Osteosynthesis/Association for the Study of Internal Fixation [AO/ASIF] classification) (95). In these cases the surrounding soft tissue usually provides reliable and rapid bone healing (96). Pubic rami fractures can either result from acute trauma or can manifest as stress fractures from osseous insufficiency or from overuse. Older women are found to be more likely to suffer pubic rami fractures due to simple falls and minimal trauma while in men such fractures tend to result from high-energy trauma (97).

Among younger and active individuals, pubic rami stress fractures also occur, though far less frequently than in the elderly. As discussed already, women have a much higher prevalence of stress fractures than men in similar training conditions in any sport. Likewise, stress fractures in the pelvis and the pubic rami are found to be more common in female than male recreational athletes (98). In runners, the site of fracture in athletes and younger individuals usually occurs at the inferior pubic ramus near the pubic symphysis (99). It has become common knowledge that among military recruits, women suffer pubic rami stress fractures much more frequently compared to men, especially in mixed training exercises with male and female recruits (100). Reports of pubic rami fractures among military recruits are comprised almost entirely of females, with one study reporting a ratio of 11:1 females to males (100) and another study finding a ratio of 67:3 females to males (101). Increased rates of pubic rami fractures were consistently associated with the introduction of integrated gender training where men and women recruits train in sessions together. When the association was made that the practice of mixed gender training resulted in higher incidence of women suffering pubic rami fractures, training sessions were segregated by gender again and the rates of pubic rami fractures subsequently decreased (99,101,102).

There are many theories about why there are such sex differences in the prevalence of pubic rami fractures among athletes. Traditionally the argument is that the prevalence of the injury reflects the increased participation of women in sport and running (99). A more updated theory argues that the gait differences in running among men and women account for the higher tendency for the female pubic ramus to fracture. Under this theory, fracture of the pubic ramus is thought to result from different pathophysiology than stress fractures, which result from stress or fatigue in runners. It is thought that the pubic ramus is a bone that is more exposed to tensile stress rather than compressive stress. As the hip is extended, muscles pull on the lateral part of the pubic ramus and ischium, creating tensile forces that are placed on the medial portion of the pubic ramus. This type of force is how a single fracture at the pubic rami may occur in a ring-like structure without a resulting secondary fracture of the pelvic ring. Also, unlike compressive stress fractures, pubic rami stress fractures tend to occur several weeks after an intense race or increase in training intensity (99–101). Researchers note that the female bone structures are more slender, the pubic symphysis shallower, the ischiopubic rami less inverted, and the obturator foramina more triangular than oval compared to men (103); however, the anatomy alone does not account for why there may be higher tensile stresses in the female pubic rami than the male. It is theorized that female runners may rely on hip-extension forces more than male runners, thus creating greater tensile stress and making the pubic ramus more susceptible to injury (99).

Among the female military recruits, most studies converge on one theory of mechanism of injury: Integration of male and female recruit training caused shorter stature women to overstride to keep up with the group. It is thought that the overstriding and an unnatural gait pattern causes increased loading of stress around the inferior pubic ramus and is the mechanism of stress fracture in women (99,100,102). As support for this theory, when the army decreased the standard stride length from 30 inches to 27 inches for all marching, no further cases of pubic rami stress fracture cases were reported through the remaining length of the studies (100,102).

In terms of prevention, it has been suggested that athletic and military training should provide cyclical exposure to stress with rest days rather than progressive and continuous increase in activity (100). As most studies show that there is a delay in the onset of symptoms in relation to the change or increase in physical activity, some investigators recommend training modifications that space high-impact activities at intervals. One study showed the reduction of stress fractures in female recruits by a rate of 7.3% per year when practicing interval training of high-impact activities and completely omitting them in the third week of training (104). It has also been recommended that military recruits be allowed to march with stride length consistent with their height and body build in order to prevent stress fractures of the pubic ramus.

SACRUM AND SI JOINT

Anatomy

The SI joint serves as a junction between the spine and the pelvis. Due to its unique location and structure, it is integral in transmitting loads between the upper and lower body during exercise. The sacrum is wider anteriorly than posteriorly, and wider superiorly than inferiorly, allowing it to become wedged between both sides of the ilium, limiting caudal and posterior translation. This keystone-like shape contributes to the stability of the SI joint (105).

The adult SI joint is generally C- or L-shaped with a long vertical pole and a short horizontal pole. The surfaces of the SI joint are initially flat and covered with hyaline cartilage on the sacral surface and fibrocartilage on the iliac surface. During childhood and particularly after puberty, roughening of the surfaces begins to occur. With increased activity and weight bearing through the SI joint, further intra-articular ridges and depressions form secondary to gravitational stress through the SI joint. Adaptive changes continue with age, with an increase in the number and size of elevations and depressions within the joint as a response to increased stress and stability of the joint.

The joint is supported by a dense, strong ligamentous network, with anterior (anterior sacroiliac ligament), dorsal, and interosseous components. The interosseous ligaments are the strongest in limiting motion between the ilium and the sacrum (106). The dorsal sacroiliac ligaments complement the interosseous ligament function and are divided into long (inferior) and short (superior) sections. The dorsal ligaments originate at the posterior superior iliac and are contiguous with the sacrotuberous and sacrospinous ligaments, connecting the sacrum to the ischial tuberosities and iliac spines, respectively (105,107,108). This dorsal ligamentous network is anchored through the thoracolumbar fascia of the back and the hamstring-sacrotuberous ligament complex of the pelvis (109) (see Figure 6.3). The iliolumbar ligaments are accessory ligaments that further support the joint by preventing anterior translation or rotation of the fifth lumbar vertebra (107).

Sex dimorphisms in SI joint anatomy emerge during puberty and mostly involved the shape and contour of the joint surface. The male SI joint has greater surface area, increased ridging, thickening of the ligaments, and decreased mobility. These differences may be functional adaptations to cope with increased biomechanical loading (105,110). These changes may progress into age-related degenerative processes involving osteophyte formation and ankylosis. Additionally, the female SI joint surface has less curvature, allowing for greater mobility (105). This finding in females is likely adaptive for the role of the female pelvis as the birth canal.

Biomechanics

The biomechanics of the SI joint are complex and affected by motion of the spine, ilium, pubic symphysis, and hips. Movement is controlled by multiple muscle groups,

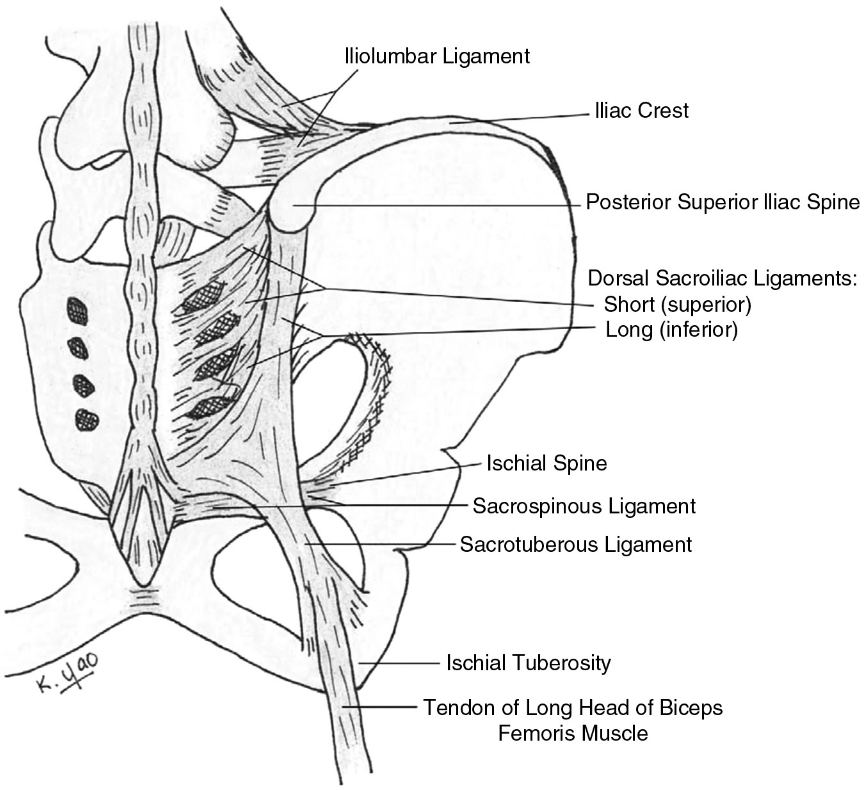

FIGURE 6.3: Dorsal sacral ligaments. Illustration created by Katherine Yao, MD.

including the gluteal muscles, hip external rotators, hamstrings, latissimus dorsi, quadratus lumborum, erector spinae, abdominals, and psoas muscles (107). The average ROM of the joint is approximately 2° in all three planes (105). The joint has a "self-locking" mechanism that was described by Vleeming et al. using both form and force closure (111).

Form closure is achieved by the shape of the SI joint and the contoured surfaces, providing inherent stability independent of external forces. Force closure is attained through the interface of the ligamentous network, fascia, and muscles in the region. There is a cross-like configuration of force from the ipsilateral latissimus dorsi to the contralateral gluteus maximus muscle, as shown in Figure 6.4 (111). These posterior forces are coupled anteriorly with support by the external obliques, internal obliques, and transverse abdominals. Appropriate conditioning and symmetry of these forces is critical in proper loading of the SI joint.

The SI joint is crucial in maintaining this lumbopelvic rhythm. Typically the first 65° of forward bending is accomplished via the lumbar spine, followed by the next 30° via the hip joints. With forward flexion, the base of the sacrum moves anteriorly and the apex moves posteriorly. Hamstring muscles, particularly the biceps femoris as it connects with the sacrotuberous ligament, along with the gluteal muscles control the degree of sagittal rotation of the pelvis (107). When contracted, they rotate the ilium posteriorly. Therefore, appropriate hamstring tension and length is important in allowing the pelvis to tilt anteriorly and maintain the lumbopelvic rhythm.

Women have a wider pelvis, decreased joint surface area, and reduced interdigitation of the sacrum with the ileum, as compared with men. The SI joint therefore depends to a greater extent on force closure rather than form closure in women, allowing for increased motion. The force closure in women is further affected by hormonal changes associated with estrogen and relaxin during menstruation, pregnancy, and menopause. These differences may put women at increased risk for SI joint dysfunction.

Mobility of the SI joint decreases in both genders from birth to puberty, but increases transiently in adult females to a peak age of about 25 years (105). Using roentgen stereophotogrammetric motion analysis in patients with pelvic girdle pain, average mobility for men was about 40% less than in women (112). Both sexes maintain normal ROM through the sixth decade, with slight reduction in movement occurring in males thereafter.

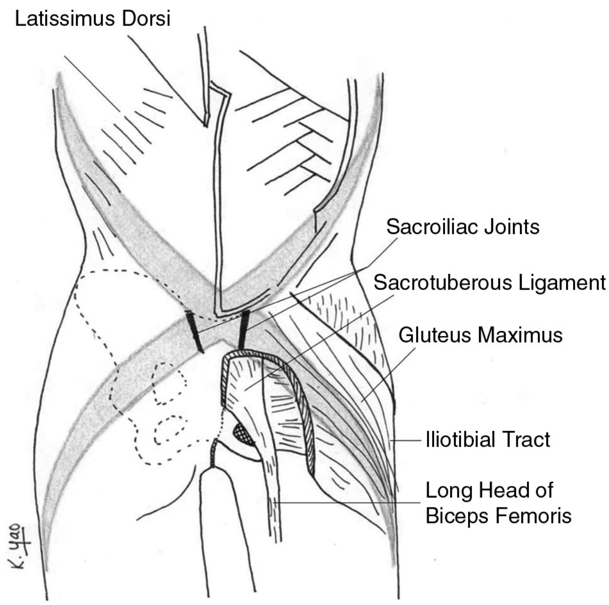

FIGURE 6.4: Force closure of the SI joint is achieved with a dense network of ligaments, fascia and muscles transmitting force in a cross-like configuration. Illustration created by Katherine Yao, MD.

Clinical Syndromes

SI Joint Dysfunction

Since stability and instability of the SI joint are dependent on both form and force closure, breakdown of the ligamentous and muscular relationships can lead to increased shear force, and adaptive movement patterns can facilitate dysfunction and cause pain (107). Degeneration of the joint may result from microtrauma secondary to either acquired hypo- or hypermobility within the joint. Greater ROM and flexibility may lead to relative imbalances in muscle length and strength that can place the female athlete at particular risk for SI joint dysfunction.

In the setting of hypomobility due to adaptive changes, there is increased stress at the lumbar spine and hips, placing these adjacent structures at risk for injury. Altered lumbopelvic rhythm can also place additional stress on the lumbar spine in the setting of reduced hamstring length. With increased tension on the biceps femoris in the shortened state, there is reduced anterior sagittal rotation of the pelvis. Additionally, if there is insufficient force generated by weak hamstring and gluteal muscles, there can be excessive anterior rotation of the pelvis. With the pelvis anteriorly rotated, there is increased lumbar lordosis, causing the psoas to fire in a shortened position and the abdominal muscles to fire in an inefficient and lengthened position.

Sports or exercise that require repetitive pelvic shear toward one direction with torsional forces (e.g., rowing, cross-country skiing, ice skating, gymnastics, golfing, bowling) may be risk factors for muscle action imbalances and SI joint dysfunction (107,113,114). Asymmetric force can also be distributed through the SI joint while training with stair climbers, ellipticals, step aerobics, or with an unaddressed leg length discrepancy. With as small as 1 cm difference in leg length, the load across the SI joint can increase fivefold (115).

The prevalence of SI joint pain is unknown; however, SI joint dysfunction may account for as much as 20% of low back pain in the general population (116–118). Athletes participating in any sport that places significant biomechanical stress through the lumbar spine and pelvis are at risk for developing SI joint pain. For instance, in a study of the U.S. Senior National Rowing Team including 36 males and 17 females, the prevalence of SI joint dysfunction was 54.1%, with 66% of sweep rowers and 34% of scullers reporting pain (113). In another study of 48 pediatric patients between the ages of 10 and 20 presenting with low back pain, the female subjects were more frequently affected by SI joint misalignment (77%) than male subjects (119). Additionally, DePalma, Ketchum, and Saullo found that among 28 patients presenting with low back pain consistent with a diagnosis of SI joint pain, 25 (89.3%) were female (120). In these studies, females had a higher prevalence of SI joint dysfunction and pain; however, gender was not found to correlate with SI joint pathology in another study of 158 patients who underwent dual comparative local anesthetic blocks to diagnose SI joint pain (121).

Despite the sex differences in anatomy of the SI joint, the treatment of sacroiliac joint dysfunction is similar among both sexes. Patients should first be treated with a trial of conservative treatment including rest, anti-inflammatory medications, and physical therapy. A comprehensive rehabilitation program should focus on improving lumbopelvic stability and rhythm as well as addressing articular, muscular, neural, and fascial restrictions, inhibitions, and deficiencies (109). Clinical assessment of lumbopelvic stability, core strength, flexibility, and identification of muscular imbalances are crucial. Targeted treatment should include strengthening and neuromuscular reeducation regarding timing and recruitment patterns during functional motion. Manual therapy techniques can be used to manage soft tissue restrictions. Additionally, ensuring that the athlete can perform an independent contraction of the transversus abdominis has been shown to increase SI joint stability, thereby possibly helping to decrease pain and improve function in the athletic population. An injection of corticosteroid into the SI joint can sometimes help to mitigate pain in the short term, but is unlikely to improve pain in the long term without addressing the underlying biomechanics.

Sacroiliitis

Sacroiliitis is inflammation of the SI joints and is often one of the earliest manifestations of ankylosing spondylitis (AS), a spondyloarthropathy. AS often presents with low back pain and stiffness that is worse in the morning and with rest and improves with activity and anti-inflammatory medications. If untreated, this disease will result in progressive loss of spinal mobility. Diagnosis may often be delayed as these symptoms are commonly described along with many routine musculoskeletal complaints (122). Therefore, in sports medicine, careful consideration of this diagnosis can aid in earlier diagnosis and treatment, potentially reducing the severity of symptoms and disease.

Diagnosis can be made with careful clinical history and examination as well as laboratory and radiographic workup. Of note, there can be absence of changes consistent with radiographic sacroiliitis in the early stage of disease and it may take years after the onset of inflammatory low back pain for these changes to appear on x-ray. This is especially true in females who may never develop radiographic changes (123). MRI can be used earlier to help aid in diagnosis and can show active inflammation in the SI joint prior to its appearance on plain radiographs. Additionally, with laboratory workup, men are more likely to have a positive human leukocyte antigen (HLA)-B27 status, which is associated with increased severity of sacroiliitis (124). Treatment includes the use of nonsteroidal anti-inflammatory and disease-modifying antirheumatic drugs in conjunction with physical therapy.

The prevalence of AS is as high as 0.9% in the U.S. population (125), most commonly presenting in young men between the ages of 15 and 30. Men are two to three times more likely than women to develop this disease (126). The pattern of affected joints varies between sexes, with the spine and pelvis being more affected in men and with more peripheral symptoms in women (127,128). There is very little published regarding the prevalence of AS in the athletic population. Wordsworth and Mowat published a socioeconomic review of 100 patients with AS and found that 61% of them participated in regular physical activity during their youth; however, these subjects had to reduce their activity level at an earlier average age of 23, compared to a healthy control group who reduced their activity level at an average age of 29. The most frequent initial symptoms were low back pain and sciatica-like symptoms (41% and 25%, respectively) (129).

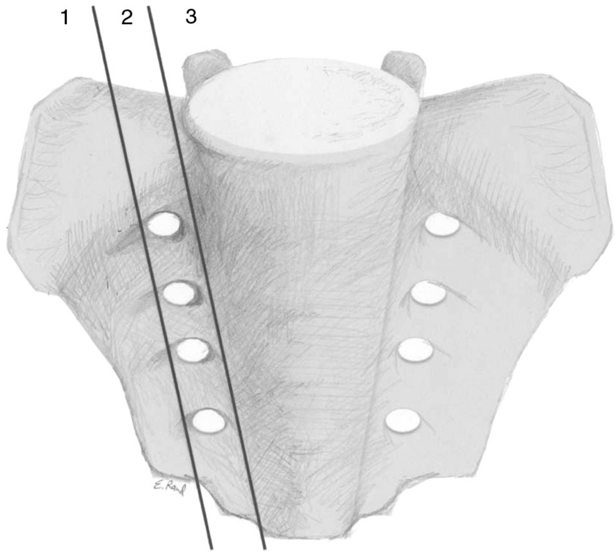

FIGURE 6.5: Zones for classifying sacral fractures. Illustration created by Ethan Rand, MD.

Sacral Stress Fractures

The sacrum is one of multiple sites where stress fractures can occur throughout the body. It is composed of a body and two sacral ala. It is divided into three zones where stress fractures may occur. Most fractures are typically vertically oriented, parallel to the SI joint and occur in Zone 1, involving the sacral ala without the central canal or foraminae (130,131). Fractures in Zone 2 involve the foraminae and those in Zone 3 involve the central canal (Figure 6.5) (131). Most patients present with insidious unilateral, localized pain in the lower back, buttock, or hip, but may occasionally present with radicular complaints or bowel or bladder changes if nerve roots are involved (132–134).

Stress fractures in athletes are rarely due to insufficiency with low bone mineral density. More commonly they are due to repetitive submaximal stress on bone resulting in "fatigue" fractures (131). The sacrum is susceptible to the same risk factors that predispose athletes to fractures at other load-bearing sites, including changes in activity level, training surface, improper footwear, and weakened supporting musculature (135,136). The sacrum is at risk for stress fracture given the vertical forces delivered through the spine into the sacrum at its junction to the pelvis. Leg length discrepancies have also been described as a risk factor for sacral stress fractures, given the uneven load transmission (137).

At younger ages female athletes are also at risk for insufficiency stress fractures due to the hormonal changes associated with the female athlete triad, pregnancy, and lactation (138). Later in life, women are at risk for developing stress fractures related to postmenopausal osteoporosis (139). The sacrum is also placed under added stress from increased pelvic anteversion in women, which is greater by 2.25° compared with men (131). Men are also at risk for developing sacral stress fractures, with the groups at highest risk being runners and military recruits (140).

The incidence and prevalence of sacral stress fractures is unclear; however, they occur less frequently at the sacrum compared with the lower limbs (131,141). Furthermore, many of these fractures are likely to go undiagnosed due to lack of familiarity with this diagnosis and low clinical suspicion (142). These fractures are often associated with coexisting pubic rami fractures because of the closed ring structure of the pelvis (131). Overall, due to increased risk factors for osteoporosis among women there is greater sex difference in the rates of insufficiency fractures, where normal stress is placed on bone of abnormal density, than that of fatigue stress fractures, where abnormal stress is placed on normal bone. In a study of 53 female and 58 male competitive track and field athletes, Bennell et al. found that pelvic stress fractures accounted for approximately 4% of stress fractures overall (143). No differences were observed in the rate among males and females. Shah and Stewart conducted a literature review of sacral stress fractures in athletes. Among 29 cases, again no difference in the rate of fracture was found between the sexes, with 15 males and 14 females (140).

Sacral stress fractures typically affect long-distance runners or athletes who engage in sports that require weight bearing for prolonged periods (132,144). These fractures have also been reported in athletes including a male amateur tennis player (145), a female volleyball player (140), and a female field hockey player (145).

COCCYX

Anatomy

The coccyx is small triangular bone consisting of three to five segments at the terminal portion of the spine. These segments may fuse with transverse grooves along the anterior surface at these lines of fusion. Proximally, the coccyx articulates with the sacrum via a symphyseal joint containing a thin intervertebral disc of fibrocartilage (146). The bilateral coccygeal cornua articulate with the sacral cornua, forming the posterior sacral foramen. Fusion of the sacrum to the coccyx may also occur after birth (147). In most adults the coccyx curves anteriorly and inferiorly. In about one third of adults it is sharply curved with its tip pointing anteriorly (148).

Minimal literature is available regarding morphological differences between the sexes. There are conflicting data regarding whether the female coccyx is less curved (149,150). Woon and Stringer performed a retrospective analysis of CT scans of 112 adults with no known sacral or coccygeal pathology. The number of coccygeal segments was not associated with sex. Sacrococcygeal fusion was present in 57% of the adults studied and was not associated with age or sex. The coccyx was significantly longer in men and tended to be more curved, but other radiologic features were not significantly different between the sexes. The mean angle between first and last coccygeal segments was 138 + 25° in men and 147 + 25° in women. The mean coccygeal length was 4.4 + 0.8 cm in men and 4.0 + 0.8 cm in women. Additionally of note, 9 of the 12 subjects with retroverted coccygeal tips were female (148).

Biomechanics

The coccyx is capable of a small amount of flexion via contraction of the levator ani muscle and passive extension. Maigne et al. classified a normal ROM of between 5° and 25°, hypomobility with less than 5°, and hypermobility with greater than 25° of coccygeal flexion with sitting (151). In a study of 47 healthy adults, the coccyx moved by a mean of 9° when transitioning from standing to sitting on a hard surface (152).

Clinical Syndrome

Coccydynia

Coccydynia constitutes less than 1% of all nontraumatic complaints of the spine (153). Maigne et al. reported 36 of 51 subjects with coccygeal pain had a history of direct trauma to the coccyx (151). In another study, Pennekamp et al. reported a 50% incidence of direct trauma (153). Women are five times more commonly affected by coccygeal pain than men (153–155). Minimal epidemiologic data are found in the literature regarding individuals with coccydynia in exercise or sport. In one study of 219 male and 99 female subjects participating in the 1997 Canadian National Taekwondo Championships, two coccygeal injuries were seen or treated by the health care team. Both of these injuries were in men (156).

Coccydynia can be due to injury to the coccyx, joints, or surrounding tissues. Both men and women may also complain of pain with defecation or sexual intercourse. The most common cause of coccygeal pain is direct trauma from a fall or childbirth, though it may also result from cumulative trauma (154). Women have a higher prevalence of coccydynia due to the sex differences in morphology of the pelvic outlet; the coccyx is more prominent in females and hence potentially more vulnerable to injury (157). Morphologically, retroversion of the coccyx increases posterior exposure of the coccyx to potential trauma. Functional retroversion can be seen in obesity, with reduced sagittal pelvic rotation (154,158). Coccygeal trauma may result in sacrococcygeal or intercoccygeal joint instability (155). In another study, patients with more of a sharp ventral angulation were considered at greater risk for developing coccydynia (150).

Degenerative changes at the sacrococcygeal, intercoccygeal, or facet joints can develop secondary to trauma or instability (148,159). Depending on the severity of trauma to the coccyx, damage to the pelvic floor muscles or ligaments may occur as well. Coccydynia can also be due to referred pain from lumbosacral nerve roots or from muscle spasm within the pelvic floor. One third of coccygeal pain is idiopathic (155,160). No specific pathophysiologic information was found in the literature regarding individuals with coccydynia in exercise or sport; however, sports with potential for coccygeal trauma (e.g., gymnastics) are likely to have the highest rates of injury. Trauma can either occur directly to the coccyx or indirectly with increased forces delivered through the muscular and ligamentous attachments.

Treatment of coccydynia typically focuses on offloading the coccyx with a cushion or sitting aid for a period of weeks to months. Physical therapy is an integral part of treatment and should focus on the pelvic floor, coccyx, and surrounding musculature. Intrarectal manipulation of the coccyx and massage of the pelvic floor muscles can be performed to relax the pelvic floor muscles and improve pain (158). Modalities such as diathermy and phonophoresis have been used with modest benefit (161).

PELVIC FLOOR

Anatomy

The pelvic floor spans from the pubic symphysis anteriorly, to the walls of the ileum laterally, and to the coccyx posteriorly. It consists of a group of striated muscles organized in a dome-shaped sheet. The pelvic floor functions to provide support to the pelvic organs, urethra, rectum and vagina. Contraction of the pelvic floor occurs in a coordinated motion, in one direction, with an inward lift and squeeze around the urethra, rectum, and vagina (162). Because of its anatomic configuration and function, the pelvic floor is often referred to as the “floor of the core” (Figure 6.6).

The deep pelvic floor contains the levator ani muscle, which is composed of the puborectalis, pubococcygeus, and iliococcygeus muscles. These muscles act in conjunction with the urethral and anal sphincters and play an important role in urinary and bowel continence. The pelvic floor has two hiatuses. The urogenital hiatus is located anteriorly and contains the urethra and vagina. Posteriorly, the anal canal passes through the rectal hiatus (Figure 6.6). The superficial pelvic floor is composed of the bulbocavernosus, ischiocavernosus, and transverse perineal muscles. In addition to providing support, these muscles are important in expulsion of urethral contents and erectile function (163).

The perineal body, also known as the central tendon of the perineum, is integral to the structure of the pelvic floor. Multiple pelvic muscles and sphincters converge and attach at the perineal body, including anterior fibers of the levator ani, superficial and deep transverse perineal, bulbospongiosus, external anal sphincters, and fibers from the urinary sphincters. It is located at the mid-portion of the perineum between the vagina or bulb of the penis and the anus. In women, it may become damaged during childbirth, potentially leading to pelvic floor dysfunction.

Biomechanics

The pelvic anatomy and biomechanical differences in women put them at risk to develop pain and/or dysfunction. As discussed previously, a woman’s pelvis is broader and shallower; therefore, the pelvic ligaments and muscle stiffness provide stability to the pelvic joints (164). Additionally, there are inherent anatomical differences in the structure of the pelvic floor between men and women and physiologic changes that occur throughout the lifecycle due to hormonal changes, pregnancy, and childbirth. For example, during adolescence females are more prone to joint hypermobility, placing them at increased risk for injury. During childbirth the pelvic floor muscles are susceptible to trauma during delivery, causing possible bone, ligament, muscle, or nerve injury. Middle-age women are more likely to undergo pelvic surgery, such as hysterectomy and bladder suspension; and finally with increased age, soft tissue atrophy can occur in the setting of decreased estrogen. Men, on the other hand, are more likely to develop pelvic floor dysfunction related to lumbar and hip pathology from degenerative changes and altered mobility at these joints. In both sexes the pelvic floor functions to control urinary and fecal continence and aids in sexual function. These

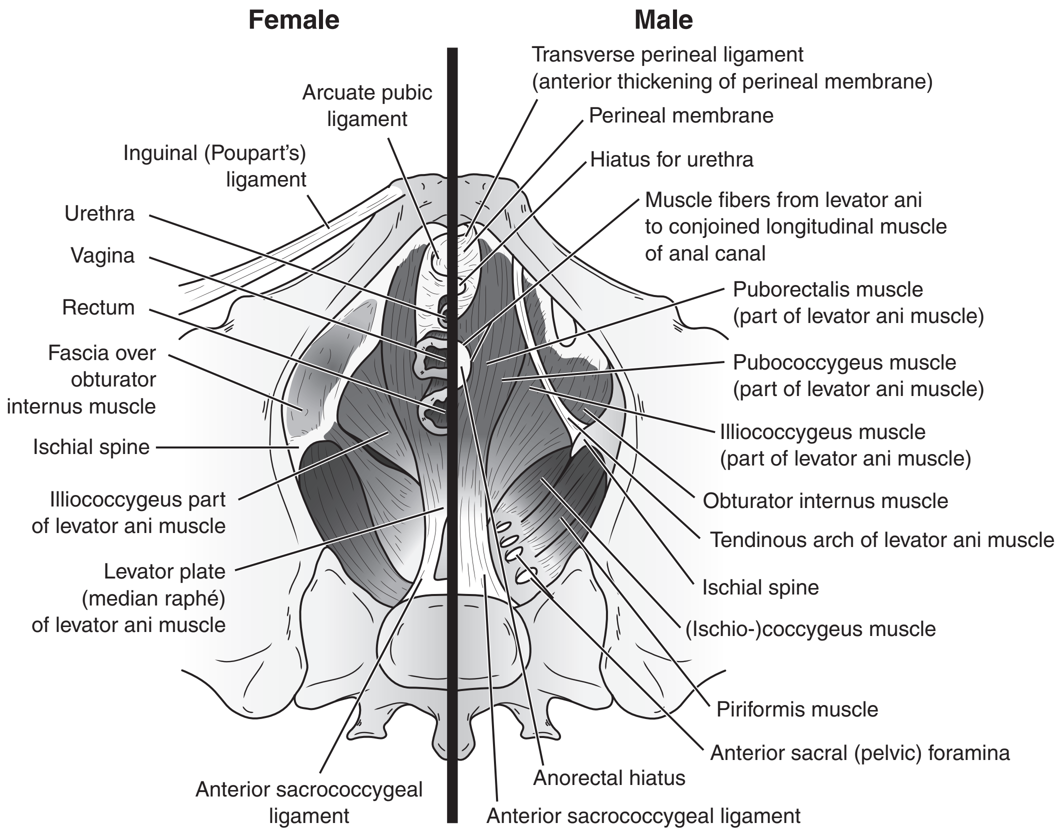

FIGURE 6.6: Difference between the female and male pelvic floor.

actions can be impaired when pelvic floor dysfunction is present. We discuss specific examples of pelvic floor dysfunction in the next sections, including addressing the etiology and prevalence of urinary incontinence and pelvic pain in athletes.

Clinical Syndromes

Urinary Incontinence

Stress urinary incontinence is the most common type of incontinence found in athletes. It involves the involuntary leakage of urine on effort or exertion (165). Urodynamic studies demonstrate involuntary loss of urine during increased intra-abdominal pressure not caused by a contraction of the detrusor muscle.

In both sexes the same neurological networks exist for control of micturition. Differences in pelvic floor structure may account for significant differences between the sexes in regard to urinary incontinence, with women being more affected than men. The etiology of stress urinary incontinence in female athletes is multifactorial, involving inadequate abdominal pressure transmission, pelvic floor muscle fatigue, connective tissue composition, and changes in the pelvic floor due to pregnancy and childbirth (166). In men, the major risk factor for stress urinary incontinence includes prostate surgery (167). High-impact sports with running and jumping cause sudden increases in intra-abdominal pressure. The pelvic floor muscles must be able to contract rapidly and forcefully to withstand the repetitive deceleration of the abdominal organs on the pelvic floor (166). Furthermore, with age, maximal urethral closing pressure tends to decrease in women, with a significant difference noted after age 36 (168).

Among all ages urinary incontinence is twice as common in women as in men (167). Of note, women are also less likely to disclose incontinence to physicians (169). In one study of female athletes, only 35% had discussed incontinence with a health care professional (166). MacLennan et al. conducted 3,010 interviews of individuals between the ages of 15 and 97 in Australia. The prevalence of self-reported urinary incontinence was 4.4% in men and 35.3% in women. Urinary incontinence was more common in nulliparous women than men and increased after pregnancy according to parity and age (170).

There is considerable literature dedicated to urinary incontinence in female athletes, but not in males. In a study of elite athletes and professional ballet dancers, Thyssen et al. studied 291 women in Denmark with a mean age of 22.8 years. They found that 51.9% of the athletes and dancers reported urine loss, 43% while participating in their sport and 42% during daily life. One third of subjects considered their incontinence a social or hygienic problem (171). Nygaard et al. reported that 47% of 326 female participants between the ages of 17 and 68 years, of which 89% exercised regularly, noted some degree of urinary incontinence. Within this group, 30% of exercisers noted incontinence during at least one type of exercise and 20% of exercisers stopped participating in an exercise because of incontinence. Among nulliparous women, one in seven noted leakage during exercise (172). In another study, 28% of 144 elite female nulliparous athletes reported stress urinary incontinence during exercise or sport (166).

The activity most likely to provoke urinary leakage is jumping with high-impact landings and running, with gymnastics having the highest degree of leakage of the different sampled sports (166). Interestingly, more athletes experienced leakage during training rather than competition, perhaps due to increased sphincter tone related to elevated catecholamine release during competition or due to ritual bowel and bladder emptying prior to competition (171). Additionally, athletes may perform an increased number of repetitions during practice compared with competition, leading to increased fatigue of the pelvic floor. In comparing elite athletes with control subjects, Bo et al. found no difference in prevalence of incontinence (41% and 39%, respectively) (162).

Pelvic floor strengthening, intravaginal support devices, voiding prior to exercise, and bladder training, as well as appropriately limiting fluid and caffeine intake prior to exercise, can all help to mitigate stress urinary incontinence in these athletes. In cases where muscles within the pelvic floor are weak, the patient can be instructed on how to strengthen these muscles. However, weakness is not always the reason behind pelvic floor dysfunction and urinary incontinence. Often, instructing the patient on appropriate relaxation and coordination can be of equal importance. Education regarding these techniques can be initiated during the internal palpatory pelvic examination and continued under the guidance of a therapist. Additionally, biofeedback can be quite helpful in helping patients improve tone, relaxation, and coordination of the pelvic floor.

With regard to anal incontinence (AI), including flatus and fecal incontinence, MacLennan et al. reported incontinence in 6.8% and 2.3% of men and in 10.9% and 3.5% of women, respectively (170). In a household survey in Wisconsin among 6,959 individuals, 2.2% reported anal incontinence, with 30% over the age of 65 and 63% women (173). With regard to anal incontinence associated with exercise or sport, in one study of 393 women (mean age of 23.52 + 5.31), the prevalence of anal incontinence was nearly three times higher among female athletes participating in intensive sports, defined as at least 8 hours per week (14.8%), compared with nonintensive sports, defined as less than 8 hours per week (4.9%) (174). Additionally, no one type of sport was significantly associated with a higher prevalence of AI than the other types of sport (174). In another study of 109 runners (78 men and 31 women) , 12% reported fecal incontinence while running (175). No specific literature was found comparing the prevalence of AI between men and women in sports.

Pelvic Pain

There are many possible causes of pelvic pain in an athlete. Adaptive patterns with increased or reduced muscle tone or dyssynergy within the pelvic floor may develop as a result of primary joint injury or muscle imbalance, causing pelvic floor dysfunction. For example, intra-articular hip dysfunction may refer pain to the groin and pelvis, or antalgic motion at the hip may cause a compensatory increase in tone within the pelvic floor. In another example, weak gluteal muscles can place extra stress on the obturator internus to assist with hip abduction (107). Improper technique with exercise that involves valsalva while bearing down rather than lifting the pelvic floor can place increased load on the pelvic floor and may facilitate dyssynergy, with the inability to coordinate contraction and relaxation (107). Muscle imbalance syndromes can also contribute to an increased resting state of the pelvic floor muscles. Myofascial pain syndromes and trigger points of these muscles can develop due to these imbalances, leading to pain and pelvic floor dysfunction. Facilitating muscle tone symmetry is key for appropriate treatment; therefore, the biomechanics of the pelvic floor should be evaluated and addressed in order to successfully improve outcomes (107).

Women are at increased risk for developing pain in the pelvic region compared with men because a woman's broader and shallower pelvis requires greater ligamentous and muscular strength to maintain joint stability. Moreover, throughout a woman's lifecycle there are physiologic changes that affect musculoskeletal function. At younger ages, the female athlete may have increased joint laxity and hypermobility (107). The pelvic floor is also susceptible to trauma through pregnancy and childbirth. With age, hormonal changes may facilitate soft tissue atrophy, which may place women at increased risk for pelvic floor dysfunction.

Pudendal nerve injury can also result in pelvic pain and sensory or motor deficits (176). The pudendal nerve is derived from the sacral plexus (S2-S4) and may be injured at several possible entrapment sites in the pelvis. Patients typically present with pain in the perineum and external genitalia, though they may also complain of incontinence or sexual dysfunction. Bony remodeling can occur as a result of repetitive microtrauma, particularly in athletes, with increased activity of the pelvic floor muscles leading to narrowing of the interligamentous space where the pudendal nerve traverses between the sacrotuberous and sacrospinous ligaments (176). Additionally, the pudendal nerve exits through the greater sciatic notch, inferior to the piriformis muscle. In athletes with an enlarged piriformis and elongation of the ischial spine, the cross-sectional area of the notch can be reduced, potentially leading to nerve compression.

Cyclists are particularly at risk for pudendal nerve injury, resulting in possible pelvic floor pain, sensory deficits, and sexual dysfunction. In cyclists this type of injury can be caused by compression of the pudendal nerves and arteries, with a decrease in the partial pressure of oxygen at the glans of the penis noted during riding (177,178). The perineum and ischial tuberosities support most of the cyclist's weight and serve as the interface between the rider and the bicycle saddle. Improper fit, saddle type, and anatomic factors can predispose one to these types of injuries. In cyclists, direct pressure of the nose of the saddle against the perineum and the pubic symphysis, exacerbated by the forward leaning of the rider, can compress the pudendal nerves where they emerge below the pubis. Excessive repetitive hip flexion while cycling may also contribute by further stretching the pudendal nerve. Since the pudendal nerve takes the same course in women, similar sexual and urinary dysfunction may occur, including difficulty with achieving orgasm, difficulty with urination, and perineal numbness and pain (179).

The prevalence of perineal, penile, or labial numbness may be as high as 50% to 91% in cyclists and is likely underreported (178,180). Cyclists older than 50 years and those with higher body weight are more likely to experience symptoms related to pudendal nerve injury (181,182). Among 282 female riders, approximately one third reported perineal trauma, and 34% of those with trauma reported perineal numbness (183). With regard to erectile dysfunction in cyclists, a study in Norway reported 13% of 4,828 riders reported symptoms of erectile dysfunction lasting 1 to 4 weeks after a 540-kilometer ride (184). In another study, Taylor et al. reported a prevalence of erectile dysfunction of 17% among 688 cyclists and noted no significant difference in the rate of erectile dysfunction among cyclists compared with historical controls (185). However, when comparing rates of erectile dysfunction among mountain bikers and road cyclists, a significant difference was noted (186).

Additionally, visceral, infectious, and psychosocial etiologies of pelvic floor dysfunction should always be evaluated, such as endometriosis, cystitis, pelvic inflammatory disease, prostatitis, a history of sexual abuse, stress, anxiety, and depression (176).

SPECIAL CONSIDERATIONS IN FEMALES

Pregnancy-Related Musculoskeletal Disorders

Pregnancy-related low back pain, pregnancy-related pelvic girdle pain, and pregnancy-related lumbopelvic pain are common and disabling conditions in women. For the sake of ease, we will use the term lumbopelvic pain (unless otherwise specified) in this chapter to include the conditions of low back and pelvic girdle pain in pregnancy. Prevalence studies have been methodologically heterogeneous and have used variable definitions; therefore, there are varying incidence and point prevalence rates of lumbopelvic pain in pregnancy in the literature from the international communities, ranging from 20% to 84% (187–189). Wang et al. found that approximately 68% of all pregnant women included in a sample population from the United States suffered from low back pain during pregnancy. Nearly 60% of these women had difficulty with sleep and performance of daily activities, and 10.6% reported taking time off from work because of low back pain (190). The prevalence of low back pain in pregnant athletes has been less studied. Since 2002, the American College of Gynecologists has recommended that healthy pregnant women engage in at least 150 minutes of moderate intense physical activity per week. There have been several studies published recognizing the benefits of exercise during pregnancy (191,192) and, therefore, more women are being encouraged to be involved in physical activity during their pregnancy and may suffer from related injuries. With regard to pregnancy-related lumbopelvic pain, Bø and Sherburn found no significant difference in the prevalence of lumbopelvic pain in elite

Norwegian athletes when compared to age-matched controls (193); however, there is limited research on this topic.

There are many hypothesized etiologies of pregnancy-related lumbopelvic pain, including mechanical, anatomical changes, and hormonal influences leading to ligamentous laxity, as well as inflammatory, vascular, and neural (peripheral and central) factors. The onset of pain can happen at any point during the pregnancy; however, a majority of studies demonstrate that the pain typically begins in weeks 18 to 22 of gestation. Clinical findings of pregnancy-related lumbopelvic pain include patient reports of low back, buttock, hip, anterior groin, or thigh pain, as well as leg pain, numbness, and tingling (194). Patients sometimes report pain with crossing of their legs and with transitional motions (e.g., sit to stand, rolling in bed). Pain is often greater with increased speed of walking, increased stride length, getting up from the floor, and climbing stairs.

During pregnancy, there may be a weight gain of approximately 20 to 40 pounds (195) and the muscles of the pelvic floor are relied upon to bear the weight of the growing uterus. Anatomical changes during pregnancy include lengthening and separation of the abdominal muscles, a shift in the center of gravity upward and forward (196), therefore leading to an increase in lumbar lordosis (196) and rotation of the pelvis on the femur (197). It was thought that hyperlordosis was the etiology of pregnancy-related low back pain, but this has been challenged in the literature. Garshasbi and Faghih Zadeh studied the effect of exercise in low back pain in pregnancy and found a weak association between pregnancy-related low back pain and hyperlordosis (198). Ostgaard et al. found that an increase in the abdominal sagittal diameter during pregnancy influenced the existence of pregnancy-related low back pain (199). The combination of lengthening/separation of the abdominal musculature, increased anterior pelvic tilt, and the shift in center of gravity places more stress on the posterior pelvis and low back including the SI joints, pelvic ligaments, and the erector spinae muscles, which have to work harder to maintain an upright posture (200).

Moreover, lumbopelvic pain may be a result of abnormal motor control and muscle firing patterns, which can perpetuate altered neurodynamics of the pelvis and lead to chronic symptoms (201). Pelvic stability is supported by well-coordinated neuromuscular and articular systems in the form and force closure models described previously. Pelvic instability is a failure of the pelvic load transfer mechanics, which can cause excessive pelvic joint movement and therefore lead to pain (202). It has been demonstrated by Damen et al. that asymmetric laxity of the SI joint as revealed by Doppler imaging is associated with moderate to severe pelvic girdle pain in pregnancy (203). Additionally, weakness of the muscles that support the pelvic girdle, including the hip abductors (specifically the gluteus medius), have also been associated with pregnancy-related low back pain. Weight gain that occurs during pregnancy can increase the stress on the gluteus medius with stance and gait, which can reduce stability of the pelvis and lead to pain (204). Based on the literature, it is likely that the etiology of pregnancy-related lumbopelvic pain is multifactorial and related to maladaptive neuromuscular patterns and musculoskeletal dysfunction as the pregnancy progresses.

Additionally, due to hormonal influences there is an increase in ligamentous laxity, especially during the second and third trimester, which has been suggested to increase pelvic girdle relaxation and be a cause of pregnancy-related lumbopelvic pain (205). This change may be due to the action of the hormone relaxin, which is an insulin-like peptide hormone that peaks during the first trimester. Relaxin stimulates collagenase to remodel the pelvic connective tissue in preparation for delivery (204), although experimental studies have not shown a direct relationship between high levels of relaxin and increased pelvic mobility or peripheral joint mobility in pregnant women (202). Different methods in these studies were used to measure pelvic and peripheral joint laxity and varying definitions of lumbopelvic pain were used. Moreover, estrogen and other sex hormones such as progesterone, testosterone, sex hormone-binding globulin, and insulin-like growth factor 1 may also contribute to the increase in joint laxity during pregnancy (206).

Relaxin has been well studied in the pregnant population with conflicting findings in regard to its correlation with lumbopelvic pain in pregnancy. MacLennan et al. found that pregnant women with the most significant amounts of low back pain were found to have the highest levels of relaxin (207). Kristiansson, Svärdsudd, and von Schoultz found a positive correlation with mean relaxin levels and pubic symphyseal pain (208,209). On the contrary, Hansen et al. found that there was no significant difference with relaxin levels and pelvic girdle pain (210). Albert et al. also found normal levels of relaxin in pregnant patients with pelvic girdle pain (211). Studies looking at peripheral joint laxity found no increase in peripheral joint laxity and relaxin levels, although it was shown that peripheral joint laxity did increase as the pregnancy progressed (212,213). Despite increasing research in this area, the true modulatory effects of sex hormones are not known, partly because of the difficulty studying this topic and partly because these hormones likely act in concert with each other to affect the metabolic properties and function of ligaments (206). Given the lack of supporting evidence for hormonal-induced lumbopelvic pain in pregnancy, this mechanism as the sole etiology of this condition has fallen out of favor (204).

Peripartum Pubic Rami Separation

Separation of the pubic symphysis is a recognized but uncommon complication of childbirth. The occurrence is not related to exercise or sports during pregnancy but, if present, would likely prohibit the mother or expecting mother from proceeding with exercises or sports due to pain. The normal width of the pubic symphysis joint in females ranges from 3 to 10 mm. Due to the hormonal changes during pregnancy and in conjunction with overall joint laxity, it is common for the pubic symphysis joint to widen up to 8 to 10 mm. Usually any separation of the pubic symphysis greater than 10 mm has been defined as pathological. The incidence of pubic symphysis separation during delivery is reported to vary between 1 in 300 and 1 in 30,000 deliveries (214,215). Case studies and series have suggested a number of clinical variables that contribute to the development of symphyseal separation. Associated factors include fetal macrosomia, multiparity, use of oxytocin, epidural anesthesia, precipitous labor, malpresentation, and forceful abduction of the thighs during labor, in addition to natural physiologic changes and joint relaxation that occur in response to hormonal changes in pregnancy (216).

The clinical presentation and diagnosis of pubic symphysis separation is relatively straightforward: Patients often experience suprapubic discomfort or sensation of separation during delivery. Subsequently there may be suprapubic pain, tenderness, swelling, and edema, with radiation of pain to the legs, hips, or back. The patient often has difficulty ambulating due to pain. Classically, pubic symphysis separation is diagnosed based on clinical symptoms and obtaining a pelvic radiograph that shows pubic symphysis separation of at least 10 to 13 mm (217) (see Figure 6.7). A review by Nitsche and Howell found the degree of widening of the pubic symphysis was up to 110 mm after delivery (218). The size of the separation does not appear to correlate well with the severity of symptoms, as significant disability and prolonged recovery has been reported with a mild degree of separation (219). Historically patients suffering pubic symphysis separation are treated conservatively with bed rest, pelvic binders, and gradual return of mobility with physical therapy over weeks to months. Physical therapy strategies include deep core muscle strengthening in the immediate recovery phase within the first week of injury to maintain pelvic stability. Patients may require walking aids as helpful initially, and pelvic corsets or SI joint belts may be used for comfort (220). Intrasymphyseal injection of corticosteroids is another adjunct therapy that has been used that can decrease pain and shorten the time of morbidity and time to complete recovery (221). Failure of conservative therapy or severe separation (greater than 40 mm) of the pubic symphysis may require invasive orthopedic interventions, including internal or external plate fixation of the pubic symphysis (222,223).

FIGURE 6.7: Anteroposterior pelvis x-ray of a female postpartum patient with a 6.2 cm pubic symphyseal separation taken after vaginal delivery of her first child.

Transient Osteoporosis of Pregnancy

Transient osteoporosis of pregnancy is a rare but perhaps underreported condition described by Curtiss and Kincaid in 1959 (224). They reported on three cases of "transitory demineralization of the hip in pregnancy" in female patients with acute hip pain in the third trimester of pregnancy. Radiography revealed spotty demineralization of the femoral head and acetabulum. Several months later the pain improved and repeated x-rays revealed recalcification of the femoral head without joint space narrowing. Since that time, over 200 cases of transient osteoporosis in pregnancy have been published (225). Steib-Furno et al. found that over a 2-year period, 3 out of 4,900 pregnancies were complicated by transient osteoporosis of pregnancy (226). Of those women who develop transient osteoporosis of pregnancy, the active exercising pregnant female is most likely to develop symptoms of pain due to the increased risk of an insufficiency fracture when exercising on osteoporotic bone. There have also been numerous reports of transient osteoporosis in middle-aged men (age 40–60). Although the condition is commonly reported in pregnant women, it is thought that it actually occurs more commonly in men with a ratio of 3:1 (227).

The etiology of transient osteoporosis in pregnancy is unclear. Several theories have been postulated, but none has garnered substantial evidence; many theories lack wide applicability and at times they even conflict with each other. The most common hypothesized etiologies of transient osteoporosis of pregnancy include genetic predisposition, neurological disruption, neurovascular compression, hematologic or vascular changes and deficiencies in bone metabolism, and calcium homeostasis (225,228). The only recognized risk factor thus far is pregnancy (228). Transient osteoporosis of pregnancy generally affects otherwise healthy women in their third trimester of pregnancy and has been described as a self-limiting condition that resolves with several months of pregnancy (229). Patients typically present with progressive and debilitating pain in the hip, although there are reports of this condition in the knee, ankle, wrist, elbow, spine, and sacrum (230–233).

At the time of presentation, a woman typically presents with a limp if the affected joint is in the lower extremities and has pain at the extremes of ROM (228). The pain can also be present bilaterally or in multiple joints (229). Laboratory results are generally nonspecific, and synovial fluid has been found to be sterile with nonspecific inflammation (234). Plain radiographs of the hip may demonstrate diffuse osteopenia of the entire femoral neck, although it may take 4 to 8 weeks after the onset of symptoms to appear (227). It is important to note that ionizing radiation exposure to the fetus should be avoided if at all possible. MRI is the imaging modality of choice given its high sensitivity and ability to detect changes consistent with transient osteoporosis of pregnancy within 48 hours of the onset of symptoms (235). Characteristic changes on MRI include decreased signal intensity of the affected bone marrow on T1-weighted images, increased signal intensity relative to normal bone marrow on T2-weighted images, and small joint effusions with resolution of these changes months later (227,236), as shown in Figure 6.8.

First-line treatment for transient osteoporosis of pregnancy is rest and weight-bearing restrictions on the affected joint with either a walker or crutches. Analgesics

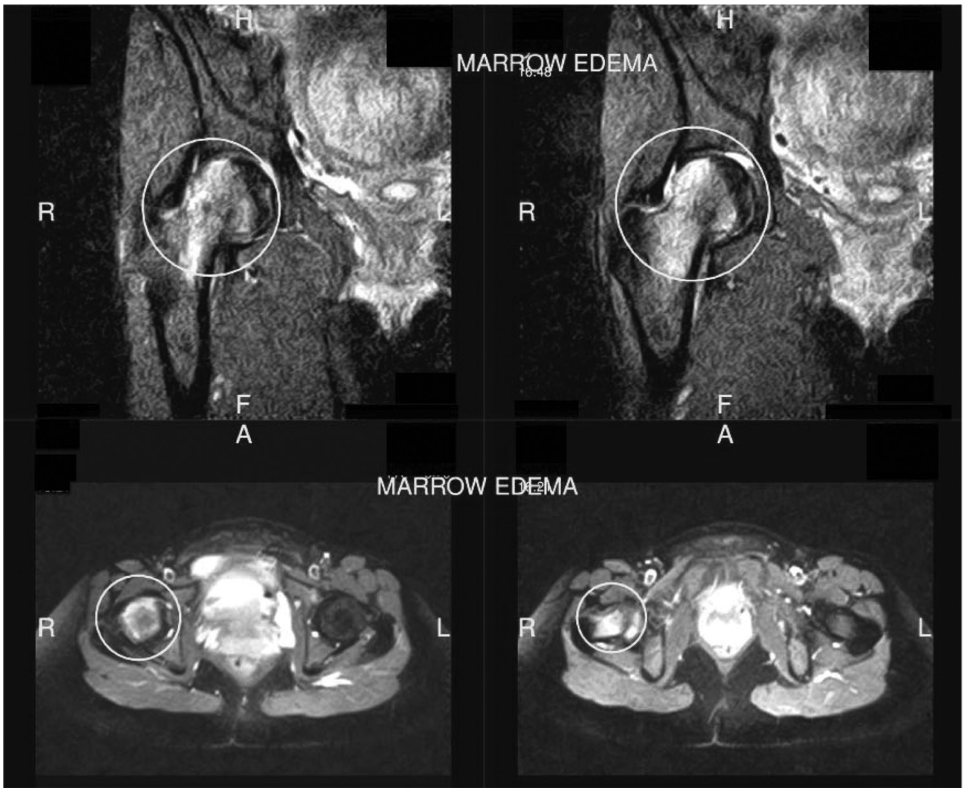

FIGURE 6.8: Coronal and axial T2 fat saturated MRI images of the right hip in a pregnant patient who is 28 weeks pregnant with transient osteoporosis of the hip.

should be avoided unless there is pain at rest, in order to allow the patient to use pain as a guide to limit mobility. Calcium (1,000 mg) and vitamin D (600 IU) supplementation can be initiated to ensure that the patient is meeting daily requirements (237). There are case reports of using calcitonin to help improve symptoms and possibly shorten duration of the illness; however, the safety of use in pregnancy is unknown (231). Transient osteoporosis also requires important considerations for labor and delivery. There are several reports in the literature of hip fractures (unilateral and bilateral) during vaginal delivery in women with this condition (238–243). Therefore, if the patient continues to be symptomatic and have hip pain at the time of delivery, cesarean section is recommended to limit the forces on the hip and reduce the risk of fracture (244).

CONCLUSION

Sex differences play a crucial role in the prevalence of various musculoskeletal injuries involving the pelvis in both males and females. These differences are outlined in summary form in the summary table for reference. As sports medicine providers it is essential that we are aware of the sex differences involved in sport to accurately diagnose and treat our patients effectively. Understanding the sex differences within the pelvis can also lead us to better understand the differences of body mechanics and etiology of injury in sports medicine. This could potentially help us develop prevention programs specifically addressing any modifiable risk factors to decrease the risk of injury and find ways to ultimately make sports safer for our patients.

Prevalence of Musculoskeletal Complaints of the Pelvis Among Males and Females

Musculoskeletal Complaint	Sex With Higher Prevalence
Adductor strain	Males (23–25)
Athletic pubalgia	Males (12,13,15,56,57)
Osteitis pubis	Males (28,81–84,88)
Pubic rami fracture	Females (97,98,100,101)
Sacroiliac joint dysfunction	Females (119,120)
Sacroiliitis	Males (124–127)
Sacral stress fracture	Similar (138,141)
Coccydynia	Females (151–153)
Urinary incontinence	Females (165,167)
Anal incontinence	Females (168,171)
Pelvic floor dysfunction	Females (107,162)

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7

HIP

Abby L. Cheng and Heidi Prather

INTRODUCTION

In the past our understanding of the hip joint, its function, and its acquisition of dysfunction was limited by the availability of only static imaging studies. Hip arthroscopy has expanded our knowledge of the cartilaginous and bony structural changes in the hip that imaging had not clearly shown. We have a better understanding of dysfunction related to structural changes that occur prior to the onset of arthritis, but we are also learning that correction of the structural changes does not always guarantee a correction of dysfunction and pain (1). This concept is particularly important when evaluating and treating young athletes because they often present with hip-related pain early in the disease course and are limited in their ability to participate in sports. We need to know how to manage this population appropriately in order to treat painful dysfunction and prevent future cartilaginous injury and adaptive movement changes that develop as a response to pain.

Now our understanding of the hip is further enhanced by three-dimensional modeling imaging with CT and MRI, which detail structural relationships, in addition to laboratory-based studies that are elucidating real-time movement relationships (2). There is emerging evidence of hip dysfunction patterns that are sex-related (3). As a result, there is an increasing awareness of a need to fill these knowledge gaps regarding the hip disorders and how they are related to each sex.

Evaluation of hip pain can be difficult because the referral pattern of hip pain is variable and overlaps in distribution with painful disorders of the lumbar spine and pelvic girdle. Furthermore, lumbar spine, pelvic girdle, and hip disorders coexist, and as a result pain may not be related to just one entity. Often the first step in coming to a hip-related diagnosis is to determine whether pain is caused by an intra-articular structural disorder (i.e., affecting the cartilage or labrum inside the hip joint) or extra-articular structural or movement disorder (i.e., affecting bone or soft tissue outside the joint capsule). This chapter refers to these concepts of differential diagnosis to review and describe hip disorders as they relate to sex, movement patterns, prearthritic conditions, hip osteoarthritis (OA), extra-articular soft tissue pathology, bone disorders, and other lumbopelvic pain conditions that are affected by hip motion.

NORMAL STRUCTURAL DIFFERENCES

Bony Differences

In addition to sex differences in pelvic girdle structure (discussed in Chapter 6), there are also sex-based differences in femur and acetabular anatomy (see Figure 7.1). Recognizing these differences is important in order to accurately define the continuum of normal versus aberrant bony hip structure.

Proximal Femur

The femoral head is often aspherical, and variations in femoral head shape can contribute to incongruent force and weight distribution across the joint. There are several radiographic measures designed to describe the femoral head shape and its relation to the acetabulum.

First, the alpha angle characterizes the “bulkiness” of the femoral head-neck junction. Larger alpha angles describe greater bulk of the proximal femoral neck (see Figure 7.2). The value for the “normal” alpha angle is still debated for two reasons: (a) the alpha angle of a given hip varies based on the plane being examined (i.e., on different radiographic views and different cuts on CT and MR imaging), and (b) for any given “normal” cutoff, abnormal proximal femur anatomy does not correlate one-to-one with symptomatic hip pain. Currently an angle above 60° in both sexes is most commonly considered to be abnormal (4).

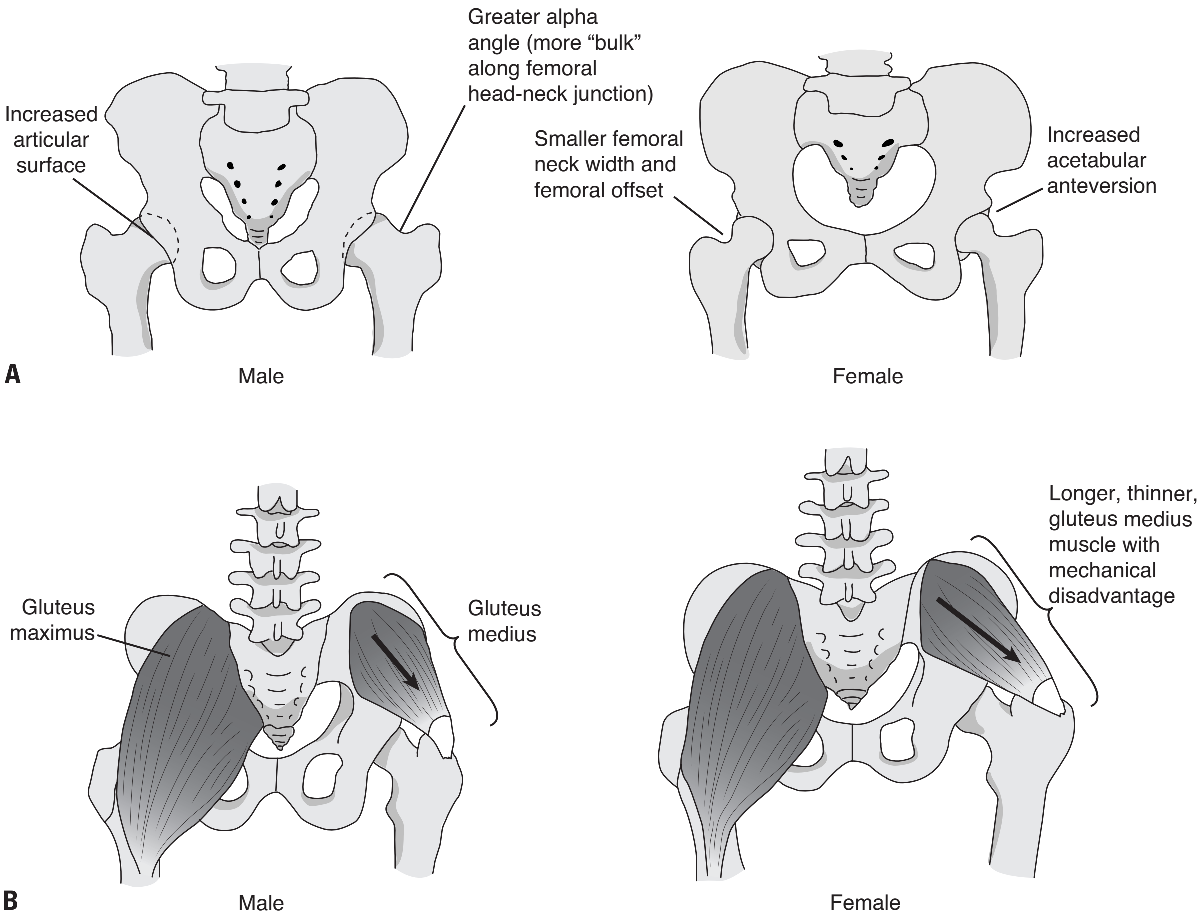

FIGURE 7.1: Sex differences of hip anatomy. (A) There are sex differences in femur and acetabular bony anatomy. (B) Because females have wider pelvises, they have longer gluteus medius muscles and must generate more torque across the hip joint in order to maintain a level pelvis.

However, several studies have shown that alpha angles are consistently larger in males than females, both in adolescents and adults (5–7). This sex difference in alpha angle suggests that in order to have the highest accuracy in diagnosing abnormal hip morphology, it may be necessary to define different reference angles for each sex. At this time, there is no expert consensus on this aspect of description by sex. Further research is needed to better quantify appropriate angles to be used as cutoff points to discriminate between the range of normal and aberrant measurements.

There are other radiographic measures also used to characterize proximal femur anatomy, but data on sex differences for these measures are less robust. The measures include femoral version, femoral head-neck offset, and femoral offset (see Figures 7.3–7.5 for descriptions of how these measurements are made). At this time in adults, there are mixed data regarding whether there is a sex difference in femoral version (2,8–10), and for femoral head-neck offset it seems there is no sex difference (5). However, for femoral offset males do have a significantly greater mean value than females (55 mm vs. 48 mm, respectively) (10). During adolescence, males also develop a proportionately greater femoral neck width, which provides increased structural integrity compared to females (11).

Lastly, the femoral head can be classified as spherical or aspherical in shape (12). While no studies have specifically evaluated for sex differences in sphericity in normal hips, there is disproportionate sex-specific representation of conditions manifesting as femoral head asphericity such as Legg-Calvé-Perthes disease (LCPD) and slipped capital femoral

FIGURE 7.2: Alpha angle. The alpha angle describes the "bulkiness" of the femoral head-neck junction. It is the angle between (a) a line drawn along the longitudinal axis of the femoral neck and (b) the point along the femoral head-neck contour that first exceeds the radius of the femoral head.

Source: From Ref. (12). Clohisy JC, Carlisle JC, Beaule PE, et al. A systematic approach to the plain radiographic evaluation of the young adult hip. *J Bone Joint Surg Am*. 2008;90(Supp 4):47–66.

epiphysis (SCFE). These conditions will be discussed later in the chapter.

Acetabulum

Radiographic measures describing acetabular anatomy include acetabular version, center-edge angle (CEA), and Tönnis angle.

Acetabular version describes the anterior/posterior orientation of the opening of the acetabulum. As depicted in Figure 7.6, it is measured on an axial image and is the angle between a line perpendicular to the plane of the ischial tuberosities and a line connecting the anterior and posterior margins of the bony acetabulum. Acetabular *ante*version refers to angles greater than 0°, and *retro*version is defined as a version angle less than 0°. Females tend to have greater acetabular anteversion angles than males (mean/standard deviation 23° ± 10° versus 18° ± 9°, respectively) (10), and acetabular retroversion is more common in males (13).

The lateral CEA describes how much coverage the acetabulum provides over the femoral head. Too much acetabular coverage is a component of femoroacetabular impingement (FAI), and too little coverage is a component of hip dysplasia. Lateral CEA is measured on an anteroposterior (AP) pelvic radiograph and, as shown in Figure 7.7, is defined as the angle between a vertical line drawn through the center of the femoral head and a line connecting the center of the femoral head to the outer edge of the acetabular roof. Historically normal lateral CEA values have been accepted as 25° to 39° for both genders (12,14), and in more recent literature the measurement for the cutoff point for sex-specific normal lateral CEA values is conflicting (2,10, 15–17). However, there are sex differences in impingement and dysplasia, and these are discussed in their respective sections later in the chapter.

Finally, acetabular inclination described by the Tönnis angle is a measure of the vertical tilt of the socket opening. As shown in Figure 7.8, it is calculated from an AP radiograph and is the angle between a horizontal line that crosses through the inferior aspect of the acetabular sourcil (i.e., the sclerotic weight-bearing aspect of the socket) and a line connecting the medial and lateral aspects of the acetabular sourcil. A normal angle is 0° to 10°, and there are no documented sex differences for this reference range (12).

Sex differences in normal acetabular structure evolve from childhood through adolescence. During adolescence, acetabular development occurs earlier in females, but males ultimately develop increased articular surface area compared to females (18). Anthropologic literature has also described variations in the shape of the inner surface of the acetabular socket. Some of these variations are unevenly represented between genders, and since bone structure is affected by its loading environment, it is possible that differences in acetabular shape are at least in part due to sex differences in movement patterns (19).

Range of Motion

Because of the differences in bony structure, it is logical to suspect that normal hip range of motion (ROM) would also be different between the sexes. In a study by Nakahara et al., evaluation of three-dimensional reconstructions of pelvic CT scans in elderly people without hip pain supports this hypothesis. Based on bony endpoints, females had greater maximum hip flexion and internal rotation at 90° of hip flexion, whereas males had greater maximum hip extension

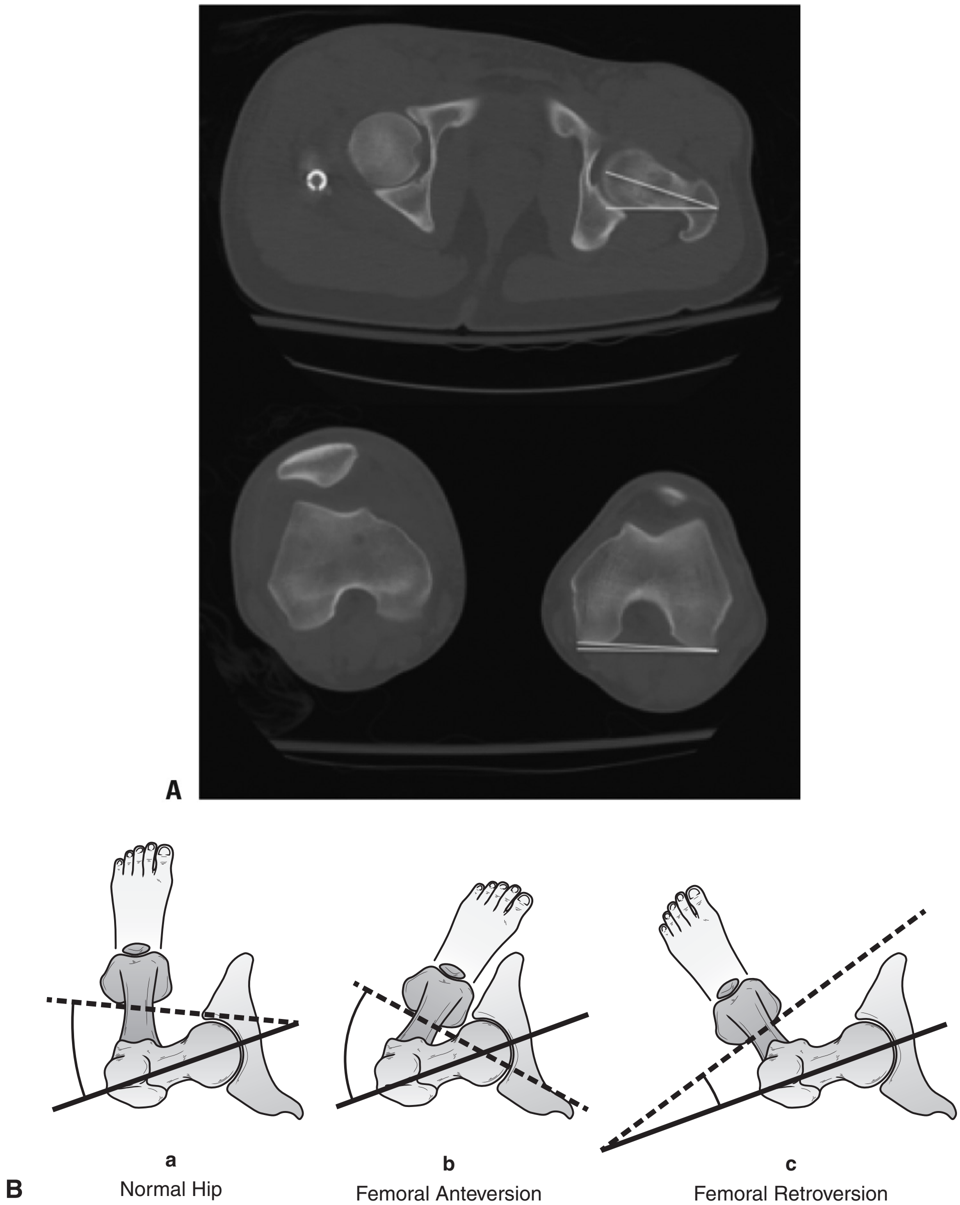

FIGURE 7.3: Femoral version. (A) Femoral version is defined as the angular difference between the femoral neck axis and the transcondylar axis of the knee. It is measured by superimposing axial CT cuts of both the femoral neck and the transcondylar axis to calculate the angle between the two. (B) Femoral version describes the "twisting" between the femoral neck and the femoral condyles. It affects rotation of the distal leg.

(A) *Source:* From Ref. (9). Koerner P, Patel NM, Yoon RS, et al. Femoral version of the general population: does "normal" vary by gender or ethnicity? *J Orthop Trauma*. 2013;27(6):308–311. (B) *Source:* Adapted from Ref. (127). Wilmerding V, Krasnow D. Turnout for Dancers: Hip Anatomy and Factors Affecting Turnout. Education and Media Committees of the International Association for Dance Medicine and Science (IADMS). 2011. www.iadms.org/?323. February 21, 2016.

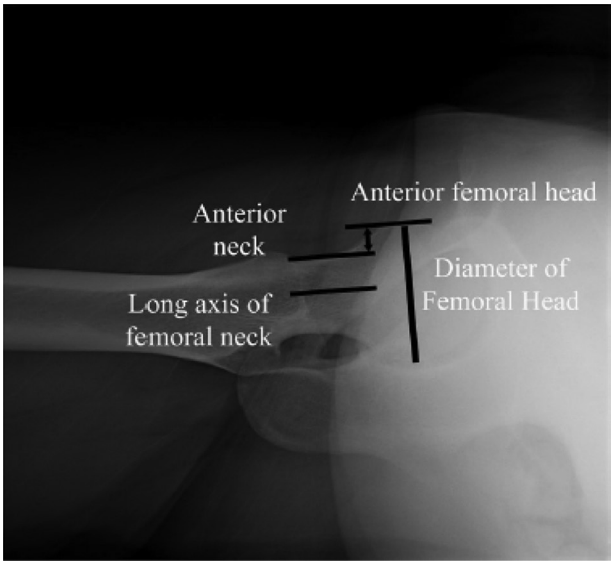

FIGURE 7.4: Femoral head-neck offset. The femoral head-neck offset describes the taper of the femoral neck. It is the perpendicular distance between (a) a line tangent to the femoral head and (b) a line that is parallel to the first and runs along through the anterior aspect of the femoral neck.

Source: From Ref. (12). Clohisy JC, Carlisle JC, Beaule PE, et al. A systematic approach to the plain radiographic evaluation of the young adult hip. *J Bone Joint Surg Am*. 2008;90(Supp 4):47–66.

FIGURE 7.5: Femoral offset. Femoral offset describes the horizontal separation between the femur and the acetabular socket. It is the perpendicular distance from the rotational center of the femoral head to a line drawn along the longitudinal axis of the femoral shaft.

Source: From Ref. (10). Atkinson HD, Johal KS, Willis-Owen C, et al. Differences in hip morphology between the sexes in patients undergoing hip resurfacing. *J Orthop Surg Res*. 2010;5:76. With permission from BioMed Central.

and external rotation at 90° of hip flexion (2). More studies are needed to support this finding in other populations (Table 7.1).

Muscular and Movement Pattern Differences

Just as there are bony gender differences of the hip, neuromuscular differences exist as well. Even among highly trained athletes, females tend to have relatively weaker hip abductors (20). This leads to a predictable movement pattern during single-leg squats, drop landings, and side-step cutting activities: females tend to have greater hip adduction and internal rotation, greater knee abduction, and less trunk and hip flexion (21,22) (see Figure 7.9). They also generate smaller hip extensor moments, and during side-step cutting activities females usually have pelvic rotation and trunk-lean toward the weight-bearing limb, whereas males have pelvic rotation and trunk-lean toward the *non*-weight-bearing limb (22,23). This combination of movements in females requires more force generation by the knee extensors and puts more stress on the knee joint (21).

One possible contributor to females' relative hip abductor weakness is the gender difference in bony anatomy. Because females have a bigger pelvic width-to-femoral length ratio, females must generate more torque across the hip in order to maintain a level pelvis (3). But, by increasing trunk flexion during squat-type activities, females can generate a pattern of energy absorption that is more similar to the typical male pattern. This is important because adapting a movement pattern to increase trunk flexion during squat activities may decrease females' risk of lower extremity injury (24).

In addition to gender differences in hip muscle strength, there are also differences in muscle stretch and possibly

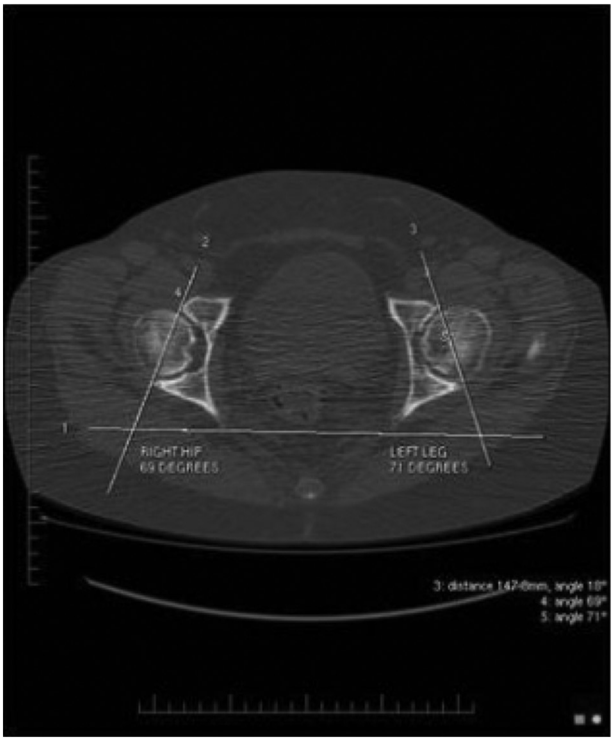

FIGURE 7.6: Acetabular version. Acetabular version is calculated from an axial image. It is the angle between (a) a line perpendicular to the plane of the ischial tuberosities and (b) a line connecting the anterior and posterior margins of the bony acetabulum.

Source: From Ref. (10). Atkinson HD, Johal KS, Willis-Owen C, et al. Differences in hip morphology between the sexes in patients undergoing hip resurfacing. *J Orthop Surg Res*. 2010;5:76. With permission from BioMed Central.

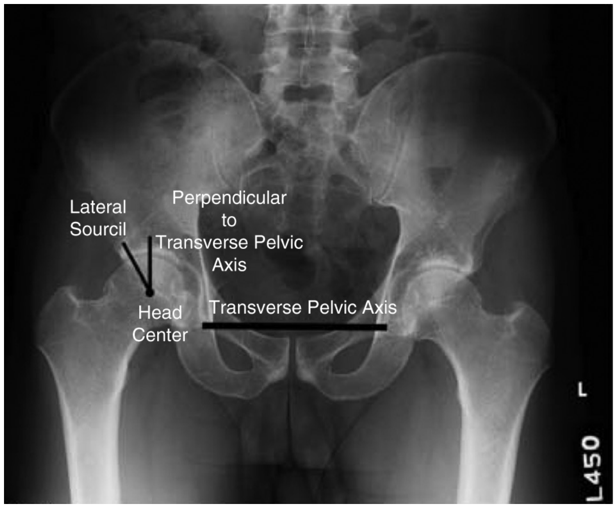

FIGURE 7.7: Lateral center-edge angle (CEA). The lateral CEA is calculated from an AP radiograph. It is the angle between (a) a vertical line drawn through the center of the femoral head and (b) a line connecting the center of the femoral head and the outer edge of the acetabular roof.

Source: From Ref. (12). Clohisy JC, Carlisle JC, Beaule PE, et al. A systematic approach to the plain radiographic evaluation of the young adult hip. *J Bone Joint Surg Am*. 2008;90(Supp 4):47–66.

differences in laxity of other surrounding soft tissue structures. Females have lower passive hamstring stiffness (25,26) and higher tolerance to stretch (27). They also have increased prevalence of symptomatic extra-articular impingement between the femur and contact points on the pelvis such as the ischial tuberosity and anterior inferior iliac spine. Eighty-five percent of diagnoses of extra-articular impingement are made in females. Some hypothesize that increased peri-articular soft tissue laxity may contribute to females' increased risk of encountering bony impingement during activities in end ROM (28).

Females are also more likely to have generalized joint laxity (29). Though not quantified at this time, it is possible that females experience hip dysfunction related to joint laxity more commonly than males. Further studies are needed to better assess and determine these potential differences (Table 7.2).

INTRA-ARTICULAR DISEASE—PREARTHRITIC CONDITIONS

While the etiology of degenerative hip OA in a given patient remains idiopathic, studies are now showing an association between early onset of hip OA and preexisting hip deformity. Some of these "prearthritic" symptomatic hip conditions occur at a disproportionately high rate in young athletes, so understanding these disorders is essential in order to appropriately manage these athletes and minimize the effect on the duration and intensity of their playing careers. This section discusses prearthritic hip conditions that have research-supported sex differences.

Legg-Calvé-Perthes Disease

Legg-Calvé-Perthes disease (LCPD) is osteonecrosis of the femoral head epiphysis in children and young adolescents. The peak age at diagnosis is 5 to 8 years old. The etiology is still unclear, but the leading hypothesis is repetitive microvascular trauma to the femoral head, possibly due to increased intra-articular pressure (30). LCPD is four to nine times more common in males than females, and males are more likely to have bilateral LCPD (31,32). However,

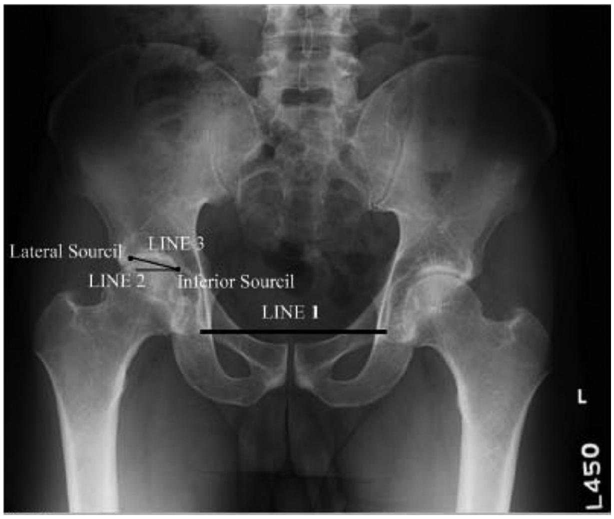

FIGURE 7.8: Acetabular inclination described by Tönnis angle. Acetabular inclination described by the Tönnis angle is calculated from an AP radiograph. To calculate this angle, first establish the transverse pelvic axis by drawing a line connecting the right- and left-sided acetabular teardrops (Line 1). The Tönnis angle is the angle between (a) a line that is parallel to the transverse pelvic axis and that crosses through the inferior aspect of the acetabular sourcil (i.e., the sclerotic weight-bearing aspect of the socket), and (b) a line connecting the medial and lateral aspects of the acetabular sourcil. A normal angle is 0° to 10° (12).

Source: From Ref. (12). Clohisy JC, Carlisle JC, Beaule PE, et al. A systematic approach to the plain radiographic evaluation of the young adult hip. *J Bone Joint Surg Am*. 2008;90(Supp 4):47–66.

TABLE 7.1: Sex Differences of Bony Hip Anatomy

Proximal Femur
Alpha angle ("bulkiness" of femoral head-neck junction): Greater in males
Femoral version ("twisting" of the femur): Unclear
Femoral head-neck offset (taper of the femoral neck): No difference
Femoral offset (horizontal separation between femur and acetabulum): Greater in males
Femoral neck width: Greater in males
Acetabulum
Acetabular anteversion angle (anterior angle of socket opening): Greater in females
Acetabular retroversion (posterior angle of socket opening): More frequent in males
Acetabular lateral center-edge angle (amount of femoral head coverage): Unclear
Acetabular Tönnis angle (vertical tilt of socket opening): No known difference
Articular surface area: Greater in males
Acetabular development: Earlier in females
Range of Motion
Greater in females:
Hip flexion
Hip internal rotation at 90° flexion
Greater in males:
Hip extension
Hip external rotation at 90° flexion

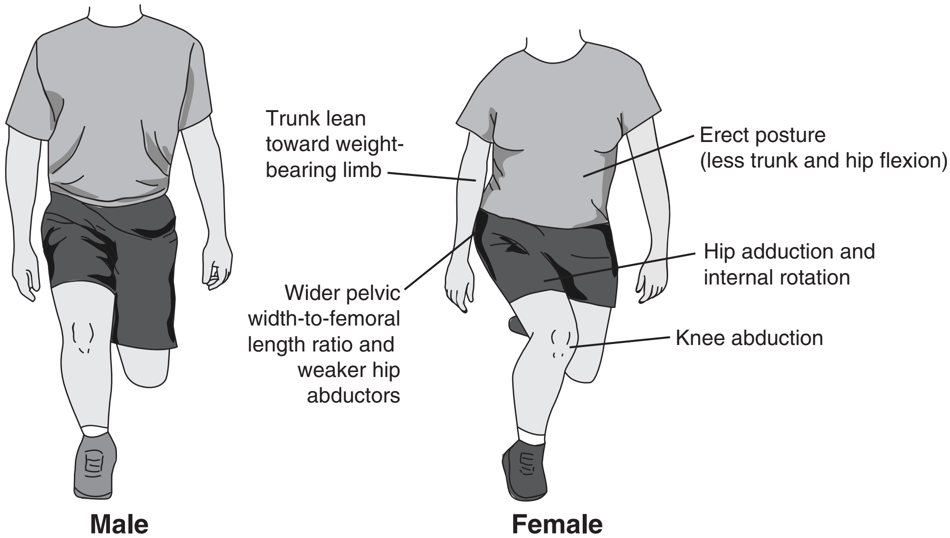

FIGURE 7.9: Movement pattern implications of common sex differences of pelvic anatomy and hip strength.

TABLE 7.2: Sex Differences of Strength and Movement Patterns Around the Hip

Compared to males, females have:
Weaker hip abduction Lower hamstring stiffness Higher tolerance to hamstring stretch
During squat exercises, compared to males, females have:
Greater hip adduction and internal rotation Greater knee abduction Less trunk flexion Smaller hip extensor moments Increased stress on knee joint
During side-step cutting:
Females have: Pelvic rotation and trunk-lean toward weight-bearing limb Males have: Pelvic rotation and trunk-lean toward non-weight-bearing limb

females tend to have a worse prognosis (33,34), possibly because the female proximal femoral physis closes at a younger age, which leaves a shorter potential period for remodeling of the femoral head (31). In contrast, the male sex is associated with more severe intra-articular hip disease in people with Perthes-*like* hip deformities. Perthes-like hip deformities include other causes of vascular insult to the proximal femur during skeletal development such as infection, trauma, and complications of treatment for hip dysplasia (35).

Since the pathophysiology of LCPD is unknown, research has focused on studying potential risk factors and associations between LCPD and other conditions. It is hypothesized that children who are more hyperactive have an increased frequency of microtrauma and stress to the vascular supply to the hip joint. Supporting this theory, people with LCPD have an increased prevalence of attention deficit hyperactivity disorder (ADHD) and a higher risk than the general population for hospitalization due to other lower extremity injuries. Both of these associations are stronger in females (30,36), even though the actual prevalence of LCPD, ADHD, and injuries requiring hospitalizations is higher in young males.

Slipped Capital Femoral Epiphysis

Similar to LCPD, SCFE is a condition affecting prepubertal children. It is the displacement between the femoral head and femoral neck at the growth plate, in which the femoral head remains in the acetabulum but the rest of the femur shifts anteriorly and rotates externally. It is well established to be most common in obese children around the time of puberty (37).

SCFE is about 1.5 times more common in males than females in the United States (38). This male predominance is present in Mexico, Japan, and Korea as well. The trend was not reproduced in the Netherlands, but this is likely because over the time period of the study, the incidence of SCFE in females rose (37,39–41). Unfortunately, SCFE is occurring more frequently and at younger ages worldwide, and these trends correlate with the rising rate of childhood obesity in each of the countries studied.

Femoroacetabular Impingement

Femoroacetabular impingement (FAI) is a term that describes a hip structural aberrancy measured by radiographic imaging. There is some confusion in nomenclature because the term is also often used to describe a bony condition associated with symptoms, even though 30% of an *asymptomatic* population has been found to have FAI on radiographs (4). In people with hip pain and FAI on their radiographs, their symptoms are thought to be related to contact between the proximal femur and the acetabular rim during hip movement and loading. Over time, this can lead to acetabular labral tears, femoral and acetabular chondrosis, and OA. There are three structural subtypes of FAI: cam, pincer, and mixed (see Figure 7.10).

Cam-Type FAI

Cam-type FAI describes the presence of extra bone along the femoral head-neck contour. Commonly called a “pistol grip” deformity, cam-type FAI is most commonly characterized radiographically by a large alpha angle. As mentioned earlier in the chapter, there is not yet a clear alpha angle cutoff value to definitively diagnose cam-type FAI by imaging, but a consensus of experts considers an alpha angle of greater than 60° to define FAI (4). Cam lesions are most common along the anterosuperior plane of the femur, and higher alpha angles directly correlate to increased risk of symptomatic FAI and subsequent cartilage damage (6).

Symptomatic cam-type FAI is most common in young, active males (42–44). It is not clear why there is a gender disparity. One theory is that cam deformities develop from participating in high-impact sports during adolescence because this kind of activity exposes the femur to intense loading during skeletal development (45–47). In the past,

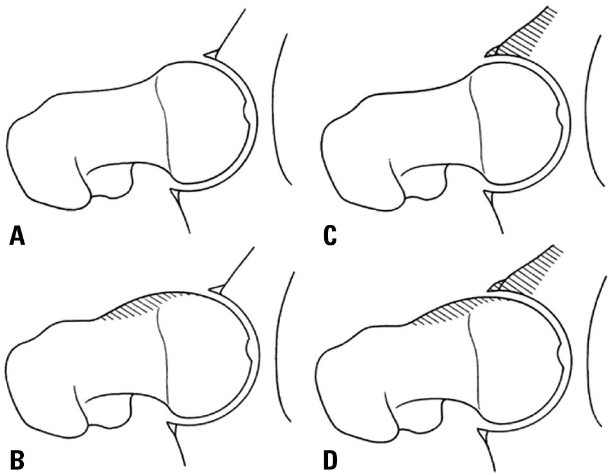

FIGURE 7.10: Types of femoroacetabular impingement. (A) Normal hip without FAI. (B) Cam-type FAI describes extra bone along the femoral head-neck contour. (C) Pincer-type FAI describes overcoverage of the femoral head by the acetabulum. (D) Mixed-type FAI describes the coexistence of both cam and pincer abnormalities in the same hip.

Source: From Ref. (128). Lavigne M, Parvizi J, Beck M, et al. Anterior Femoroacetabular Impingement: Part I. Techniques of Joint Preserving Surgery. *Clin Orthop Relat Res*. 2004;418:61–66.

boys have been more involved in these high-impact sports, which would be consistent with the higher prevalence of cam-type FAI in males. However, this participation gap is narrowing, so if the hypothesis is correct, the gender difference in cam-type FAI should narrow, too. Another theory to explain the gender disparity is that cam deformities are subclinical slipped capital femoral epiphyses, which are also more common in boys. Since SCFE is more common in sedentary, overweight children as opposed to active youth involved in high-impact sports, this theory somewhat contradicts the first (6).

Pincer-Type FAI

Pincer-type FAI describes overcoverage of the femoral head by the acetabulum. It is commonly defined radiographically by a lateral CEA of at least 40° or a Tönnis angle less than 0° (48). Pincer-type FAI is more common in middle-aged females. Again, the etiology of this gender discrepancy is unknown. In fact pincer-type FAI is commonly associated with acetabular retroversion, and as mentioned previously, acetabular retroversion is more common in males even though they have a lower prevalence of pincer-type FAI (13).

Mixed-Type FAI

Although it is thought that cam and pincer deformities have different etiologies, they commonly exist simultaneously in the same hip. This is called mixed-type FAI and is more common in males (49,50). Reporting of prevalence and outcomes of people with mixed deformity is evolving. In a 2009 study by Allen et al., 42% of hips with cam deformities also had a pincer deformity (51). In a study by Byrd and Jones in 2011, there were 159 cam, 10 pincer, and 31 combined lesions (52).

Sex Differences in Symptomatic FAI Clinical Presentation

Just as asymptomatic females may have smaller "normal" alpha angles than males, females with symptomatic FAI tend to present with pain and labral tears associated with smaller alpha angles as compared to males with symptomatic FAI (49,53). Hetsroni et al. theorize that females' increased sensitivity to develop symptoms associated with smaller alpha angles may be due either to weaker hip stabilizing muscles, leading to increased force through the hip joint, or to increased soft tissue laxity and subsequent greater ROM, allowing frequent contact of the proximal femur and the acetabulum (53). Another theory is based on the observation that pincer-type FAI causes more direct damage to the labrum compared to cam-type FAI, which tends to cause more separation between the labrum and articular cartilage. Because the labrum is richly innervated by nociceptive fibers, pain is likely to be more severe after direct damage to the labrum. Pincer-type FAI is more common in women and may be a more painful form of FAI. (54).

Despite females' increased predilection for pain and labral pathology associated with small cam lesions, males tend to have more severe structural abnormalities at the time of presentation. This includes more severe cam lesions, a higher frequency of labral tears, and more advanced acetabular hyaline cartilage lesions (49,55,56). Males are also more likely to develop bilateral symptomatic FAI (57). Advanced intra-articular cartilage injury and degeneration is a poor prognostic factor for satisfactory joint preservation surgery outcomes, so as a result this gender difference in injury and degenerative severity at presentation is important to consider when counseling patients regarding treatment options.

Interestingly, though males tend to have more severe structural abnormalities, FAI has a larger impact on quality of life in females (58). In patients who decide to proceed with hip preservation surgery, postoperative quality of life measures are still lower in females than males (59). This draws further attention to the need for prospective studies related to gender-specific differences and needs in order to improve outcomes.

Developmental Dysplasia of the Hip

Like FAI, developmental dysplasia of the hip (DDH) is a hip deformity associated with intra-articular pain and also is a known risk factor for the development of OA. However, in contrast to the *excessive* contact between the femur and acetabulum as in FAI, DDH is characterized by *inadequate* femoral head coverage by the acetabulum. DDH is commonly defined radiographically as a lateral CEA less than 25° or, in severe cases, less than 20°.

DDH is more common in females than males, regardless of patients' age at presentation (60). Diagnosis of DDH is often made in infancy during routine screening exams. In this population, females have a 2.5- to 4-fold increased risk of DDH (61–63). Sometimes, though, DDH is not diagnosed until a person develops hip pain in adolescence or early adulthood. In this group of older patients, the female predominance is present but less pronounced (60). While risk factors for DDH have been identified, the exact etiology remains unclear. In light of this difference in gender demographics based on patients' age at presentation, it is possible that DDH diagnosed in young adults is a distinct condition that develops after infancy, rather than a milder version of the condition diagnosed with newborn screening exams (60,64).

Aside from research proving the female predominance of DDH, there have been few gender-focused studies on this condition. From the scattered research that has been done, it seems there is no gender difference in clinical response to the Pavlik harness in infants (65) or to hip preservation surgery—namely, eccentric rotational acetabular osteotomy—in young adults (66). There is, however, a stronger association between DDH and subsequent degenerative joint-space narrowing in females than males (67). Females with DDH also have a higher incidence than the general population of spina bifida occulta, but this association is not seen in males (68). The reason for this gender difference is unknown, but it could help identify at-risk newborns who would benefit from hip screening programs through adolescence.

Acetabular Labral Tear

The acetabular labrum is a ring of cartilage around the outer rim of the bony acetabulum. It serves to deepen the hip socket and provide increased area of contact between the femoral head and hip socket. Even in hips with normal bony structure the labrum can become damaged from repetitive mechanical stress and trauma, but abnormal hip structure such as FAI and DDH deformities further expose the labrum to increased load and risk for tear (69). Labral tears are clinically important because they can be painful, limit patients' desired activity, and predispose to degenerative OA.

The sex differences in patients with acetabular labral tears mirror those seen in people with normal hips and with FAI: Males have larger alpha angles and generally less acetabular anteversion (4). There is no gender difference in CEA (53). Most labral tears occur in the setting of hip deformity. When presenting for surgery for labral tears, males tend to have larger tears (70) but females require a longer recovery period (71). Again, it is important to be aware of these differences in order to optimally manage and counsel patients. Specifically, females with hip pain and only mild cam-type FAI deformities on imaging still warrant suspicion and evaluation for labral tears, and recovery time estimates after FAI surgery can be tailored by gender.

There are also special patient populations who are at increased risk of acetabular labral tears and have uneven gender representation. First, labral tears can occur during pregnancy and labor (72). Physiological increased ligamentous laxity and altered cartilage matrix may play a role in peripartum labral tears (73), and laboring positions involving extreme hip flexion and internal rotation also increase the risk for acute tears. Women who have epidural anesthesia will not experience the pain right away and may only notice hip dysfunction as they become more active again. Second, dancers have a high prevalence of labral tears. In this population, especially at the professional level, labral tears appear to more often be the result of repetitive joint stress at extreme ranges of motion in structurally normal hips, rather than the result of bony deformity such as FAI or DDH. Also, labral tears in this population occur more frequently in the superior and posterosuperior region, rather than in the anterior and anterosuperior region as in the general population (74) (Table 7.3).

INTRA-ARTICULAR DISEASE—OSTEOARTHRITIS

Epidemiology

The entities of LCPD, SCFE, FAI, DDH, and acetabular labral tears described here are considered prearthritic hip diseases because they all increase a person's risk for developing degenerative hip OA. Not surprisingly, since there are sex differences in the conditions that predispose to hip

TABLE 7.3: Sex Differences in Pre-Arthritic Hip Disorders

Legg-Calvé-Perthes Disease (LCPD)
More common in males. Tends to be more severe in females.
Slipped Capital Femoral Epiphysis (SCFE)
More common in males.
Femoroacetabular Impingement (FAI)
Cam-type FAI: More common in young, active males. Pincer-type FAI: More common in middle-aged females. Mixed-type FAI: More common in males. Males have increased severity of structural lesions. Females have lower quality-of-life ratings, despite more subtle structural abnormalities.
Developmental Dysplasia of the Hip (DDH)
More common in females. Stronger association between DDH and joint-space narrowing in females.
Acetabular Labral Tears
Males have less acetabular anteversion. Females have smaller alpha angles and more subtle cam-type deformities. When presenting for surgery: Males tend to have larger tears. Females tend to require longer recovery time. Special populations: Females can develop tears during pregnancy and labor. Dancers can develop labral tears despite normal bony anatomy. Their tears are in a different location than the general population.

OA, there are also sex-specific differences in the prevalence and manifestations of hip OA.

While study results have occasionally differed, possibly due to the inclusion of slightly different patient populations, most research suggests that hip OA is more common in females than males (50,75,76). The gender gap widens with age until people are about 70 to 75 years old, and then it narrows again (77). The female predominance is confirmed to be present in physically active populations (78), but it narrows in the obese population because obesity is associated with a minimally increased prevalence of hip OA in males but not females (79). Interestingly, in people with hip OA, the prevalence of coexisting prearthritic hip malformations is significantly higher in males than females, suggesting females may be at higher risk for idiopathic primary OA (50,80).

Among people who present for medical care for hip OA, females also tend to be older and have increased pain and disability compared to males (75,81). In addition, a greater proportion of females has been found to have rapid structural progression (82), and it follows that more total hip arthroplasties (THAs) to treat symptomatic hip OA are performed in females (75,82).

Response to Treatment

Because the severity of symptoms related to hip OA are usually greater in females at the time of presentation, it is not surprising that females have a poorer response to operative management for hip OA. Following THA and revision THA, females report lower quality-of-life measures as compared to males (83,84). However, THA results in greater *improvement* in quality-of-life measures for females compared to males (85).

Surgical complication rates also differ between the sexes, but specific effects vary somewhat based on the exact surgical procedure and prosthesis used. In general, for primary THA, males have a higher revision rate due to aseptic loosening and infection (86), but obese females have a greater risk of infection than obese males (87). Females seem to have a higher overall rate of requiring revision arthroplasty (88). One study suggests this may be more related to the size of the femoral component rather than to sex itself (89). There has been consideration of developing sex-specific THA components to improve outcomes, but multiple studies support that the variety of implant systems currently available provides adequate customizability for both sexes (90,91).

Potential Contributors to the Sex Differences in the Prevalence of Hip OA

While not yet definitively proven, structural and hormonal sex differences likely play a role in the increased prevalence of hip OA in females as compared to males. First, because of the sex-specific structural differences of the normal hip joint (as described earlier in the chapter), mathematical modeling shows females have higher peak contact pressure, abductor force, and joint contact force within the hip (92). This increased exposure to loading could contribute to the increased prevalence of hip OA in females.

Second, hormonal factors likely influence risk of developing hip OA. Bone and articular cartilage have estrogen receptors, and it has been noted that asymptomatic males have a relatively unchanged joint space width throughout life, whereas after menopause asymptomatic females have a progressive decline in joint space width (93,94). Additionally, the incidence of THA in elderly females varies based on differences in concentrations of patients' innate sex hormones (95), and multiple studies have shown that long-term use of hormone replacement therapy in postmenopausal females provides a protective effect against hip OA (96) (Table 7.4).

EXTRA-ARTICULAR CONDITIONS

Dysfunction associated with extra-articular soft tissue structures of the hip can also be associated with hip pain. There are documented sex differences in two of these hip disorders that can be seen in athletes.

Greater Trochanteric Pain Syndrome

Greater trochanteric pain syndrome (GTPS) is a term used to describe persistent pain over the greater trochanter. Previously called "greater trochanteric bursitis," GTPS was renamed because it is not always associated with inflammation, and it is oftentimes not due to pathology of a bursa. Since GTPS simply describes a pain pattern, there are many potential underlying movement impairments and structural sources contributing to pain. Among the most common are gluteus medius tendinitis, tendinopathy, and muscle tears (97).

GTPS is up to five times more common in females (98–100). Similar to many other conditions described in this chapter, the reason for the gender discrepancy is unknown but is hypothesized to be related to the difference in pelvic structure. The greater pelvic width-to-femoral length ratio in females alters the direction of force created by the gluteal muscles and the iliotibial band, which may result in more friction of the soft tissues overlying the greater trochanter.

TABLE 7.4: Sex Differences in Hip Osteoarthritis (OA)

Males with hip OA have an increased prevalence of concomitant prearthritic structural malformations.
Hip OA is more common in females.
Females tend to present later in the disease process and with more severe pain and disability.
After THA, females have more improvement but still report lower quality of life compared to males.
Surgical complication rates from THA differ between sexes.
Structural and hormonal differences likely play a role in sex differences in hip OA.

THA, total hip arthroplasty.

Snapping Hip

Coxa saltans, more commonly referred to as "snapping hip," describes any reproducible palpable or auditory snapping around the hip joint during movements. Snapping hip can be asymptomatic in the general population, but it is more common and more frequently symptomatic in athletes who routinely use full hip ROM.

Extra-articular snapping hip is divided into two subcategories. *External* snapping hip refers to snapping over the lateral aspect of the hip and is usually due to rubbing of the iliotibial band or gluteus maximus muscle over the greater trochanter. There is not a documented sex difference in this condition (101).

Internal snapping hip occurs over the anterior aspect of the hip during hip flexion and is attributed to sudden movement of the iliopsoas tendon over structures such as the femoral head, iliopectineal ridge, lesser trochanter, and paralabral cysts. There is a high rate of co-occurrence of internal snapping hip with acetabular labral tears, and it is possible that extra-articular impingement of the iliopsoas tendon contributes to tears in the labrum (102). In contrast to external snapping hip, in several case series internal snapping hip is described repeatedly more often in females (103–106). It is common in athletes who perform repetitive hip flexion, external rotation, and abduction to extreme ranges of motion, so not surprisingly it is extremely common in elite ballet dancers (101,107) (Table 7.5).

BONE DISORDERS

Femoral Neck Stress Fracture

Sex differences of stress fractures are discussed in Chapter 12, but it is worthwhile to mention a few differences specifically relevant to stress fractures at the femoral neck. Femoral neck stress fractures (FNSFs) are relatively rare and account for less than 10% of all stress fractures (108,109). However, they cause disproportionate morbidity due to their high risk for femoral nonunion and avascular necrosis, both of which can lead to long-term pain and disability.

TABLE 7.5: Sex Differences in Extra-Articular Hip Conditions

GTPS is more common in females.
External snapping hip does not have a documented sex difference.
Internal snapping hip is more common in females.

GTPS, greater trochanteric pain syndrome.

Classically, people with FNSFs describe insidious onset, aching groin pain that increases with exercise and is relieved with rest. FNSFs usually occur in skeletally mature military personnel and distance runners, and they often occur after a sudden, significant increase in training intensity. Interestingly, people who develop FNSFs also have an increased prevalence of FAI (110).

Females have a higher incidence of FNSFs (111–114). Of course, the female athlete triad likely plays an important role in this gender difference, and it has been found that the number of menstrual cycles in the previous year is predictive of femoral neck bone mineral density (115). However, especially in military personnel, there is another potential contributor to the female predominance: In most training protocols, all recruits start with the same exercise regimen and with the same carrying load, even though this results in a proportionately greater increase in musculoskeletal stress to most females due to their smaller stature (111). This larger sudden increase in training intensity may put female recruits at relatively higher risk for FNSFs. At one U.S. Army Basic Training center, when fitness programs were tailored to recruits' baseline strength levels, the incidence of FNSFs was subsequently halved in both genders (109) (Table 7.6).

TABLE 7.6: Sex Differences in Bony Hip Disorders

Femoral neck stress fractures are more common in females.

HIP-SPINE SYNDROME

Sex differences in musculoskeletal disorders of the spine and pelvis are discussed in other chapters. However, it is important to recognize that because the hip and lumbopelvic region are linked closely in the kinetic chain, movements of the hip affect the lumbopelvic region, and vice versa. Pathology of one of these regions can result in secondary degeneration of the other region due to compensatory changes in movement patterns. Furthermore, people with degenerative changes of the hip on radiographs were found to more likely complain of low back pain (LBP) (116). Both of these examples are included in Offierski and MacNab's description of the "hip-spine syndrome" (117). Gender-specific correlations of this disorder have not been prospectively studied. However, in patients treated for LBP within 2 years preceding or following THA, women were found to have worse pain and function as compared to men (118).

Effect of Lumbopelvic Posture on Femoral Head Coverage

First, while equally applicable to both genders, it is important to recognize that lumbopelvic posture can affect the interaction between the femoral head and acetabulum.

As shown in Figure 7.11, standing in lumbar hyperlordosis with exaggerated anterior pelvic tilt rotates the anterior edge of the acetabular rim further anterior and inferior. This functionally increases the anterior acetabular coverage

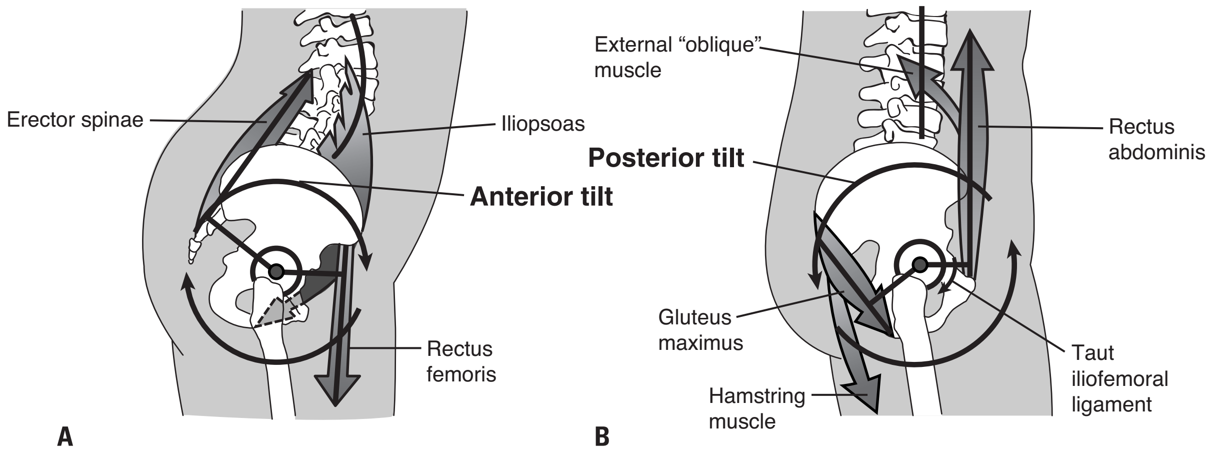

FIGURE 7.11: Effect of lumbopelvic posture on hip impingement and hip instability. (A) Lordotic posture and anterior pelvic tilt functionally increase anterior acetabular coverage of the femoral head. In people with bony femoroacetabular impingement, this posture increases the likelihood of contact between the femur and acetabulum. (B) Flat-backed posture and posterior pelvic tilt functionally decrease anterior acetabular coverage of the femoral head. In people with hip dysplasia, this posture further decreases stability of the hip.

of the femoral head, and so in people with FAI, hyperlordotic posture increases the likelihood of contact between the femur and acetabulum.

On the other hand, standing in a flat-backed posture with exaggerated posterior pelvic tilt functionally retracts the anterior edge of the acetabular rim. This decreases anterior coverage of the femoral head by the acetabulum, and in people with hip dysplasia, this posture further decreases stability of the hip. In females with hip dysplasia and increased soft tissue laxity, this flat-backed posture puts them at especially high risk for joint instability. Posture assessments as they relate to hip disorders need further study.

Lumbopelvic Rotation During Hip Rotation

Because net lumbopelvic rotation is the sum of rotation around the spine and the hips, people with decreased hip ROM require more lumbar spine ROM to achieve a given amount of total rotation. As a result, people with decreased hip ROM put more torsional stress through their lumbar spines and have a higher incidence of LBP (119).

A series of studies has shown that males are likely at higher risk for LBP related to poor hip ROM than females. Van Dillen and colleagues found that when performing hip medial rotation, men with LBP have greater and earlier involvement of lumbopelvic rotation, as compared to females with LBP. Males are also more likely to report back pain during this maneuver (120). These gender trends are found with hip lateral rotation as well (121). Therefore, in rotation-related sports such as tennis and golf, males rotate through the lumbopelvic regions at a faster rate than females. As a result, they may be at higher risk for LBP during these activities, especially if they have restricted hip motion at baseline such as from FAI (122). Fortunately, with physical therapy directed at modifying this excessive motion, pain improves and both genders can decrease and delay lumbopelvic motion during hip medial rotation. However, males still have greater and earlier lumbopelvic motion than females posttreatment (123).

TABLE 7.7: Sex Differences in the Hip-Spine Syndrome

Males have greater, earlier, and more frequently symptomatic lumbopelvic rotation during hip rotation.
Side-to-side asymmetry of hip muscle strength is associated with the development of low back pain in female athletes but not in male athletes.

Association Between Asymmetric Hip Strength and Low Back Pain

Just as hip ROM affects a person's risk for LBP, so can hip *strength*. Nadler et al. studied a cohort of collegiate athletes and found that females with recent LBP or lower extremity injury had a significant side-to-side difference in hip extension strength. This asymmetry was not present in asymptomatic females, nor in males (regardless of the presence or absence of symptoms) (124). In fact, the percent difference between side-to-side hip extensor and abductor strength might even be predictive for the development of LBP in females but not in males (125,126). These findings suggest that hip muscle imbalance predisposes females but not males to LBP and injury. Perhaps this is because males tend to have adequate strength of their hip stabilizing muscles even on their nondominant side, or perhaps the increased stiffness of their soft tissues helps prevent a predisposition for LBP despite strength asymmetry (Table 7.7).

CONCLUSION

Evidence presented in this chapter demonstrates that imaging, surgery, and laboratory-based advancements in recent decades have exponentially enhanced our understanding of normal and pathologic hip structure and function. Through these endeavors, sex differences have been found in hip bony structure, muscle properties, and movement patterns, and these differences likely contribute to the uneven sex-specific prevalence and outcomes of many intra- and extra-articular hip disorders, in addition to disorders affecting both the hip and spine. Despite recent progress, further research is needed in order to best serve our patients and optimally diagnose, counsel, and treat both males and females with hip pain and disorders.

Summary of Sex Differences in the Prevalence of Hip Disorders

Musculoskeletal Complaint	Sex With Higher Prevalence
Legg-Calvé-Perthes disease	Males (31,32)
Slipped capital femoral epiphysis	Males (37–41)
Femoroacetabular impingement, cam-type	Males (42–44)
Femoroacetabular impingement, pincer-type	Females (13)
Femoroacetabular impingement, mixed-type	Males (49,50)
Developmental dysplasia of the hip	Females (60–63)
Hip osteoarthritis	Females (50,75,76)
Greater trochanteric pain syndrome	Females (98–100)
Internal snapping hip	Females (103–106)
Femoral neck stress fracture	Females (111–114)

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8

NONTRAUMATIC KNEE INJURIES

Cindy Y. Lin and Kelvin T. Chew

INTRODUCTION

While sex differences in traumatic knee injuries are more commonly described in the literature, a subset of nontraumatic knee injuries also have demonstrated sex differences that are important to note in the athletic population. Patellofemoral pain syndrome (PFPS), iliotibial band syndrome (ITBS) and pes anserine tendinitis bursitis (PATB) are common nontraumatic knee injuries typically related to overuse. Gender differences have been described in their incidence and risk factors (see the table in the Conclusion section). These differences should be considered in the evaluation and treatment of common nontraumatic knee injuries in a sports medicine population.

Patellofemoral Pain Syndrome

PFPS is anterior knee pain characterized by retropatellar or peripatellar discomfort (1). Symptoms are typically provoked when the patellofemoral joint is loaded, such as in stair climbing, running, cycling, squatting, or rising from a seated position.

Epidemiology

Several studies report a higher incidence of PFPS in female than in male athletes, while other studies report a similar incidence in both sexes, such as in military populations (2–8). In a retrospective study of over 4,000 runners, PFPS accounted for more injuries in women than in men (2). PFPS comprised 19.6% of all injuries in females compared to 7.4% of males presenting to an academic sports medicine center (3). In a retrospective review, Taunton et al. reported a PFPS prevalence approximately 1.5 times greater in females than in males (4). A prospective study of 810 adolescent basketball players also found that patellofemoral dysfunction was significantly more common in females than in males (7.3% versus 1.2%; $P < .05$) (5).

PFPS prevalence and incidence has also been examined in military populations where the literature is mixed. In a prospective study of United States Naval Academy enrollees, there was no statistically significant sex difference in PFPS rates on enrollment; however, females were 2.23 times more likely to develop PFPS (95% confidence interval [CI]: 1.19–4.20) compared with males over 2.5 years of follow-up (6). In contrast, a study of 97,000 Israeli defense force recruits found that males had a 4.56% prevalence of anterior knee pain compared to 2.39% in females (7). Almeida et al. reported that female military recruits reported more musculoskeletal injuries than males (relative risk [RR]: 1.72, 95% CI: 1.29–2.30) (8). Furthermore, PFPS was the most commonly reported injury affecting 10% of female recruits (8). However, when reported and unreported musculoskeletal injuries were combined, total injury rates were similar between the groups, indicating possible sex differences in symptom reporting (8).

Risk Factors

PFPS pathogenesis is multifactorial in origin and relates to several intrinsic and extrinsic risk factors (1). Intrinsic risk factors include anatomic, biomechanical, and hormonal factors and abnormal neuromuscular control, while extrinsic risk factors include training and environmental conditions.

Sex differences in PFPS incidence have been evaluated with respect to proximal and distal kinetic chain factors that contribute to dynamic maltracking of the patellofemoral joint. Abnormal or lateral patellar tracking

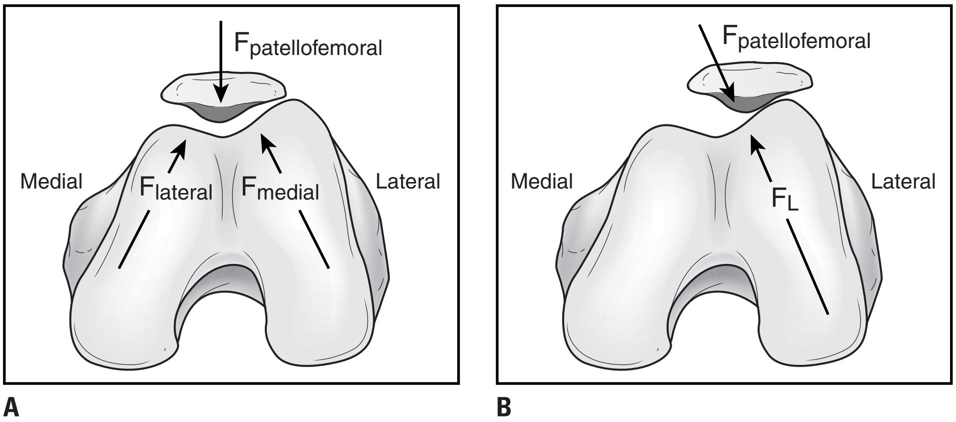

FIGURE 8.1: Diagram shows distribution of patellofemoral compressive forces with normal patellar tracking (A) and with abnormal, lateral patellar tracking (B). A laterally tracking patella may result in a decreased patellofemoral contact area, causing the same amount of force applied over a more focal region.

results in decreased patellofemoral contact area and causes the same amount of patellofemoral force to be applied over a smaller area (see Figure 8.1).

Historically, the wider pelvis in women has been associated with a larger quadriceps femoris muscle angle (Q angle), which is defined as the acute angle formed by the vector for the combined pull of the quadriceps femoris muscle and the patellar tendon (9). The resultant abnormal patellar tracking is believed to play a role in PFPS development. Horton and Hall reported a mean Q angle for women of 15.8 ± 45° and for men of 11.2 ± 30° (10). Several studies have cited a Q angle greater than 20° as abnormal (11,12). The larger Q angle of women has been associated with greater dynamic lateral patellar shift during quadriceps contraction (10), thereby making them more prone to developing PFPS.

However, recent studies suggest that a greater Q angle as well as other anatomic factors may not be as significant of risk factors as previously thought for PFPS (13–15). Contrary to conventional belief, a study by Park and Stefanyshyn found a negative correlation between Q angle and the magnitude of peak knee abduction moment ($P = .005$) (15). Further substantiating this discovery was an MRI study that found that increased Q angle correlates with medial rather than lateral patellar displacement and tilt (13). In a study of women with PFPS compared to controls, no significant difference was identified between the patients' symptomatic versus nonsymptomatic knee, nor between the patients' and controls' Q angle and leg-heel alignment measurements (16). Another prospective study by Barber Foss et al. found no relationship between relative body composition and relative body mass to height ratio and the development of PFPS in middle school-age female basketball players (17).

Muscle imbalance in terms of strength and flexibility differences have also been described inconsistently as a risk factor for PFPS in females (1). The greater flexibility and generalized ligamentous laxity of women, as well as the higher incidence of benign hypermobility syndrome, is a risk factor for patellar hypermobility (18–21). Patellar hypermobility may lead to PFPS due to the increased tendency for patellar maltracking.

While local factors that influence patellofemoral biomechanics such as patellar hypermobility, lateral patellar tilt, and vastus medialis strength have been well described in the literature (22), recent studies have highlighted the importance of proximal kinetic chain factors.

Hip strength deficits are another identified risk factor for PFPS in women. When hip isometric strength was measured using a handheld dynamometer in females with and without PFPS, the hip adductor/abductor isometric strength ratio in the PFPS group was 23% higher than the control group ($P = .01$), suggesting a tendency towards increased dynamic knee valgus and patellofemoral loading in this group (23). Lower hip abduction strength, lower knee extension peak torque, and less hip external rotation strength have also been reported in females with PFPS compared to controls (24). Females with PFPS had less gluteus medius muscle activation ($P = .017$) during the single-leg squat compared to controls (25). Prins and van der Wurff also found that females with PFPS had decreased hip abduction, external rotation, and extension strength compared to controls (26). However, a study by Thijs et al. found no significant difference in baseline isometric strength of the hip flexor, extensor, abductor, adductor, and external and internal rotator muscles between healthy female novice runners who did and did not develop PFPS (27). Hip strength deficits in men with PFPS have not been identified consistently (28). While some studies may disagree, the current body of evidence suggests that evaluating and addressing proximal kinetic chain deficits in hip muscle strength is important in the rehabilitation of PFPS in males and females.

Sex differences in lower limb dynamic alignment, strength, and central motor planning may contribute to altered neuromuscular control patterns during activities such as single-leg squat, running, and jump landings. Reduced lower limb frontal plane neuromuscular control has been described in female athletes (29). Females with PFPS had more hip internal rotation ($P<.05$) during the single-leg squat compared to controls (30). In adolescent girls, elevated (greater than 15 Nm) knee abduction load during jump landing was associated with a greater likelihood of developing PFPS (31). A prospective study of male military recruits found that those who developed PFPS had significant delay of vastus medialis obliquus electromyographic activity onset compared with controls ($P=.023$), even before basic military training (32). This finding suggests that altered quadriceps muscle activation timing may be a risk factor for PFPS in men (32).

Running gait mechanic differences have been evaluated as a possible risk factor for PFPS. Females with PFPS demonstrated greater hip internal rotation ($P=.04$) compared to controls when ground reaction forces were greatest during running, suggesting that altered transverse plane hip kinematics may be involved in the etiology or exacerbation of PFPS (33). When running mechanics were compared, males with PFPS ran and squatted with greater peak knee adduction and demonstrated a greater peak knee external adduction moment compared with healthy male controls. In addition, males with PFPS ran and squatted with less peak hip adduction and greater peak knee adduction compared with females with PFPS (34).

The role of menstrual phase and hormonal factors in the development of PFPS is inconclusive, although preliminary studies suggest a possible link (35,36). Menstrual cycle fluctuations in female sex hormones may influence ligament mechanical properties and increased knee laxity has been related to ACL injuries (35). Tenan et al. found that vastus medialis and vastus medialis oblique initial firing rates differ across the menstrual cycle during an isometric ramp knee extension exercise (36). However, whether these hormonal factors relate to PFPS needs further investigation.

Potential extrinsic risk factors that might contribute to sex differences in PFPS include training volume, intensity, type, and environment. As PFPS pain is typically associated with increased activities or athletic training, some studies suggest that the cause of PFPS is overloading and overuse of the patellofemoral joint, rather than anatomic or biomechanical malalignment (16). Abrupt increases in running mileage have been identified as a risk factor for PFPS (37). Early specialization in a single sport also increases the relative risk of PFPS incidence by 1.5 fold (95% CI: 1.0–2.2; $P=.038$) in adolescent females (38). These studies highlight the importance of identifying training factors during history taking in both sexes when PFPS is suspected.

Clinical Evaluation

PFPS is a clinical diagnosis based on history and physical exam. However, no single physical exam maneuver reliably confirms PFPS, and the reliability of individual tests for PFPS is generally low (39). Sex differences in the physical exam for PFPS have not been well described in the literature. The history taking should include evaluation of common intrinsic and extrinsic risk factors described previously. The physical exam of any patient with suspected PFPS should include evaluation of anatomic factors as well as static and dynamic alignment of the lower limb kinetic chain. On standing examination, it is helpful to evaluate for abnormal foot position such as pes planus. Navicular drop, a measure of foot pronation, has been identified as a risk factor for running-related injuries in novice female but not in novice male runners (40).

Dynamic patellar tracking and stability is best evaluated by a functional test such as single-leg partial squat (see Figure 8.2), step up or step down, single-leg sit to stand from a chair, or a sports-specific movement that is associated with symptom onset. Performing a functional, weight-bearing activity test allows for a visual assessment of patellar kinematics over a range of knee flexion angles (41). A running gait evaluation via a video gait analysis may be helpful to identify factors related to running mechanics. Abnormal biomechanics at the hip, knee, foot, or ankle joint should be identified and addressed in the rehabilitation of PFPS as these factors can contribute to dynamic knee valgus. If generalized ligamentous laxity is suspected, the Beighton score evaluation is useful. One should also assess for tightness of the iliotibial band and quadriceps and hip abductor strength (39).

Preparticipation screening may be useful for identifying athletes at risk for PFPS and other common musculoskeletal injuries. In a preparticipation screening study of middle and high school female basketball players, 26.6% had anterior knee pain (42). Risk factors, prior injuries,

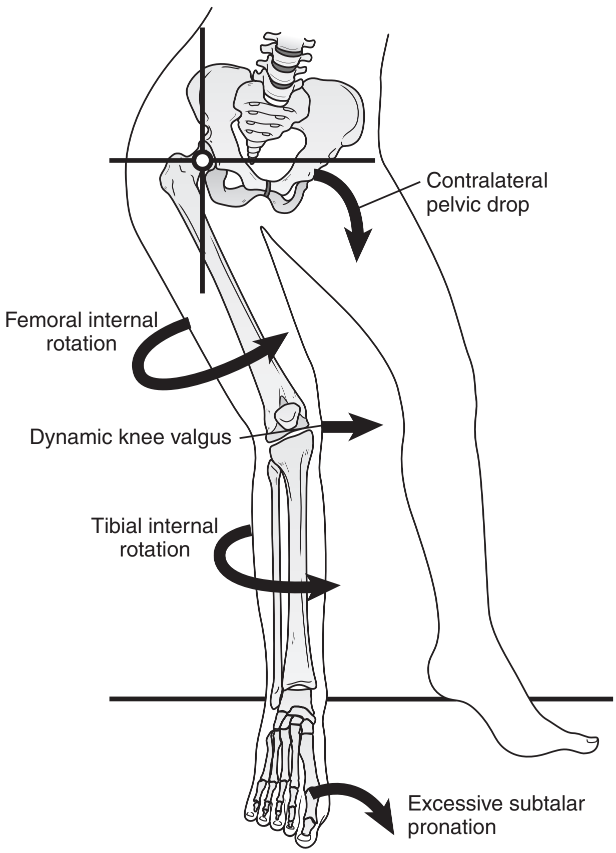

FIGURE 8.2: Performing a kinetic chain evaluation, during a functional movement such as a single leg partial squat, is an integral component of assessing the causative factors for abnormal dynamic knee valgus. Abnormal segmental alignment or biomechanics at the hip, knee, foot, and ankle are all potential contributing factors that should be identified and addressed in the rehabilitation of patellofemoral pain syndrome (PFPS).

Source: Adapted from Ref. (69). Powers CM. The influence of altered lower-extremity kinematics on patellofemoral joint dysfunction: a theoretical perspective. *J Orthop Sports Phys Ther*. 2003;33(11):639-646.

muscle imbalance, or functional deficits identified during the screening can be used to guide a prehabilitation injury prevention program (43). Waryasz and McDermott suggest that prehabilitation programs may help prevent PFPS (44). The role of prehabilitation programs in preventing anterior cruciate ligament (ACL) injuries in females is described in Chapter 9 on traumatic injuries of the knee; this framework may be a useful guide for PFPS prevention as dynamic knee valgus, which is a risk factor for ACL injuries, also increases patellofemoral loading.

As PFPS is a clinical diagnosis based on history and physical examination, diagnostic imaging is typically not indicated. Sex differences in the indications for diagnostic imaging in PFPS have not been described. Radiographs may help identify excessive patellar tilt, patellar alta, or trochlear dysplasia, as these factors may predispose patellar instability (45).

Treatment and Rehabilitation

The treatment of PFPS should be individualized based on modifiable risk factors identified during the history and physical examination. Exercise therapy is generally beneficial in reducing pain and improving functional outcomes in PFPS (46,47). Sex differences in PFPS risk factors suggest a potential benefit of sex-specific interventions for individuals with PFPS.

Hip abductor strengthening and neuromuscular control training should be included in the rehabilitation of females with PFPS (31). Knee exercises supplemented by hip posterolateral muscle-strengthening exercises were more effective than knee exercises alone in improving long-term function and reducing pain in sedentary women with PFPS (48). Another study of women with PFPS also found that a functional stabilization program including hip muscle strengthening and lower-limb and trunk movement control exercises was more beneficial in improving pain, physical function, and muscle strength compared to a program of quadriceps-strengthening exercises alone (49).

Pain can limit the ability of a person with PFPS to participate actively in rehabilitation. An exercise progression involving 4 weeks of initial hip strengthening has been found to result in earlier pain reduction than exercises focused on the quadriceps alone in females with PFPS (50). Adolescent females with PFPS have lower mechanical pressure pain thresholds, characterized by localized and distal hyperalgesia, than those with no musculoskeletal pain (51). These findings may have implications for treating PFPS, as both peripheral and central mechanisms may influence pain sensitization in females.

Iliotibial Band Syndrome

ITBS is well described in the active population including runners, cyclists, and military recruits (52–54). ITBS is characterized by lateral knee pain associated with repetitive motion activities. Proposed etiologies include friction of the iliotibial band against the lateral femoral condyle, compression of the fat and connective tissue deep to the iliotibial band, and inflammation of the iliotibial band bursa (53).

Epidemiology

The prevalence and incidence of ITBS have been described in military recruits and runners. A study of running injuries presenting to a sports medicine clinic found that ITBS was the second most common injury following PFPS for both females and males. ITBS was diagnosed in 62% of the females and 38% of the males (4). Among U.S. Marine Corps male and female recruits, there was no significant difference in reported rates of ITBS, at 5.8% and 4.0%, respectively (8).

Risk Factors

Biomechanical differences related to altered hip frontal plane running mechanics have been described between females with and without ITBS. Greater knee internal rotation and increased hip adduction angles may play a role in ITBS pathogenesis (55). Phinyomark et al. found that females with ITBS demonstrated greater hip external rotation during the stance phase of running as compared with males with ITBS (56). Females with ITBS also have a significantly greater peak rearfoot inversion moment, peak knee internal rotation angle, and peak hip adduction angle compared to controls while running (57). However, causality is not clear as Foch and Milner found that of 34 female runners with and without ITBS, both groups had similar peak trunk lateral flexion, peak contralateral pelvic drop, peak hip adduction, and peak external knee adduction moment during running (58).

Male runners with ITBS had significantly less ITB flexibility on Ober test measurement, weaker hip external rotators, greater hip internal rotation, and greater knee adduction than controls on handheld dynamometer testing (59).

The literature is inconclusive as to whether specific patterns of muscle strength deficits exist in runners with ITBS (55). Some studies have suggested a role of gluteus medius and minimus muscle weakness or inhibition during running, resulting in decreased ability to stabilize the pelvis during the single leg support phase (52). A case series of male and female long-distance runners with ITBS found that those with ITBS had weaker hip abduction strength in the affected leg compared with their unaffected leg than healthy long-distance runners. The runners' successful return to their preinjury training program paralleled improvement in hip abductor strength (60). Further sex-specific prospective studies are needed to evaluate the anatomic, biomechanical, strength, and neuromuscular control factors contributing to ITBS.

Sex differences have not been described in extrinsic risk factors in the development of ITBS. It is important in both sexes to evaluate for inciting factors such as changes in training volume, intensity, equipment, and environment. In cyclists, ITBS can be aggravated by improper seat height and training errors (61). In runners, a repetitive knee flexion angle between 20° and 30° can increase iliotibial band friction against the underlying lateral femoral epicondyle (62,63). Thus, jogging or running at slower speeds or running downhill is more likely to aggravate symptoms than sprinting or faster running (63).

Clinical Evaluation

Sex differences have not been described in the physical examination and diagnostic imaging indications for ITBS. The diagnosis of ITBS is made from a thorough history and clinical examination, with an infrequent need for imaging studies.

Treatment and Rehabilitation

Given the lack of consensus regarding sex-specific biomechanical risk factors for ITBS, there are also no clear guidelines regarding the sex-specific rehabilitation of ITBS. Noehren et al. suggested that men with ITBS may benefit from intervention strategies that target neuromuscular control of the hip and knee (59). Phinyomark et al. found that female ITBS runners exhibited significant differences in transverse plane hip kinematic gait patterns while male ITBS runners exhibited significant differences in transverse plane ankle kinematic gait patterns as compared with controls (56). These results suggest that female runners may benefit from focusing on proximal muscle strengthening, whereas male runners should focus on distal muscle strengthening to prevent ITBS (56). Individualized assessment of contributing risk factors and tailored treatment are advised for both sexes in ITBS.

Pes Anserine Tendinopathy Bursitis Syndrome

The pes anserine bursa is located at the anteromedial aspect of the proximal tibia at the tendinous insertion of the sartorius, gracilis, and semi-tendinosus muscles. This bursa can become inflamed due to overuse or from direct trauma. Tendinitis or tendinopathy can occur at the pes anserine site as well.

PATB has been more commonly reported in women than in men, although the exact difference in prevalence rates has not been well-defined (64–67). Risk factors that have been proposed, although controversial, include diabetes mellitus, obesity, and knee osteoarthritis (64,68). The presence of valgus knee deformity alone or in conjunction with ligamentous instability has been cited as a risk factor (64).

There are no published studies specifically describing sex differences in the diagnosis, imaging, treatment, and rehabilitation of PATB syndrome. Risk factors that may be helpful to consider during diagnosis and treatment planning include proximal kinetic chain gluteal weakness and lumbopelvic and core instability. Imaging is typically not necessary in the diagnosis of PATB syndrome. Diagnostic ultrasound, if readily available, may be a useful supplement to the physical exam.

CONCLUSION

While some studies suggest sex differences in the incidence and prevalence of common nontraumatic knee injuries such as PFPS, ITBS, and PATB syndrome, the literature is still inconclusive as to whether diagnosis and rehabilitation of these disorders should be sex specific. Based on the current literature, an individualized assessment taking into consideration possible intrinsic and extrinsic risk factors should be undertaken for each patient, whether male or female, and the rehabilitation and treatment planned accordingly.

Summary of Sex Differences in Prevalence of Nontraumatic Knee Injuries

Musculoskeletal Complaint	Sex With Higher Prevalence
Patellofemoral pain syndrome	Possibly women (2–8)
Iliotibial band syndrome	Inconclusive, similar overall between sexes (4,8)
Pes anserine tendinopathy bursitis syndrome	Women (64–67)

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9

TRAUMATIC KNEE INJURIES

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OVERVIEW

Traumatic knee injuries are a common occurrence in sports medicine and may greatly impact an athlete's health and quality of life. With regard to sex-related differences, perhaps no entity has received as much attention as a tear of the anterior cruciate ligament (ACL). Although evidence is less conclusive, other traumatic knee injuries, including meniscal tear, patellar dislocation, and ligamentous injury involving the lateral collateral ligament (LCL) or medial collateral ligament (MCL), may also show sex differences. A thorough understanding of the manner in which these injuries affect male versus female athletes is imperative in the design of patient-specific surveillance, prevention, and treatment strategies.

ANTERIOR CRUCIATE LIGAMENT INJURY

One of the most discussed and studied knee injuries in sports medicine is a rupture of the ACL. The ACL is one of the four main stabilizing ligaments of the knee along with the posterior cruciate ligament (PCL), MCL, and LCL. The ACL extends from the anterior intercondylar region of the tibia to the posteromedial aspect of the lateral femoral condyle and prevents anterior displacement of the tibia (1). The ACL is essential in control of pivoting and cutting movements, and if ruptured, the stability of the knee is compromised (2). Injury to the ACL occurs through two main mechanisms: either by way of contact or noncontact (3,4).

Regardless of how the injury occurs, an ACL tear is a major injury for most athletes. While most athletes returning to cutting and rotational sports choose to undergo surgical reconstruction, recovery usually ranges from 6 to 12 months even if a nonoperative course is pursued (5). An ACL injury also leads to altered biomechanics, muscle weakness, and reduced functional and academic performance, and may lead to the loss of an entire athletic season (6,7). In fact, after an ACL injury only about half of athletes return to a competitive level of sport (8). Additionally, an athlete's function for many years into the future may also be impacted, as evidence reveals that individuals who tear their ACL have up to an 80% increased risk of developing knee osteoarthritis (OA) 10 to 15 years after injury (6,9–12). From a societal perspective, an ACL rupture is costly, with conservative estimates of surgery and rehabilitation ranging from $17,000 to $25,000 per injury (13,14).

Epidemiology

It has been estimated that 80,000 to 250,000 ACL injuries occur each year in the United States, with more than 50% of injuries occurring in athletes 15 to 25 years of age (15). A study evaluating nationwide incidence of athletes requiring ACL reconstruction found a significant increase between the years 1994 (86,687 injuries or 32.9 injuries per 100,000 person-years) and 2006 (129,836 injuries or 43.5 injuries per 100,000 person-years). This trend disproportionately affected females and those younger than 20 and older than 40 years of age (16).

Significant sex differences exist with regard to the epidemiology of ACL injuries. Female athletes are two to eight times more likely to sustain an ACL injury compared to their male counterparts (16–19). With increasing participation of females in competitive sports, this sex difference takes on even greater importance. Since the enactment of Title IX in 1972, the number of females involved in athletics has grown considerably. The percentage of girls participating in sports at the high school level increased almost 10-fold from 1971 (3.7%) to 1998 (33%). By 1998, females represented 40% of all high school and college athletic participants (20).

The National Collegiate Athletic Association (NCAA) Injury Surveillance System compiled data for eight men's and eight women's sports over a 16-year period (1988–2004) from a sample of colleges and universities. In total, the greatest number of injuries occurred in American football. However, if ACL injuries were ranked as a percentage of the total injuries on a team, female sports such as women's basketball (4.9%), women's gymnastics (4.9%), women's lacrosse (4.3%), and women's soccer (3.7%) showed disproportionate rates of injury. When evaluating the incidence of ACL injury per 1,000 athletic exposures, female gymnastics and men's spring football showed the highest injury rate (0.33), followed by women's soccer (0.28) and women's basketball (0.23) (21,22). Overall, high school athletes show lower rates of ACL injury when compared to collegiate athletes (5.5 versus 15 per 100,000 athlete exposures), however, with a similar distribution of injury across sports (23,24). At the high school level, ACL injuries represent a higher proportion of all injuries in female versus male athletes (4.6% versus 2.5%), with girls' basketball being the highest (6%), followed by girls' soccer, girls' gymnastics, and girls' volleyball (each 5%) (23). In gender-comparable sports at the professional level, ACL injury rates are similar between sexes (17,22).

The incidence of ACL injury is both sex- and sport-specific. For example, a meta-analysis evaluating sex differences according to sport found a female-to-male ACL tear ratio of 3.5 for basketball and 2.67 for soccer across all age groups and levels. The ratios with lacrosse and alpine skiing were found to be much more equivalent at 1.18 and 1.0, respectively (25). A recent study found that being a college athlete, female, and participating in the sports of soccer or rugby were independent risk factors for having a first-time noncontact ACL injury. After adjustment for sport and level of play, females were more than twice as likely as males to have a first-time ACL injury (relative risk [RR]: 2.10) (26).

Mechanism of Injury

The two main mechanisms of ACL injury are contact and noncontact. Over two thirds of all reported ACL injuries are noncontact in origin, with the remainder originating from contact through an outside force such as another player (3,4). Noncontact ACL injuries typically occur during a deceleration maneuver combined with a change of direction while the foot is in a closed-chain position. When the foot is in a closed-chain position and pronated, the tibia is internally rotated and the knee is at or near full extension (0° to 20° of flexion), the athlete is at particularly high risk. If the athlete attempts to change direction, the result is an excessive torsional force pulling the tibia into internal rotation while the femur is in external rotation, resulting in potential strain or rupture of the ACL (4). Furthermore, the interaction between the trunk and knee is better understood by way of evaluating the hip joint. The kinetic chain directly links the hip to the trunk, which comprises what is known as the lumbopelvic hip complex (27). Hip adduction, internal rotation, and flexion have been described during ACL injury (27–30).

In a study using video analysis to evaluate the biomechanical mechanism of ACL injury during a jumping maneuver, four common motor control strategies were more commonly observed in females. During landing, the injured knee deviated medially, the knee remained in a greater degree of extension, the majority of weight was on a single leg, and the trunk was tilted ipsilaterally. The combination of these components resulted in the center of mass being located outside the base of support during landing, placing the athlete at particularly high risk of ACL injury (29,31). With injury, hip flexion angles have been found to be greater in females compared to males (28,30).

Although noncontact ACL injuries are the most common mechanism of ACL injury, contact injuries can occur, typically via a distinct mechanism. Sports with the highest incidence of contact ACL injuries occur in men's collegiate American football, ice hockey, and wrestling (22). Soccer has also been found to have a higher percentage of contact injuries than many other sports, accounting for up to 46% of ACL tears (32). The majority of contact ACL injuries in soccer have been found to occur specifically when a player is being tackled (33). Studies from the 1990s showed an incidence of 37% to 48% for contact ACL injuries in soccer (18,32). However, a more recent 2009 study has shown a reduced incidence of 23% (33), possibly due to increasingly strict rules regarding foul play in many contact sports (33).

Due to the preponderance of literature focused on noncontact ACL injury, we focus on this mechanism of injury for the remainder of our discussion. However, it should be noted that the specific definition of "noncontact" ACL injury varies among studies. While some define a noncontact injury as one that occurs in the absence of player-to-player contact, others define it as the absence of a direct blow to the knee (23). Additionally, risk factors for experiencing a noncontact ACL injury can generally be categorized by their ability to be modified (Table 9.1).

Anatomical Risk Factors

There are many proposed anatomical differences between males and females that are important in ACL injury. These

TABLE 9.1: Summary of Risk Factors for First-Time Noncontact ACL Injury

	Nonmodifiable	Potentially Modifiable	Modifiable
Anatomic			
	• Smaller ACL (area and volume) • Greater lateral posterior-inferior tibial plateau slope • Smaller femoral notch width • Greater anterior knee laxity • Greater generalized laxity • Greater internal rotation knee laxity • Genu recurvatum	BMI	
Hormonal			
	Fluctuations of estrogen, progesterone, testosterone, and relaxin across the menstrual cycle	Hormonal effects might be modifiable with the use of hormonal contraceptives	
Neuromechanical			
			Landing Mechanics • Dynamic knee valgus, tibial internal rotation, and femoral adduction • Decreased hip/knee flexion in landing • Increased lateral trunk displacement • Posterior center of mass Quadriceps Dominance • Higher quadriceps/hamstring recruitment ratio Leg Dominance • Asymmetries in muscle strength and neuromuscular control Trunk Control • Increased lateral trunk displacement • Core weakness
Genetic			
	COL1A1 polymorphism *COL5A1* polymorphism		

ACL, anterior cruciate ligament; BMI, body mass index.

sex differences can be divided into primary knee factors and those involving other regions, such as the hip or body mass index (26,34,35). (See Figure 9.1.)

Intercondylar Notch

There has been extensive research evaluating the link between the size and geometric shape of the femoral intercondylar notch and the risk of ACL injury. Two measures of intercondylar notch anatomy include the intercondylar notch width as well as the notch width index (NWI)—that is, the ratio of the width of the anterior outlet of the femoral intercondylar notch divided by the total condylar width at the level of the popliteal groove on a tunnel radiograph (36). Use of this measurement attempts to standardize the notch width relative to overall distal femoral width for individuals of varied body habitus (36). The intercondylar notch has also been classified by geometric shape. An

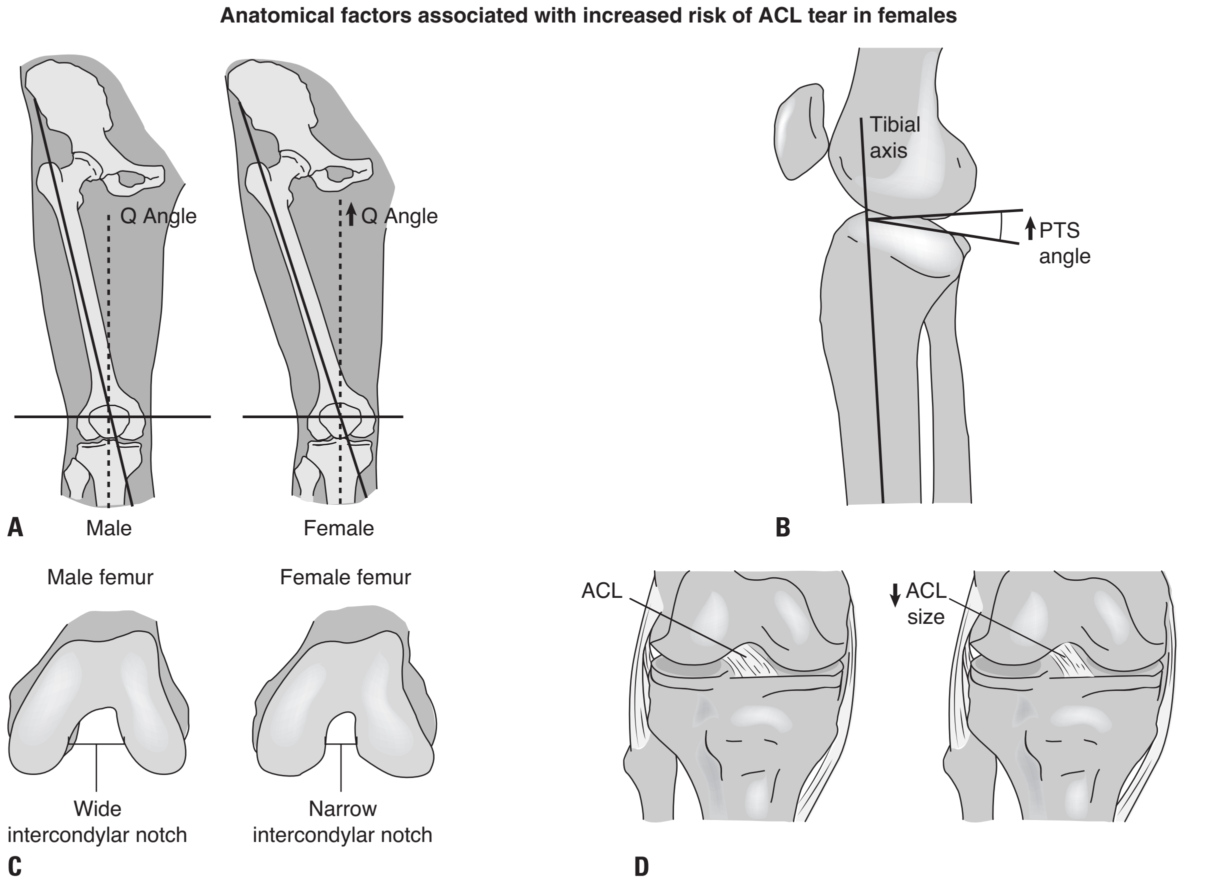

FIGURE 9.1: Sex difference in intrinsic risk factors for ACL tear. (A) Q-angle. (B) Posterior inferior tibial slope. (C) Intercondylar notch width. (D) ACL size.

ACL, anterior cruciate ligament.

A-shaped notch narrows from the base to the midsection and apex. In U-shaped notches, the midsection does not taper from the base, whereas a W-shaped notch has two apices instead of a classic flat roof (37). There are contradictory findings regarding sex differences in intercondylar notch anatomy. For example, a prospective study of 213 Division I athletes demonstrated that athletes with intercondylar notch stenosis (NWI < 0.2) were at increased risk of noncontact ACL injuries. However, no statistically significant difference was found between the sex of the athlete and notch width indices or rate of ACL tears (38). Another study compared 294 radiographs of athletes both with and without ACL injuries, evaluating notch width and shape. Women were found to have a significantly higher proportion of A-shaped notches when compared to men (34.9% versus 16.7%, respectively), although this was not significantly related to ACL injury given that a smaller notch width and NWI were found in ACL-injured athletes regardless of notch shape or sex (39).

Posterior Tibial Slope

An additional anatomical measure called posterior tibial slope (PTS) has been evaluated for its association with ACL injury. PTS is defined as the angle between a line perpendicular to the mid-diaphysis of the tibia and the posterior inclination of the tibial plateau (40). (See Figure 9.1B.) An increase in PTS places the tibia more anterior relative to the femur during quadriceps contraction, which may result in an increased force through the ACL (37).

Studies evaluating sex differences with regard to ACL injury and PTS are conflicting, but it seems that there may be an association between PTS and ACL injury, particularly in females. (41–44). A retrospective chart review evaluating radiographs of 199 males and 73 females found that the PTS of the medial plateau was higher in ACL injured females when compared to controls. Additionally, females with ACL injury had a higher PTS than did males with ACL injury (42). Another study used MRI to compare the PTS of those who had experienced a noncontact ACL injury with controls, including both males and females. In the female ACL injured group, the mean tibial posterior slope angle was 10.9° compared to 8.2° in controls ($P = .003$). Males showed no significant difference between the ACL injured and control groups with regard to PTS (43). Yet another study was done on U.S. Military Academy recruits, in which the PTS was measured on plain film radiographs of 140 individuals with noncontact ACL injuries and compared with controls. Subjects in the noncontact ACL group had significantly greater PTS ($P = .003$). When broken down by sex, this difference was statistically significant for female subjects ($P = .002$), however not for males ($P = .113$) (44). Utilizing MRI, PTS was measured in 100 athletes with a deficient ACL versus 100 control athletes with patellofemoral pain and an intact ACL. An increased PTS was associated with ACL rupture ($P < .001$) in both males and females; however, there was no statistically significant sex-related difference between groups (41). In sum, emerging evidence points to the contribution of increased PTS as an anatomical risk factor associated with ACL injury in female athletes.

Structure and Function of the ACL

An additional anatomic factor related to sex differences in ACL injury is ligament size. The female ACL has been shown to be inferior in strength and smaller in size than males, which is additionally proven to be unrelated to height (45–48). A cadaveric study found that the ACL in females was smaller in length, cross-sectional area (CSA), volume, and mass when compared to that in males (49). Using MRI in normal individuals, the mid-substance CSA of the ACL was measured. Females were found to have a smaller mid-substance CSA when compared to males even when looking at matched pairs of the same height ($P = .008$). On average, the CSA was found to be 40% to 50% smaller in females (47). A subsequent cadaveric study evaluating 10 male and 10 female knees revealed that the female ACL may have reduced mechanical strength when compared to the male ACL, even when adjusting for age, body anthropometric measurements, and ACL anthropometric measurements. In this sample, the female ACL was found to fail at 14.3% lower stress when compared to males. The female ACL also had a 22.49% lower modulus of elasticity, meaning that the female ACL offered less resistance during strain (45).

Quadriceps Angle

The quadriceps angle (Q angle) is defined as the angle created between a line drawn from the anterior superior iliac spine to the center of the patella and from the center of the patella to the middle of the anterior tibia1 tuberosity (50). The Q angle has been shown to range from 3.4° to 4.9° greater in females when compared to males and when measured in a standing position (51). Although an increased Q angle in females may lead to more laterally directed pull of the quadriceps at the knee, thus placing the ACL in a position more prone to rupture (20), evidence has not definitively revealed a clear relationship between an increased Q angle and ACL injury (52). A classic study by Shambaugh, Klein, and Herbert evaluated 45 basketball players (sex not specified) and found that the Q angle was higher in those who sustained a knee myotendinous injury or bone contusion compared to those who did not (53). A more recent study from 2004 investigating lower extremity alignment compared 10 male and 10 female subjects with a history of ACL tear with 20 controls. Subjects were assessed on the basis of navicular drop, Q angle, pelvic tilt, hip internal and external rotation range, and true versus apparent leg length discrepancy. Although females had significantly larger Q angles when compared to males, no correlation with ACL injuries was demonstrated. Of these parameters, increased navicular drop and anterior pelvic tilt were found to be statistically significant predictors of ACL injury; however this did not vary by sex (54). There has also been the suggestion that the sex differences in Q angle size can be explained by height, such that taller individuals have smaller Q angles. When males and females of equal height were compared, similar Q angles were found (55). Furthermore, considerable disagreement on the reliability and validity of the clinical Q angle measurement has been noted, possibly due to a lack of standardization (56).

Combination Factors

Combinations of multiple different risk factors for ACL injury have been investigated. A large study involving 895 military cadets found that significant risk factors included a small femoral notch width, generalized joint laxity, and, in women, a higher than normal body mass index (BMI). A combination of these factors greatly increased the risk of injury in females. In females, a multivariate stepwise logistic regression model accounting for narrow femoral notch width, higher-than-average BMI, and generalized joint laxity correctly predicted 75% of noncontact ACL injuries (35). More recently, Sturnick et al. conducted a study to evaluate combinations of intrinsic knee measurements and found these to be more highly associated with risk of experiencing a noncontact ACL injury than individual measurements alone. For example, a smaller femoral intercondylar notch width combined with an increased posterior-inferior slope of the tibial lateral compartment articular surface conferred the greatest risk. Females with both of these variables had double the risk of sustaining an ACL injury. For males, the presence of a smaller ACL volume concomitant with smaller lateral posterior meniscal horn wedge angle increased the risk of ACL injury by 1.76 times (57).

Neuromuscular Control as a Risk Factor

The relationship between neuromuscular control, particularly in movements such as landing and cutting, and ACL injury has been extensively studied (58–60). One reason this area has garnered much interest is that neuromuscular control is considered a modifiable risk factor (34). Additionally, when clinicians and researchers watch athletes sustain a noncontact ACL injury (particularly via video analysis), it appears that there are several common movement patterns that are so prevalent that they are considered “high-risk biomechanical strategies.” Furthermore, these risky patterns are more likely to be displayed by female than male athletes’ positioning (31,61). When evaluated in closer detail, the cumulative forces observed in this landing pattern have been distilled down to four main neuromuscular imbalances that contribute to ACL injury. They are termed ligament dominance, quadriceps dominance, leg dominance, and trunk dominance (29). Each of these is discussed in greater detail in the following sections.

Ligament Dominance

Ligament dominance is characterized by the reliance on bony morphology and static stabilizers such as the ligament to absorb ground reaction force, rather than the larger muscle groups of the lower limb. This results in a high amount of force being translated through the ACL over a very short period of time, which may result in ligament rupture (29). As noted previously, the ACL is the primary static restraint to anterior tibial translation. Through cadaveric testing it has been shown that the greatest forces through the ACL occur with a combination of either (a) anterior tibial shear with internal tibial torque at full extension or hyperextension, or (b) anterior tibial shear with a valgus moment when the knee is at greater than 10° of flexion (62). This corresponds to the aforementioned findings of video analysis of ACL injuries, notably the high-risk position of landing on a straight knee with an accompanying valgus force (29).

Although there have been numerous studies evaluating landing biomechanics in athletes, there is a lack of consistency in the literature regarding typical sex-related differences of knee flexion angles during landing. Although few studies have demonstrated that females land with greater knee extension at initial contact versus males (63,64), most indicate that males and females land with a similar degree of knee flexion (65–68). Similarly, evidence with regard to hip flexion is inconclusive, although most studies reveal no sex differences in the degree of hip flexion during vertical landing tasks (65).

Although most sex-related differences in landing biomechanics lack consistency, one exception is that females have repeatedly been shown to have greater peak knee abduction angles compared to males (66,67,69). It is thought that the peak knee abduction angle in females may represent a lack of ability to control frontal-plane motion of the knee joint, given that females have diminished reflex muscle activation in response to valgus perturbations at the knee (70). This said, video analysis has estimated the time of ACL injury to occur anywhere from 17 to 50 msec after initial contact, while the peak knee abduction angle occurs well past this time period (30,65). Thus, conclusive evidence connecting peak knee abduction angles in females during landing and ACL injury is lacking.

Quadriceps Dominance

Quadriceps dominance refers to the tendency to utilize quadriceps activation to a greater degree than hamstring activation in order to stabilize the knee joint during dynamic movements. Engagement of the quadriceps results in anterior tibial shear force at low knee flexion angles, such as during high-risk landing and pivoting maneuvers, thereby translating a high degree of force through the ACL (29,71). In general, females appear to use the quadriceps to stabilize the knee to a greater degree than males (72). Sex differences have been observed in muscular electromyogram (EMG) firing patterns, with females typically having a higher ratio of quadriceps-to-hamstring recruitment (73,74). For example, one study used an experimental device to translate the tibia anteriorly while asking subjects to resist the force as soon as movement was felt. In these conditions, it was noted that males first activated their hamstrings while females first activated their quadriceps (75). Additionally, findings demonstrate that co-contractions of the hamstring and quadriceps muscles actually decrease the total knee anterior shear force and thus the stress on the ACL (74). If the quadriceps is used primarily for limb stabilization, this only offers a single tendinous insertion for stability and control. Contrast this with the hamstrings that have multiple attachment points, both medially and laterally. The hamstrings can be thought of as a synergist with the ACL because they are able to pull the tibia posteriorly, thus decreasing stress through the ligament (72).

Leg Dominance

In tasks that require symmetry in the lower extremities, females tend to use one leg more dominantly than males. When a female tears her ACL, most of her weight is usually found on a single leg (31). Although most athletes have a preferred plant leg and a preferred kicking leg or jumping leg, the associated asymmetries in muscle strength and recruitment patterns tend to be greater in women than in men (61,69,76,77). Significant differences in knee valgus angles between dominant and nondominant legs have been demonstrated in female high school athletes (69). Another study of female high school athletes revealed significant side-to-side differences in hamstring peak torque and hamstring-to-quadriceps peak torque ratios. It was noted that these side-to-side imbalances were lessened after completing a neuromuscular training program (72). Side-to-side differences in knee abduction angles and knee abduction moments have also shown to be predictive of future ACL tear (58). Leg dominance puts both the dominant and nondominant limbs at increased risk of injury by placing excessive forces on the dominant leg and affording the nondominant limb decreased ability to handle average joint forces (69). Identifying limb asymmetries is therefore an important component of a neuromuscular screening exam.

Trunk Dominance

Trunk dominance is defined as the inability to precisely control the trunk in three-dimensional space (29). Athletes who do not adequately control their trunk have been found to have a greater risk of knee and ACL injury. In a prospective study of athletes, it was found that trunk displacement after a sudden force release was significantly greater ($P<.05$) in those who went on to have knee, ligament, and ACL injuries. Lateral displacement was the strongest predictor of ligament injury ($P=.009$). Factors related to core stability predicted risk of athletic knee, ligament, and ACL injuries with high sensitivity and moderate specificity (91% and 68%, $P=.001$) in female, but not male, athletes (78). Video analysis of ACL injury has also shown a greater mean lateral trunk angle in female compared to male athletes during ACL tear (31). After the pubescent period, females typically experience a shift of weight distribution to their trunk, placing their center of mass further from the ground, although they may not obtain a proportionate increase in neuromuscular development and power unless these factors are specifically addressed in a training program. This excessive trunk motion creates greater torque at the knee joint, further stressing the ACL (58,79).

Dynamic Neuromuscular Control

Although evidence exists in support of each of the four neuromuscular imbalances in relation to ACL injury, limited information is available on the coexistence of multiple biomechanical deficits in the same athlete (Figure 9.2). Biomechanical deficits consistent with ligament and quadriceps dominance have previously been found to coexist in the same group of athletes during drop landing tasks (80). It has also been suggested that athletes who exhibit trunk control deficits in the frontal plane have higher knee valgus moments as the center of mass displaces more laterally (78,81). Recently, the prevalence of biomechanical deficit patterns was quantified in 721 high school female athletes during performance of an unanticipated cutting task. Approximately 40% of females demonstrated no deficits and were categorized as low risk. The next most prevalent profile at 24% was a combination of high quadriceps and leg dominance deficits, labeled as "quadriceps-leg." This was followed by 22% of females who demonstrated a combination of trunk, leg, and ligament dominance deficits labeled as "trunk-leg-ligament." The fourth and final profile at 14% demonstrated high ligament dominance deficits only. Further research is needed, but the goal is to better tailor injury prevention programs in relation to an athlete's specific biomechanical deficit profile (60).

Dynamic control in a jump-landing task has revealed several distinct biomechanical risk factors for ACL injury. Hewett et al. performed a study on 205 female athletes in the high-risk sports of soccer, basketball, and volleyball. Neuromuscular control of the knee joint was prospectively measured using three-dimensional kinematics (joint angles) and kinetics (joint moments) during a jump-landing task. Nine of the athletes went on to sustain an

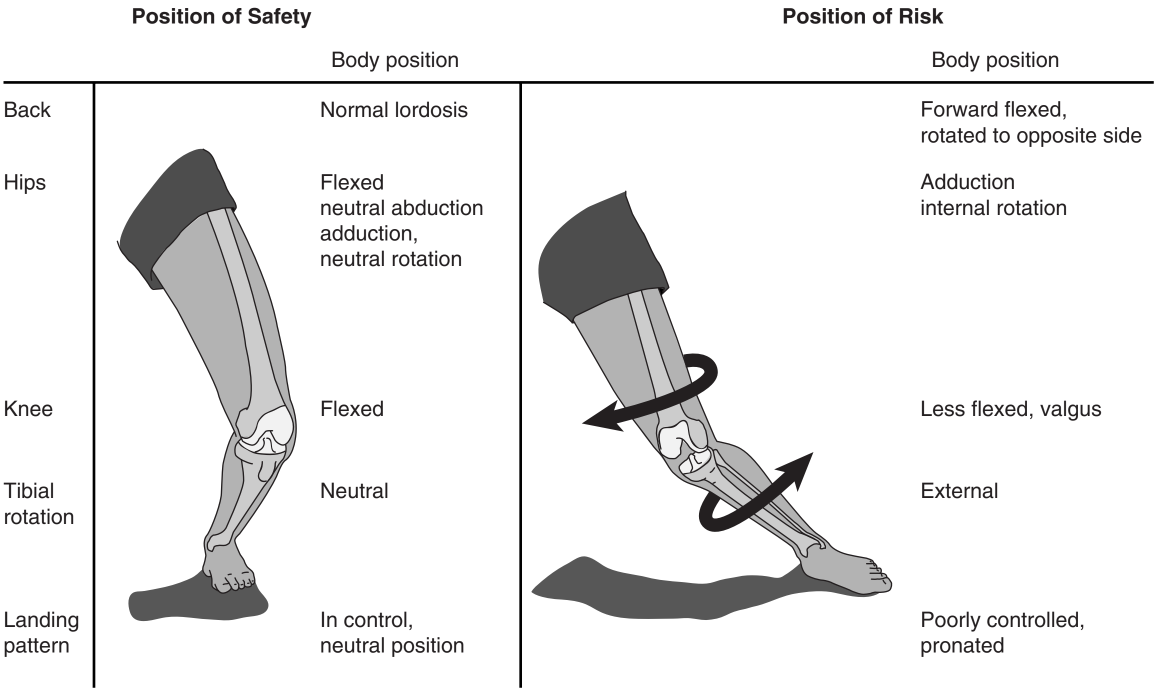

FIGURE 9.2: Knee neuromechanics that have been identified as culprits in anterior cruciate ligament (ACL) injury.

ACL rupture. Comparison of the preseason data demonstrated that ACL injured athletes had knee abduction angles that were 8.4° greater at initial contact and 7.6° greater at maximum displacement during landing. Athletes with ACL injuries had increased angular motion, which took place at a faster pace and with higher forces than in noninjured athletes. Of interest, the authors commented that preseason knee abduction moment measurements could predict which female athletes were at higher risk of ACL injury with a 73% sensitivity and 78% specificity (58). A much simpler instrument, the Landing Error Scoring System (LESS), has recently been examined as a tool for identifying individuals at risk for ACL injury in elite youth soccer. The LESS is a field assessment tool that identifies high risk patterns during a jump-landing maneuver, with higher scores indicating more errors (82). It was found that athletes with a LESS score of five or more were at higher risk. A score of five was optimal as a cutoff point as this produced a sensitivity of 86% and a specificity of 64% as a predictive factor for future noncontact ACL injury (83).

Another recent study evaluated 215 intercollegiate athletes grouped by sex and self-reported history of knee injury. Jump-landing patterns were found to be impacted by sex, but not injury history (84). It was noted that males demonstrated more at-risk landing patterns in the sagittal plane including limited trunk, knee, and hip flexion at initial contact, as well as limited hip flexion throughout the landing. Conversely, females demonstrated more at-risk landing patterns in the frontal plane including knee valgus at initial ground contact and maximum knee flexion, as well as more frontal plane movement throughout the landing (84).

Mechanisms of growth and development in females may underlie the altered neuromuscular control that leads to ACL injury. A study of pubertal males and females was conducted using drop vertical landings. Each subject was evaluated 1 year apart. Interestingly, pubertal females were found to have an increased peak knee abduction angle in the second year when compared to the first year ($P<.001$), while males showed no change in matched developmental stages ($P=.90$). It was also found that in postpubertal females, peak knee abduction angle and moment were greater relative to postpubertal males (85).

Fatigue has also been evaluated as a contributing factor to ACL injury. In one study, team sport athletes were compared with dancers during single leg drop landings. Both groups demonstrated suboptimal landing mechanics after a fatiguing protocol, including increased peak knee valgus moment and increased lateral and forward trunk flexion. However, it was noted that dancers took significantly longer to reach fatigue than did the team sport athletes (86). A similar study, again comparing dancers to team sport athletes with single leg drop landings, found female team sport athletes landed with significantly greater peak knee valgus ($P = .007$) than male team sport athletes and also as compared to both male and female dancers (87). It is hypothesized that slower onset to landing fatigue and better landing mechanics in dancers may be due to the fact that they specifically practice landing technique with high repetitions from a young age. This information may play a future role in preventive strategies.

Sex Hormones as a Risk Factor

Evidence continues to evolve regarding the role of sex hormones in noncontact ACL injury. This body of literature is discussed extensively in Chapter 1 on the influence of sex hormones on the neuromusculoskeletal system.

Genetic Risk Factors

Several studies have suggested that genetic contributions may be considered among intrinsic risk factors for ACL injury. For example, a small study on female twins suggested that neuromuscular imbalance, increased joint laxity, and smaller intercondylar notch width may be associated with ACL injury, each defined as an individual risk factor (as noted previously) but also with a genetic predisposition (88). The background reasons for such familial associations are currently under investigation.

Genetic differences in collagen have also been evaluated as a contributing factor for ACL rupture. A major structural component of ligaments is collagen, predominantly types I and IV, which are encoded by the *COL1A1* and *COL5A1* genes, respectively. Variations of sequence within these genes may lead to an increased risk of ACL injury (89). For example, a Swedish study found that cruciate ligament injuries were associated with a polymorphism in the *COL1A1* gene. Compared with the homozygous ss genotype, the heterozygous participants displayed a similar risk (odds ratio [OR]: 1.06), whereas those with the ss genotype were less likely to experience ACL injury (OR: 0.15) (90). A South African study also revealed that the TT genotype of the *COL1A1* Sp1 binding site polymorphism was underrepresented in those with ACL ruptures (91). Another South African study specifically evaluated the *COL5A1* gene. It was found that the CC genotype of the *COL5A1* BstUI restriction fragment length polymorphism in the female participants was significantly underrepresented in the ACL rupture group compared with controls (27.4% versus 5.6%; OR: 6.6). Male subjects did not reveal a similar correlation (92). Although it is premature to definitively state that genetics play a significant role in the increased risk of ACL rupture in female athletes when compared to males, further study may reveal significant findings in this regard (37).

Injury Prevention

The aforementioned neuromuscular imbalances of ligament dominance, quadriceps dominance, leg dominance, and trunk dominance are each thought to play a role in the underlying modifiable factors contributing to ACL injury. Therefore, many ACL injury prevention programs seek to evaluate for these “high risk” biomechanical strategies in individual athletes during a preseason screening examination, allowing for the implementation of specific neuromuscular training to correct deficits and therefore prevent ACL injury (14,93,94). For example, pre-enrollment drop vertical tests can be administered as a simple, low-cost screen to identify at-risk athletes. Details about the athlete’s knee kinematics can be analyzed (37). In a drop vertical test, the athlete begins by standing on a box (31 cm above ground) with the feet positioned 35 cm apart, then drops directly down off the box and immediately performs a maximum vertical jump, raising both arms as if jumping for a basketball rebound (58). Observations regarding neuromuscular control can include factors such as lower limb alignment, trunk posture, and landing technique, thus helping to focus an individual athlete’s neuromuscular training program. As noted previously in the discussion on neuromuscular control, another simple field assessment screening tool is the LESS, which identifies high-risk patterns during a jump-landing maneuver by simply counting the number of landing “errors” during a jump. Participants jump from a 30-cm-high box to a distance of 50% of their height away from the box, followed immediately by a maximum vertical jump. There are 17 scored items that include assessment of lower extremity, trunk, and foot positioning (82). Good interrater and intrarater reliability can be obtained, and there is concurrent validity using three-dimensional motion analysis (82).

A recent systematic review evaluated the available literature regarding the efficacy of neuromuscular retraining programs in reducing the risk of noncontact ACL injuries. According to the authors, three specific intervention programs were found to be particularly effective:

(a) Sportsmetrics, (b) Prevent Injury and Enhance Performance (PEP) program, and (c) the Knee Injury Prevention Program (KIPP). Across these three programs, 70 to 99 athletes needed to be trained in order to prevent one ACL injury, with a relative risk reduction of 75% to 100% (95). Another systematic review evaluated nine ACL injury prevention programs from 1996 to 2008 and found that programs reported a cumulative risk reduction of 52% in females and 85% in male athletes (96).

The Sportsmetrics training program included female high school teams in the sports of soccer, volleyball, and basketball. Participants completed a 6-week preseason neuromuscular training program with a certified athletic trainer and physical therapist involving stretching and plyometric techniques with an emphasis on proper form. Training sessions lasted 60 to 90 minutes, 3 days per week (14). Jump training was based on a prior study that included three phases. The technique phase (Phase I) took place during the first 2 weeks and focused on demonstration and reinforcement of proper jump form. Four basic techniques were emphasized, including maintaining a correct posture (shoulders back, chest over knees, and spine erect), jumping vertically without excessive lean, landing softly with toe-to-heel rocking and bent knees, and lastly, instant recoil preparation for the next jump. The fundamentals phase (Phase II) concentrated on the use of proper technique to build a base of strength and power. The performance phase (Phase III) focused on achieving maximal vertical jump height (72). Throughout the season following Sportsmetrics program implementation, 14 serious injuries occurred in 1,263 athletes, nine of which were noncontact ACL tears. Untrained female athletes were 3.6 times more likely to experience a knee injury than trained female athletes ($P = .05$) and 4.8 times more likely than trained male athletes ($P = .03$). The incidence of noncontact knee injuries was significantly lower in the trained versus the untrained female athletes ($P = .01$) (14).

The PEP program study consisted of female soccer players between the ages of 14 and 18. Each participating team was provided a 20-minute instructional video designed to replace the traditional warm-up performed prior to training and competition. The video consisted of basic warm-up activities, trunk and lower extremity stretching techniques, strengthening exercises, plyometric activities, and soccer-specific agility drills. A heavy emphasis was placed on proper landing technique; for example, maintaining a "soft landing" with deep hip and knee flexion. In the season after program implementation, there was an 88% decrease in ACL injury in the PEP-enrolled subjects compared to an age- and skill-matched control group. In year 2, there was a 74% reduction in ACL tears in the PEP intervention group compared to controls (94).

As another example, the KIPP study evaluated high school female soccer and basketball players and risk of lower extremity injuries. Coaches in the intervention group attended a 2-hour training session 2 weeks before the start of the season, learning how to implement a 20-minute neuromuscular warm-up before team practices and an abbreviated version before games. The warm-up protocol included a combination of progressive strengthening, plyometric, balance, and agility exercises. Athletes were instructed to avoid dynamic knee valgus and to land with flexed hips and knees. After implementation of the program, athletes in the intervention group demonstrated a lower incidence of gradual-onset lower extremity injuries (0.43 versus 1.22, $P < .01$) and acute-onset noncontact lower extremity injuries (0.71 versus 1.61, $P < .01$) compared with a control group performing a typical warm-up program. Athletes involved in the program experienced significantly fewer noncontact ACL injuries (Incidence Rate Ratio [IRR]: 0.20; 95% Confidence Interval [CI]: 0.04–0.95). The number needed to treat in order to prevent one noncontact ACL injury was 191 (93).

Soccer is a high-risk sport that has worldwide popularity and is played by almost 300 million people on an amateur or recreational level (97). The FIFA 11+ was developed as a complete warm-up program to prevent injuries in amateur soccer players (98). The program consists of three different components. The first involves running exercises at slow speed combined with active stretching and controlled contacts with a partner. The second component progresses to six different sets of exercises that focus on strength, balance, and jumping. The final component involves speed running combined with soccer-specific movements simulating sudden changes in direction (99). Studies have demonstrated significant benefit of the FIFA 11+ in prevention of ACL injuries in females (100) and in lower extremity injuries in males (101).

Despite these and several other studies demonstrating the benefits of neuromuscular training in the prevention of ACL injuries, the specifics of the composition and duration of the optimal program is still uncertain. A recent systematic review evaluating the ACL neuromuscular training components across 13 studies found that training sessions ranged from 10 to 45 minutes and the total number of sessions ranged from 10 to 108. The emphasis also varied considerably among programs, though most placed the greatest emphasis on balance and agility training (102). It has been suggested that, at a minimum, a prevention program include at least 10 minutes of exercise three times per week with an emphasis on neuromuscular facilitation (96). In 2008, the International Olympic Committee stated that well-designed injury prevention programs should include strength and power exercises, neuromuscular training, plyometric exercises, and agility exercises, along with regular warm-up. The goal of the program should attempt to alter dynamic loading of the tibiofemoral joint through neuromuscular and proprioceptive training and emphasize proper landing and cutting techniques—for example, landing softly on the forefoot and rolling back to the rearfoot, engaging knee and hip flexion, and, where possible, landing on two feet. Training should also avoid excessive dynamic valgus of the knee and focus on the "knee over toe position" when cutting (22). Based on prior evidence it is believed that programs should be 8 or more weeks in duration in order to allow sufficient neuromuscular changes and performance training effects (103). Finally, it is important to note that deconditioning after termination of a program can occur quite quickly. Aerobic deconditioning has been reported as soon as 1 to 2 months after program cessation, and anaerobic deconditioning in as little time as 2 weeks, implying that prevention programs should remain ongoing throughout an athlete's career (15).

Outcomes After ACL Injury

As outlined so far, there is ample evidence to support that female athletes are at higher risk for ACL injury when compared to males. Additionally, females are known to have a greater risk with regard to re-tears of their ACL surgical grafts as well as of the contralateral knee upon return to sport (37). In a study of 1,415 athletes followed prospectively for 5 years after primary ACL reconstruction using a patellar tendon autograft, females experienced more injuries to the contralateral knee when compared to males (7.8% vs. 3.7%; $P<.001$). There was no sex-related difference in injury incidence to the reconstructed knee (104). Paterno et al. found that almost 30% of young athletes who returned to pivoting and cutting sports after ACL reconstruction suffered a second ACL injury within 24 months after return to sport. Of those who suffered a second injury, contralateral tear occurred 20.5% of the time and ipsilateral graft tear occurred 9.0% of the time. Most injuries occurred early, within 72 athlete exposures. With regard to sex-specific differences, the rate of injury for female athletes in the ACL reconstruction group was almost five times greater ($P=.0004$) than female controls. Also, a trend was found toward a higher proportion of female participants (23.7%) who suffered a contralateral injury compared with male participants (10.5%), while ipsilateral injuries between males (10.5%) and females (8.5%) were similar. Findings in males were limited due to the small sample size (105). Countering this, a more recent meta-analysis evaluated outcomes of ACL reconstruction, noting no sex-related difference in risk of graft failure or contralateral ACL tear, the latter showing rates of 4% for males and 7.4% for females ($P=.13$). That said, only a small amount of studies were sufficiently homogeneous to be included in the analysis (106).

With regard to ACL reconstruction, a large epidemiological study evaluated the 3-year cumulative incidence of ACL reconstruction in adult patients. Overall, males were more likely than females to undergo ACL reconstruction after injury (26% versus 19%; $P<.001$). It should be noted, however, that only adults age 20 and older were included in the study. As one would expect, the likelihood of undergoing ACL reconstruction decreased with each decade of age. For example, 45% of patients age 20 to 29 underwent reconstruction compared with only 8% of patients 60 to 69 years of age (107). Although the majority of orthopedic surgeons recommend ACL reconstruction for those who wish to return to sport (108), not all patients have this goal (109). In fact, a meta-analysis on return to sport after ACL reconstruction found that only 65% returned to their preinjury level of sport and only 55% returned to competitive sport (8). It also demonstrated that males were approximately 1.5 times more likely than females to return to either level of sport (8). Data from the Multicenter Orthopaedic Outcomes Network (MOON) ACL cohort study also found that within the sport of soccer, female athletes are less likely to return to play when compared to their male counterparts (110).

Rupture of the ACL has been found to be a risk factor for future development of knee osteoarthritis (OA). It is commonly stated that, on average, 50% of patients with ACL injury will progress to the development of knee OA later in life (10). With a combined ACL and meniscus injury, this prevalence is even higher (111). The increased risk of OA is most likely related to the extent of the injury to the bone, chondral surface, and meniscus at the time of the ACL tear given that rates of OA are similar regardless of surgical versus nonsurgical management (10,112). A large population-based study in Sweden with a mean follow-up of 9 years found no sex-related difference in the risk of OA after ACL injury (113). Additionally, a systematic review and meta-analysis looking specifically at knee OA after ACL reconstruction concluded the effect of sex could not be determined given that the majority of studies did not publish separate results for males and females (114).

Supporting sex-related differences, a 2015 study used MRI to evaluate for the presence of knee OA only 1 year after ACL reconstruction, comparing postoperative subjects with age, sex, and activity-level matched controls. Among those with ACL tear, males were found to have a five to six times greater likelihood of both patellofemoral osteoarthritic changes and the presence of osteophytes (115). Another study from 2014 likewise found sex-related differences with regard to the outcome of progressing to total knee replacement in a 15-year period after cruciate ligament reconstruction. Although the incidence of knee arthroplasty was low at 1.4%, this was seven times greater when compared to a cohort of matched controls. With regard to sex-related differences, being female increased the likelihood of undergoing total knee arthroplasty (hazard ratio [HR]: 1.58; $P=.001$) (116). More research is needed to determine if a sex-based difference exists with regard to development of OA after ACL injury.

MEDIAL COLLATERAL LIGAMENT/ LATERAL COLLATERAL LIGAMENT

Although an abundance of literature exists concerning sex differences in ACL injury, the impact of sex on the knee collateral ligaments is less certain. The two collateral ligaments of the knee, the medial collateral ligament (MCL) and the lateral collateral ligament (LCL), provide medial and lateral stability to the knee joint, respectively. The MCL primarily restricts excessive valgus of the tibiofemoral joint (2). The superficial portion of the MCL is extracapsular while the deep MCL has two attachment points to the medial meniscus (117). The LCL primarily prevents excessive varus of the tibiofemoral joint and has no connection to the meniscus (2).

Overall, the available literature reveals a lack of significant sex-related differences in collateral ligament injury patterns. Two available studies reported the incidence of collateral ligament injuries to be higher in females compared to males, however to a lesser degree than the differences noted with ACL injury. These studies did not differentiate between the lateral versus medial collateral ligaments (17,18). One additional study evaluated the "stiffness" of the medial tibiofemoral joint, comparing sex as well as age in three distinct groups (prepubertal children, postpubertal young adults, and older adults). No sex-related difference was found across the three age groups. However, after puberty, medial tibiofemoral joint stiffness was greater and was significantly influenced by height and mass, regardless of sex (118).

MENISCUS

The knee meniscus is a wedge-shaped section of semilunar cartilage located between the femoral condyle and tibial plateau (119). Both the medial and lateral meniscus play an important role in knee joint stability, shock absorption, as well as nutrition and lubrication of the articular cartilage (120). In one MRI-based study, the cross-sectional shape of the medial meniscus varied significantly between males and females, although much of this was attributable to size-related differences (121). Acute meniscal injuries typically occur when the shear stress generated within the knee during flexion/compression combined with femoral rotation exceeds the meniscal collagen's ability to resist these forces (2).

Acute meniscal injuries commonly occur in conjunction with ACL tears, and variable sex-related differences with regard to meniscal injury have been reported. A prospective study evaluating meniscal tears during ACL reconstructive surgery found that female high school soccer athletes had fewer medial meniscal tears than did their male counterparts ($P=.02$), despite finding no sex-related difference in mechanism of injury (122). Another prospective study of 9,023 male and 1,396 female military academy cadets with ACL injury found no significant sex-related difference in the incidence of meniscal injury at arthroscopy (123).

Although less commonly discussed, the incidence of meniscal tear in individuals with intact ligamentous structures has been reported. A case series of meniscal injuries diagnosed at arthroscopy in athletes age 16 to 32 found that males were three times as likely to have the presence of an isolated meniscal tear (120). This finding was similar to that found in a much older review of meniscal injuries (124). A recent study specifically evaluated the prevalence and sex-related variance of isolated meniscal tears in patients younger than 40, revealing that the overall prevalence of meniscal tears was less in females compared with males. In males, the presence of medial meniscal tears increased with age, whereas females revealed a lower prevalence along with no age-related variability. Strikingly, males under 30 were nearly four times as likely to have the presence of an isolated medial meniscal tear compared with females (OR: 3.95 versus 0.25, $P=.002$) (125). Similar trends have been noted in younger populations. In a study of youth aged 10 to 19 with mixed ligamentous integrity status, complex meniscal tears were more common in male than female children (defined by the presence of open growth plates) ($P<.01$) (126).

The posterior horn of the medial meniscus is particularly vulnerable to tears as it is relatively immobile compared to other portions of the meniscus. In a single study, radial tears of the medial meniscus posterior horn were uniquely found to be associated with older age and obesity and were more commonly found in females when compared with males ($P<.001$). In addition, radial tears were strongly associated with an increased incidence and severity of cartilage degeneration compared to horizontal tears (127).

Related to genetic risk factors, molecular analysis of meniscal tissue harvested at the time of arthroscopic meniscectomy has been performed, noting that the expression of the cytokine *CCL3L1* was higher in women of all ages with concomitant ACL and meniscal injury. Of note, higher expression of this catabolic marker in patients with a combined injury pattern indicates an increased catabolic response that may lead to greater likelihood of development of post-traumatic osteoarthritis (128).

QUADRICEPS TENDON

Quadriceps tendon ruptures are uncommon and typically occur when the quadriceps muscle rapidly and eccentrically contracts with the knee in a semi-flexed position (129). Males have been reported to incur this injury four to eight times more often than females (129–132), potentially due to the disproportionately increased prevalence of systemic risk factors such as gout, metabolic disease, and chronic renal failure within the male population (133,134). Rupture typically occurs in the sixth decade of life (129,132,135). The most commonly reported scenarios of injury occur with a simple fall (61.5%) or a fall from stairs (23.4%). Injury during an actual sporting activity is reported to be far more rare (6%) (135). Treatment typically involves surgical repair, for which one study revealed no sex differences in outcomes (136).

PATELLAR DISLOCATION

An acute traumatic patellar dislocation usually occurs in young, active individuals (137–139). The typical mechanism of injury underlying acute patellar dislocation is partial flexion of the knee with tibial valgus (139). Athletes displaying an increased Q angle at 30° of flexion may be at higher risk (140), and one cadaveric study revealed that relaxation of the vastus medialis oblique (VMO) also reduced lateral stability (144). A similar incidence of injury between males and females has been reported (137,141). However, when evaluating young, active individuals, there is a definite female predisposition toward injury that lessens with age (137–139,142). A prospective, population-based study found that the risk of first-time patellar dislocation is 33% higher among females than males when examining individuals age 10 to 17, which is a high-risk age group. The risk of patellar dislocation was three times higher in females with a prior history of either dislocation or subluxation (138).

Knowledge regarding specific characteristics of anatomical risk factors between males and females is limited. Anatomic differences in females have been found to include joint hypermobility, increased femoral torsion, and extensor mechanism malalignment (138). One study specifically used MRI to evaluate for anatomical sex differences in those who sustained a patellar dislocation, comparing these with a control group. Trochlear asymmetry was higher in females, whereas trochlear depth was higher in males (143). This bears importance given prior studies demonstrating that a flattened trochlear groove reduced lateral knee stability by 70% at 30° of flexion (144). A significant interaction between patellar dislocation and sex was also observed for the tibial tubercle–trochlear groove (TT-TG) distance ($P=.02$), which was longer in females and also correlated with an increased Q angle (145). In this particular study group, injury during low-risk and no-risk pivoting injuries were more common in females, whereas first time dislocations in males occurred predominantly during high-risk pivoting activities (143).

CONCLUSION

Many acute knee injuries such as ACL tear show clear sex-related differences with regard to the incidence of injury as well as injury mechanisms and risk factors. Multiple contributors to injury such as anatomical variation, biomechanical alterations, genetic factors, and sex hormone variability may play a role. Through the thorough evaluation of the manner in which these injuries impact male versus female athletes, sports medicine practitioners can be better prepared to prevent acute knee injuries and ensure appropriate treatment in the event that an injury occurs.

Summary of Sex Differences in Traumatic Knee Injuries

Musculoskeletal Factor	Sex With Higher Prevalence
ACL tear	• Females, 2 to 8 times greater (16–19)
ACL tear by level of play	• High school: Females (22,24) • College: Females (21) • Professional: Similar rates (17,22)
Anatomic risk factors for ACL tear	• Increased PTS: Females (41–44) • ACL size and function: Weaker in strength and smaller in size in females (45–48) • Q angle: Larger in females, but evidence for increased ACL tear risk lacking (51,54)
Neuromuscular risk factors for ACL tear	• Greater peak knee abduction angles during landing: Females (66,67,69) • Preferential use of quadriceps to stabilize the knee: Females (64,72–74) • Inadequate trunk control: Females (31,58,78,79)
Risk of ACL injury to the contralateral knee after ipsilateral reconstruction	• Females (104,105)
Undergoing ACL reconstruction surgery after injury	• Males (107)
Return to preinjury level of sport or competitive sport	• Males (5,8,110)
Collateral ligament injury	• Possibly females (17,18)
Isolated meniscal tear	• Males (120,124–126)
Quadriceps tendon rupture	• Males (129–132)
Patellar dislocation	• Younger females (137–139,142)

ACL, anterior cruciate ligament; PTS, posterior tibial slope.

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10

FOOT AND ANKLE

Dan Cushman

DIFFERENCES BETWEEN THE SEXES IN THE FOOT AND ANKLE

Numerous intrinsic differences exist between men and women with regard to the foot and ankle. The shape, size, and architecture of the structures exhibit many distinctions between the sexes. The appearance of a photographed foot, for example, often can be described as masculine or feminine purely based on its appearance. Furthermore, social and cultural factors influence the feet, which also add to the dichotomy. These intrinsic and extrinsic differences play an important role in injuries. As will be demonstrated, women tend to have more disorders of the foot and ankle compared to men.

Anatomy of the Foot and Ankle

The foot is proportional to body size for both sexes. Numerous studies have demonstrated, however, that despite men's larger body size, men's feet are not simply larger versions of women's feet (see Figure 10.1). The male foot, as expected due to the larger body size, is larger than the female foot in all foot measurements—the 20th percentile for foot length for men is 257 mm, which is the 80th percentile for women (1,2). When normalized to body height, however, men have a longer foot length and breadth than women. Women's feet have been shown to be wider in the forefoot, with a shorter arch length and shorter metatarsal length than a man's foot (2). They also have smaller calcaneus bones (3). Men have been shown to have a greater first toe height and outside of the ball of the foot length (2). For both sexes, longer feet tend to be narrower (4). It should be noted that some studies have found contradictory results, including no relevant differences between sexes (4); geographical and cultural variations may play a part. It has been theorized that women have undergone intersexual selection for smaller foot size (5). In other words, men may have chosen female partners with smaller feet.

Men also display larger ankle circumference, calf girth, and tibial size than women (2,6), again owing to the larger body size. When normalized to body height, however, other findings appear. Women have larger ankle circumference, calf height, and calf circumference (2). Men, in turn, have a larger ankle height, medial malleolus height, ankle girth, and bimalleolar breadth (2). They also demonstrate a thicker distal third of their tibias than women, with thicker cortices, when assessed by dual-energy x-ray absorptiometry (DXA) and histologic sectioning (6). Comparison of ankle cartilage between the sexes by MRI shows less cartilage (in volume, thickness, and joint surface area) in the distal tibia, proximal talus, distal talus, calcaneus, and total hind foot in men than women (7).

Differences in the muscles that control the foot and ankle also exist between the sexes. The tibialis anterior, lateral gastrocnemius, medial gastrocnemius, and soleus all demonstrated larger optimal pennation angles in men than women (8). This may account for differences in force production or risk for musculotendinous injury (9). Although men have demonstrated greater absolute strength than women in the foot, when normalized to body size, no large differences in strength between the sexes have been shown (10–12). Toe flexor muscle strength has been demonstrated to decrease more rapidly over time in women than men, however (10).

Biomechanics of the Foot and Ankle

Biomechanical studies of the foot and ankle with regard to difference between the sexes mainly focus on gait, both in walking and running. During the first years of walking, boys and girls already demonstrate differences in foot shape and dynamic loading parameters. Girls exhibit greater heel

FIGURE 10.1: The human foot.

and forefoot dynamic loading, while boys demonstrate a broader midfoot, suggestive of a lower arch (13). As adults, however, women have greater contact area in the midfoot; men have higher peak pressure and peak force in the medial toe and forefoot as well as greater contact area in the central forefoot and heel areas (14). This has potential medical implications as high metatarsal pressure has been linked to an increased risk of foot/ankle disorders (15). Women also tend to walk slower due to a shorter stride length and also demonstrate a narrower step width (16).

For the foot, women have demonstrated a higher amount of first metatarsophalangeal (MTP) joint extension compared to men while running (17). Men demonstrate significantly greater peak rearfoot eversion (18), which has been theorized to contribute to increased strain on the iliotibial (IT) band. In runners, men had significantly decreased contact area in the medial and middle forefoot with an increased maximal force in the lateral forefoot, neither of which was seen in women (19). In jumping tasks, men and women load their feet differently during landings, with men displaying greater force-time integrals in the medial midfoot, lateral midfoot, medial forefoot, and lateral forefoot compared to women (20).

The ankle joint has been shown to have a greater range of motion (ROM) in all three axes for girls/women aged 9 to 20 (21). Interestingly, as they age, there is a greater decrease in the ankle joint ROM for women compared to men (21). While walking, this increase in stiffness for men is most prominent in the fourth subphase of the stance phase (22). However, women's ankle joint flexor moments are significantly smaller than men's throughout the stance phase (16). Women generate greater plantar flexion ROM with greater power during the pre-swing phase of gait (12,23). When examining ankle stability, professional female dancers exhibit longer time to stability compared to their male counterparts (24). In unanticipated cutting tasks, women had significantly larger peak eversion angle and significantly smaller peak inversion angle during stance phase (25).

The Effect of Shoes

Although men and women have distinct anthropometric characteristics, shoe-wear has been demonstrated to have an increasingly important part in injury and is the most extensively studied extrinsic factor causing injury to women (26). The two most commonly implicated shoe characteristics, often found in the same shoe, are an elevated heel and narrow toe box.

Men and women have different priorities when it comes to the health of their feet. In a study by Baumhauer, Mcintosh, and Rechtine (27), men and women were asked about the most important outcome factors with regard to their feet and ankles. These factors are listed in Table 10.1. Men chose "foot and ankle weakness" more commonly than women, while women chose "difficulty fitting into shoes" significantly more than men.

The high-heeled shoe (Figure 10.2) has been studied extensively in its relationship to injury (26,28). As heel height increases, plantar pressure shifts from the midfoot to the medial forefoot, with an increased vertical and anteroposterior ground-reaction force (29). These biomechanical factors lead to an increased rate of plantar loading, increased peak pressures beneath the metatarsal heads, and decreased time to maximal peak pressure (26). As the heel height increases, there is an associated increase in subjective discomfort. This is likely a significant part of the reason that

TABLE 10.1: The Most Important Factors, in Order of Priority, for Each Sex in Terms of Outcomes for Their Feet and Ankles

Men	Women
1. Limitations in walking	1. Limitations in walking
2. Activity-related pain	2. Activity-related pain
3. Constant pain	3. Constant pain
4. Inability to do a job or housework	4. Difficulty fitting into shoes
5. Difficulty with prolonged standing	5. Difficulty with prolonged standing

Source: Adapted from Ref. (27). Baumhauer, JF, Mcintosh S, Rechtine G. Age and sex differences between patient and physician-derived outcome measures in the foot and ankle. *Journal of Bone and Joint Surgery (American Volume).* 2013;95(3):209–214.

FIGURE 10.2: High-heeled shoes, which are likely related to foot and ankle problems in women.

women who wear shoes with high heels complain of foot pain and deformity compared to women who wear flats (26). In fact, there are reports that the frequency of foot problems in populations that have never worn shoes is low (30). Narrow toe-box shoes have also been correlated to rates of injury. Hallux valgus was not found until the development of narrow shoes during the late medieval period, when examining human remains (31).

Hammer toes, neuromas, bunionettes, and hallux valgus have all been implicated from high-heeled, narrow toe-box shoes causing excessively high plantar pressures and toe crowding (26). Women bear the brunt of shoe-related injuries, which are felt to be related to high-heel shoes. Forefoot deformities are prevalent in 76% of women during their lifetime (32), with hallux valgus and hammertoes being the most common maladies. In the same study, it was reported that 88% of women wore shoes with a width smaller than their feet by an average of 1.3 to 2.5 cm. When examining groups of women with and without foot pain or deformity, the average difference between their foot and shoe width was only 0.6 cm in each group.

Of note, shoe-wear may play a larger effect on injuries in men in one subgroup—rock climbers. In one study of 144 rock climbers, male sex was independently related to the onset of foot disorders, as well as the use of high-type shoes (33). However, this may also be related to the higher degree of climbing difficulty with men.

Last, manufacturers of running shoes have long purported performance and injury-prevention benefits of their shoes. The high prevalence of running-related injuries has allowed for decades of advice about the "correct" type of shoe for runners. However, this still remains anecdotal and there remains scant evidence proving the effectiveness of running shoe type with injury prevention (34,35). Barefoot running and minimalist shoes, which are lightweight running shoes designed to promote more of a forefoot strike, have also been studied over the last few years as they had a surge in popularity. It is believed that more anterior foot strike and increased cadence afforded by these shoes may help limit injury rates, as evidenced by decreased ground-reaction force and impulse data (36), but data demonstrating decreased risk of injury are lacking. Some studies even suggest increased injury (37,38). It should be noted that minimalist shoes have been demonstrated to show more foot bone marrow edema (39) and increased plantar pressure (40) compared to subjects with conventional running footwear. Regardless of the footwear, male and female runners appear to have similar foot-strike patterns (41).

MUSCULOSKELETAL COMPLAINTS OF THE FOOT AND ANKLE

Ankle Sprains

Ankle sprains are one of the most common musculoskeletal complaints encountered in modern practice, with half occurring during athletic activity (53). Most commonly, the anterior talofibular ligament is affected, but the calcaneofibular, posterior talofibular, and anterior tibiofibular ligaments may also be affected. The sex-difference literature is mixed on this topic, primarily due to the differences among age groups and sprain types. Women have repeatedly demonstrated higher injury incidence rates than men (44), with rates for women and men at 13.6 and 6.94 sprains per 1,000 exposures, respectively (44). Interestingly, the prevalence between sexes is equivalent (10.6% women, 11.0% men) (44) and the risk of suffering a first-time ankle sprain was not significantly higher in one sex than the other (42). Rates of ankle sprains in high school athletes, as a whole, occur at a rate of approximately 3.1 ankle sprains per 10,000 athletic exposures (52).

Studies for ankle sprain incidence in younger patients are mixed (43,45–54). Men/boys between the ages of 15 to 24 have been shown to have higher rates of ankle sprains than their female counterparts, which is likely related to the high rate of injury with athletic activity and increased risk-taking behavior in that cohort (43,46,50,53). The highest incidence has been reported in young males, while it is more common in older women compared to older men (108). Girls have been shown to experience the injury 1.25 times as often as boys in sex-comparable sports (e.g., sports played by both sexes such as basketball or soccer) (52). Both boys and girls sustain ankle sprains more often in competition than practice, with risk ratios of 3.42 and 2.71, respectively (52). High school- and college-age women have demonstrated more Grade I injuries compared to males; however, there are similar rates of more severe ankle sprains (Grades II and III) between the sexes (47).

An examination of ankle injuries (predominated by ankle sprains, but not exclusive to that injury) in high school athletes by Nelson et al. (50) demonstrated the following:

- Boys' basketball had the highest rate of injury, followed by girls' basketball, then boys' football.
- Ankle injury rates were similar between the sexes.
- In sports played by both sexes (e.g., soccer, basketball, baseball, or softball), boys had higher rates of practice-related ankle injuries while girls had higher rates of competition-related ankle injuries.
- Injuries to the ankle were the most frequent injury in both boys' and girls' soccer, but the proportion of ankle injuries to total soccer injuries was higher among girls (31.5%) than it was among boys (23.5%).

After ankle sprain, men demonstrated an increased risk of residual symptoms compared to women (odds ratio [OR]: 4.78) (109). In this study, however, the male cohort included a larger percentage of athletes than the female cohort, which may have introduced bias.

In young athletes, 23% report chronic ankle instability, which was more commonly reported in high school athletes compared to collegiate. Women report chronic ankle instability significantly more than men (55). The higher incidence of ankle instability may be related to the increased time to stability (the time period that it takes for the ankle musculature to return to a baseline variation after jumping) exhibited in asymptomatic women than in men (24).

When examining medial ankle sprains, men outnumber women in incidence by a ratio of 3:1 (56). Medial ankle sprains tend to be higher-force injuries, in which men are more often involved. Due to the uncommon nature of medial ankle sprains, there is little in the literature looking at the sex differences.

In contrast, high ankle sprains and syndesmotic injuries have been studied most in military populations. Waterman et al. (56) found the incidence of syndesmotic injury to be 480 per 100,000 person-years with a nonsignificantly higher incidence in men (490) than in women (460). This value is felt to be much higher than the general population, however, as the cohort included those participating in rigorous physical activity on a daily basis. In a large cohort of emergency department visits in eight states, the incidence rate was lower than the previously mentioned study—2.15 per 100,000 person-years for men and 1.65 for women (57). The statistical comparison was not reported, but was likely significant given the large amount of subjects. In this study, the 18- to 34-year-old age group contained the highest rate of incidence. The incidence rate in the general population most likely lies somewhere between these two rates, and it is likely that men have a slightly increased risk of injury. The difference between sexes may be accounted for by anatomical differences (110), where men tend to have larger tibiofibular clear space with larger tibiofibular overlap (111). Additionally, as men tend to be more commonly involved in high-energy trauma, they are more at risk for unstable syndesmotic injuries (112).

Differences in incidence rates of ankle sprains between the sexes is likely due to many causes. A variety of hypotheses have been raised, including hormonal differences, neuromuscular control differences, anatomic variances, and ligamentous laxity differences (57,113).

Pes Planus

The foot is often viewed as three sets of arches—an anterior transverse arch, a lateral longitudinal arch, and a medial longitudinal arch, as seen in Figure 10.3. Pes planus, or flatfoot, is defined as a flattening of the medial arch (114). Ligamentous, tendinous, fascial, and muscular structures all play a role in the stabilization of the medial arch. Asymptomatic pes planus is generally considered to not be pathologic and is not commonly treated. Arch height has been shown to be a risk factor for lower extremity injury (115). Figure 10.4 demonstrates an x-ray of a patient with pes planus.

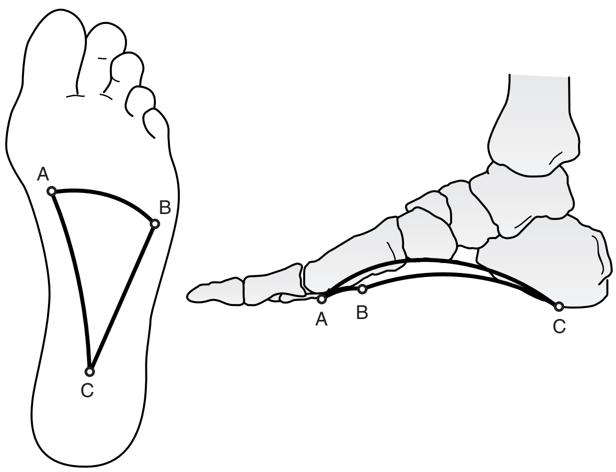

FIGURE 10.3: Arches of the human foot. (A,B) Anterior transverse arch. (B,C) Lateral longitudinal arch. (A–C) Medial longitudinal arch.

FIGURE 10.4: Lateral x-ray image of a 16-year-old girl with pes planus (flatfoot).

TABLE 10.2: Flatfoot Rates for Children

Cohort	Boys vs. Girls
Ages 3 to 10; 940 children, Colombia	18.2% prevalence in boys and 13.1% in girls (OR: 1.55) (67)
Ages 3 to 6; 835 children, Austria	52% prevalence in boys and 36% in girls (62)
Ages 3 to 6; 1,598 children, Taiwan	43.8% in boys and 30.6% in girls (59)
Ages 7 to 12; 2,083 children, Taiwan	67% of boys and 49% of girls (58)
Age 17; 825,964 adolescents, Israel	16.2% of boys and 11.7% of girls with flexible pes planus (66)

The prevalence rates for this condition have been studied in numerous populations, particularly in children, for which a greater array of management options exist, including plaster casting, splints, muscle training, orthoses, and specialty shoes. The prevalence rates of pes planus are shown in Table 10.2. A general trend is that boys have a higher prevalence rate than girls, but the rates are variable depending on diagnostic criteria and population studied. The arch height for boys has also been studied, and a significant increase occurs around the ages of 12 to 15 for boys and 10 to 15 for girls (116). The arch heights in boys age 7 to 15 tend to be lower than those in girls (116), which is not the case in adults (117). Boys also have a thicker midfoot fat pad, which may also play a part in the diagnosis of pes planus (118).

In adults, men have been shown to have flat feet significantly more often compared to women, with an odds ratio of 1.23 (65). Other associated factors include advanced age, greater body mass index (BMI), bunion, hammertoe, poor health, Asian and African American races, and white-collar occupation (63,64). One interesting factor for men is that those with pes planus were twice as likely to also have hallux valgus compared to men without pes planus (61). Men also tend to have a greater navicular drop in asymptomatic individuals, which may predispose them to the higher incidence (61).

In one prospective study of military cadets (60), 33 of 512 new cadets were identified as having pes planus, using relatively rigid inclusion criteria. Similar to the other adult pes planus studies, women had smaller feet and a lesser degree of pes planus, yet still sustained more injuries than men.

Hallux Valgus

Hallux valgus (Figure 10.5) is a deformity of the foot with first MTP joint subluxation and medial bony enlargement over time and is also commonly called a bunion. It has been shown to be more prevalent in older patients, African Americans, those with pes planus, and those with knee/hip osteoarthritis (61,69). Surgical correction for hallux valgus is a common orthopedic procedure (119). As previously

FIGURE 10.5: Weight-bearing x-ray image of a 50-year-old man with hallux valgus.

mentioned, this malady appears to be related to the effect of shoe-wear—women who wore high-heeled shoes during the ages of 20 to 64 had an increased likelihood of hallux valgus (61).

Women show a greater incidence of hallux valgus than men in several studies (26,30,68–72). One author (71,72) reports treating 53 male feet over a 20-year period, compared to 812 female feet. The female predominance in hallux valgus is not only isolated to the older population—girls are also more likely to seek treatment than boys for the condition (120). The effect of BMI on hallux valgus appears to also differ between the sexes. In women, a higher BMI is inversely associated with the presence of hallux valgus, while in men, those with a BMI between 25.0 and 29.9 had an increased likelihood of hallux valgus compared to those with a normal BMI (61). The authors felt that the likely reason for this sex-based difference was that women with lower BMI may tend to wear more fashionable (narrow toe-box) shoes, but this was not proven. Additionally, as mentioned previously, there is a correlation between the presence of hallux valgus with the presence of pes planus seen only in men (61).

Plantar Fasciitis

Plantar fasciitis, which is more appropriately termed plantar fasciopathy, is a disorder of the plantar fascia, which extends from the plantar tubercle of the calcaneus to the metatarsal heads. It presents most commonly with pain in the medial portion of the plantar tubercle and affects approximately 2 million people in the United States alone (73). Common treatments include steroid injections, deep-tissue mobilization, foot orthotics, night splints, extra-corporeal shockwave therapy, and surgical release. One study demonstrated that men had lower levels of postoperative pain from plantar fascia release and a quicker return of function (121).

Differences in the prevalence of plantar fasciitis between the sexes are mixed, and the majority of the literature demonstrates similar rates between them (73,74). Women aged 40 to 60 have been described as having the highest incidence of the disorder (73). When looking at U.S. military recruits, women have demonstrated an increased rate of plantar fasciitis (1.96 times more than men). Women also tend to have more plantar heel spurs than men (3), which may suggest increased traction on the plantar fascia. The plantar fascia thickness at the point 1 cm distal to the insertion has been demonstrated to have different values between the sexes (122), which may play a part in these potential differences. Conversely, male runners have demonstrated a greater incidence compared to female runners (97). A major concern with plantar fasciitis is progression to plantar fascia rupture, which is associated with steroid injection and appears to happen equally between the sexes (123).

Morton's Neuroma

Morton's neuroma is a common forefoot complaint due to an inflamed plantar nerve without a known etiology. It affects the third web space of the forefoot most commonly and results in pain and numbness or tingling that radiates to the affected nerve distribution to the toes. Due to the debility caused by the pain, foot and ankle surgeons are commonly called on to perform neuroma excisions (78). One of the theories related to the etiology of the condition is narrow shoe-wear. It thus comes as no surprise that women are more commonly affected than men (75–78).

Morton's neuroma accounted for approximately 50.2 out of 100,000 presentations to primary care providers in the year 2000 for men, and 87.5 out of 100,000 presentations for women (76). Middle-aged women appear to be the most commonly affected (75,77,78). In an Australian study, when patients required hospitalization for Morton's neuroma, the condition was three times more likely to happen to a woman than a man. Most cases occurred in the 50- to 54-year-old age group in women (age 55 to 59 in men) (77).

Chronic Exertional Compartment Syndrome

Chronic exertional compartment syndrome (CECS) is a condition that most commonly affects the legs, with a reported incidence of up to 30% (124). It is characterized by reversible ischemia in an enclosed fibrosseous space leading to decreased perfusion and pain. Symptoms usually resolve with rest and without permanent damage, unless an athlete continues to exercise through the pain, which can lead to acute compartment syndrome. The increased pressure in the compartment can be measured, and this intramuscular pressure is used for diagnosis. This diagnostic method has been called into question (125) as it is common to have high pressures in asymptomatic individuals.

In a study by Baltopoulos et al. (79), 48 asymptomatic participants underwent compartment pressure testing before, during, and after exercise testing. The 48 participants consisted of 12 female high-level runners, 12 male high-level runners, 12 female recreational athletes, and 12 male recreational athletes. Compartment pressures increased during the test in all subjects, and decreased after exercise in all subjects, but not to the point of pre-exercise levels. The recreational athletes had lower compartment pressures than the high-level athletes. Men had higher compartment pressures than women in the pre-exercise and during-exercise time points, but no difference post-exercise.

Though the Baltopoulos et al. study may seem to suggest that men would be at a greater risk for compartment syndrome, this study was done on asymptomatic individuals. Some studies suggest that symptomatic CECS is similar between the sexes (81,82). A retrospective study by Davis et al. (80) looked at 153 subjects with CECS that were verified by elevated compartment pressures; women accounted for 60% of the patients. Women accounted for more of the CECS diagnoses in competitive soccer, track/cross-country, lacrosse, and field hockey. Men accounted for more of the CECS diagnoses in noncompetitive running. A study of Army servicepersons also found that female sex was significantly correlated with an elevated risk for CECS (83).

Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy (RSD), is a poorly understood condition that is characterized by a painful limb that is disproportionate to any inciting event and contains sensory, vasomotor, sudomotor, and/or motor signs and symptoms (126). It has two subtypes—type I, which does not relate to a dermatomal or peripheral nerve distribution; and type II (causalgia), which relates to a peripheral nerve lesion. CRPS is likely to have elements of psychological, sympathetic, inflammatory, and genetic factors all involved in its pathophysiology (84).

Women are affected more commonly than men with CRPS (84–87), though it should be noted that most studies encompass all areas of the body, not just the foot/ankle. Women of European descent have a 3.4- to 4-fold higher incidence rate than men, while two thirds of Japanese cases are women (84). However, Korean men seem to be slightly more affected than women (84). In children, more than 80% of those with CRPS are girls (84). Interestingly, overall outcome may not be related to sex (85). Female sex has also been identified as a risk factor for CRPS type I, particularly postmenopausal females with ankle fractures or dislocations (87).

Osteoarthritis

It is estimated that 10% of all people over the age of 65 have foot pain attributed to osteoarthritis (OA) (88). Despite its high prevalence, OA of the foot has received less attention than other joints. OA in the foot has been found to have the highest radiologic prevalence in the second cuneometatarsal joint (88), but the first MTP joint is the most common symptomatic joint (90). The prevalence of OA in the ankle is generally accepted to be lower, in the range of 5 to 100 persons per 10,000 (127,128) and most often attributed to a history of prior trauma (95,129). It can have a similar impact on quality of life as hip OA (130).

When comparing the radiographic rates of OA in the foot, women likely are more commonly affected. Though statistical significance was not reported, Van Saase et al. (90) reported larger female prevalence rates of radiologic grade 2+ OA in a large Dutch cohort in the tarsometatarsal joint and the MTP joints, for all ages over 40 (see Figure 10.6). Men had a greater prevalence only in the proximal interphalangeal (PIP) joints of the foot. For both sexes, the rates of OA increased with age, as would be expected. In a separate study, women were found to have a greater median number of foot joints affected by OA (diagnosed by x-ray) than men (88). Similarly, Roddy et al. examined the prevalence of symptomatic radiologic OA of the foot (89). This study demonstrated that the first MTP joint was most commonly affected. Women were more likely to have symptomatic OA than men, particularly in the older age groups. They were also more likely to have disabling symptomatic OA compared to men.

Hallux rigidus is a condition seen with degenerative osteoarthritis of the first MTP joint with corresponding reduced sagittal motion in the first ray. It affects approximately 2.5% of people aged 50 or greater (131). Women are more commonly affected than men (91–93). One potential contributing etiology may be evidenced in a study of ballet dancers, in which females with longer second toes had a higher incidence of hallux rigidus and correspondingly increased pain scores, while men had no ideal pattern of toe lengths (132). Hallux rigidus was found not to be associated with shoe-wear or elevated first ray (91), but there have been correlations with metatarsal head articular shape (i.e., flat versus chevron) and metatarsal adductus (92).

For the ankle, men and women appear to have similar prevalence rates of OA (Figure 10.7). Over a decade-long study, Valderrabano et al. (95) collected information on 390 patients with end-stage ankle OA, and the split between sexes was almost 50/50. A study examining total ankle replacements in Finland showed that 63% of surgeries were performed on women (94), but sex had no effect on outcome after total ankle replacement. As opposed to the foot, the majority of ankle OA comes from prior trauma. This appears to balance between the sexes, where men have a greater incidence of ankle ligament lesions while women have more malleolar fractures (95). Primary OA is relatively rare in the ankle and may be more common in men (95).

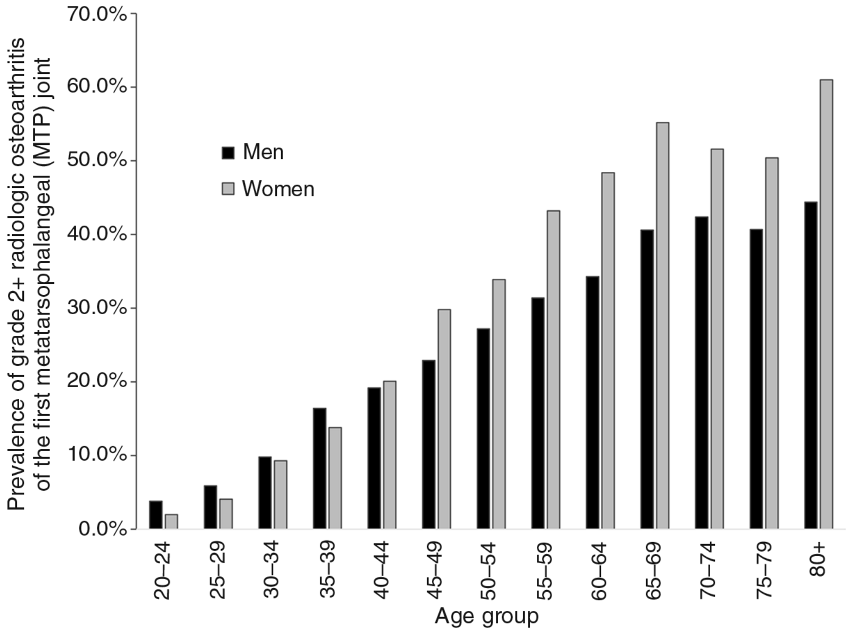

FIGURE 10.6: Prevalence of osteoarthritis in the first metatarsophalangeal joints of men and women.

Source: Adapted from Ref. (90). Van Saase JL, Van Romunde LK, Cats A, et al. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. *Annals of the Rheumatic Diseases*, 1989;48(4):271–280.

FIGURE 10.7: Mortise view x-ray image of a 68-year-old man with post-traumatic osteoarthritis of the ankle.

Stress Fractures

Stress fractures are covered more in-depth in Chapter 12. However, specific to the lower leg, a few studies have shed some light on differences between the sexes. Common locations of stress fracture include the tibia, navicular, metatarsals, and fibula (133). A study by Changstrom et al. (134) tracked stress fractures in U.S. high school athletes and found that the foot and lower leg were the most common locations of stress fractures for all athletes. In sex-comparable sports (basketball, soccer, volleyball, track and field, and cross-country), girls had a greater number of stress fractures, though these were counts and not rates. The combined effect of sex and body location was not reported in the study. By comparison, out of a total of 387 stress fractures, there were 135 in the foot and 156 in the lower leg compared to only 12 in the ankle. A separate study (97) examined 2,002 patients with running-related injuries in British Columbia and did not show a difference in tibial stress fractures between the sexes, but it did show that lower BMI in female runners was associated with more tibial stress fractures, which has been demonstrated elsewhere (135). Metatarsal stress fractures have been demonstrated to be more common in male high school runners (135).

Other Musculoskeletal Disorders

- For **overall foot pain**, a prospective study of older adults demonstrated a 4-to-1 female predominance (96). Interestingly, a subgroup analysis was performed demonstrating that impaired foot protective sensation was associated with falls in men (OR: 5.1).
- **Posterior tibialis** tendon rupture has been shown to occur more commonly in middle-aged and obese women (136). No significant difference was seen in posterior tibialis injury in a running population between men and women (97).
- In a study examining the results of surgical intervention on 34 patients with **tarsal tunnel syndrome** (137), 74% of the subjects were women, though it was not stated that these were consecutive patients, so it is heavily subject to selection bias.
- In a running population, there was no difference between the sexes in the incidence of **metatarsalgia** (97).
- **Sesamoid** prevalence in the feet was examined in a comprehensive systematic review and meta-analysis (138). Men and women had no difference in partition (lateral and/or medial sesamoid bones). There were more commonly fifth MTP joint sesamoid prevalence (1.47 times more common) seen in men, otherwise there were no other differences in sesamoid prevalence in the other joints between the sexes. Sesamoid pain was not studied.
- A prospective study examining **anterior ankle impingement** without ankle arthritis (98) collected 42 male patients and just 4 female patients with a mean age of 29 years, though this is also subject to selection bias as they were all patients who elected to undergo surgery. Patient sex had no effect on postoperative outcome. A similar study of 55 consecutive patients with **posterior ankle impingement** who underwent endoscopic removal of bone fragments and/or scar tissue was performed (99), of which 30 were male and 25 were female (median age 29 years).
- **Lisfranc injury** prevalence does not appear to be affected by a patient's sex (101). Additionally, 2 years after isolated Lisfranc injury surgery, there was no association between sex and functional outcome (100). Densitometric differences have been identified between the sexes in the bones of the first tarsometatarsal joint (139).
- **Toe fractures** are extremely common, with a prevalence of around 3% (103). In a Dutch study (103), over 30 months of consecutive phalangeal fractures of the foot were collected, of which incidence was split evenly between men and women. Prior studies have demonstrated male predominance, however (102). In the aforementioned Dutch study, women tended to have worse outcomes than men, though most respondents had excellent outcomes.
- For **metatarsal fractures** treated conservatively, men have been shown to have better functional outcomes than women (105). Fifth metatarsal fractures of the Jones type occurred more frequently in men, while avulsion fractures occurred more frequently in women, and functional outcomes were equal between the sexes (104).
- **Ankle fractures** that were treated surgically tend to have better functional improvement in men than women (140,141). Incidence of ankle fractures is roughly equal between the sexes (102,106), though talus fractures occur more commonly in men. Ankle fractures are more likely to occur in young men or older women (106). Men have a greater chance of having a Weber C ankle fracture than women (106).
- **Avascular necrosis of the sesamoid** is uncommon, but is more commonly associated with women (107).

CONCLUSION

Women tend to have more foot and ankle disorders than men. Biomechanical and extrinsic factors, mainly shoe-wear and activity differences, are likely the main contributors to these disparities.

Summary of Prevalence of Foot and Ankle Disorders Between Men and Women

Musculoskeletal Complaint	Sex With Higher Prevalence
Shoe-related pain	Women (26,28–31)
Ankle sprains	Similar overall between sexes, though likely higher for boys/men in younger age groups and higher for women in older age groups (42–54)
Chronic ankle instability	Women (55)
Medial ankle sprains	Men (56)
High ankle sprains	Possibly men (56,57)
Pes planus/flatfoot	Boys and men (58–67)
Hallux valgus	Women (30,68–72)
Plantar fasciitis	Similar between sexes (73,74)
Morton's neuroma	Women (75–78)
Chronic exertional compartment syndrome (CECS)	Possibly women (79–83)
Complex regional pain syndrome (CRPS)	Women (84–87)
Osteoarthritis of the foot	Women (88–90)
Hallux rigidus	Women (91–93)
Osteoarthritis of the ankle	Similar (94,95)
Foot pain	Women (96)
Metatarsalgia	Similar (97)
Anterior ankle impingement	Men (98)
Posterior ankle impingement	Similar (99)
Lisfranc injury	Similar (100,101)
Toe fractures	Possibly men (102,103)
Fifth metatarsal fractures	Jones type more common in men, avulsion type more common in women (104,105)
Ankle fractures	Similar (102,106)
Avascular necrosis of the sesamoid	Likely women (107)

The terms "boys" and "girls" are used for those under the age of 18, while "men" and "women" refer to those aged 18 and over.

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11

RUNNING

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Running is one of the most common forms of exercise that is used by a wide variety of elite and recreational athletes. Nearly all sports involve some type of running, if not during play, then certainly as a part of training. The incidence of lower extremity running injuries ranges from 19.4% to 79.3% (1). The most common area of injury is the knee; other areas of injury from running include the shin, Achilles tendon, calf, heel, foot, hamstring, and quadriceps (1). Other chapters of this book describe the sex-specific difference in these lower extremity injuries. This chapter is dedicated to understanding the sex-specific differences of lower extremity biomechanics that may predispose an athlete to injury during running. Sex differences in static lower extremity alignment have been well described. Differences in static structure have been theorized to contribute to running injuries. Females generally have greater anterior pelvic tilt, femoral internal rotation, genus valgus, and recurvatum than males (2). More recently, sex-specific differences in running mechanics have been reported in the literature. The most consistent trend is with frontal and transverse plane hip and knee kinematics. Female runners most consistently demonstrate increased femoral adduction and internal rotation. In addition to kinematic differences, sex-specific differences in kinetics, spatiotemporal differences, muscle activation, and timing as well as pathomechanics have been reported. Controversy exists though, as not all studies support these differences between sexes. This chapter reviews the literature regarding sex-specific running mechanics and attempts to draw some meaningful clinical conclusions to guide the clinician in specific management of runners with musculoskeletal pain related to running pathomechanics.

BIOMECHANICS AND MOTOR CONTROL

Running requires a complicated series of muscle activations throughout a range of multiple joint motions occurring within the gait cycle. The gait cycle of running includes a stance phase (40% of the cycle) and a swing phase (30% of the cycle), but the main difference between running and walking is due to the period between stance and swing phases. In running, there are two float phases (15% of the cycle each) in which neither limbs are on the ground. During walking, the phase between stance and swing consists of a period of double support, where both limbs are in contact with the ground. Running is a complex process that cannot easily be summarized by one measure. Sex differences can exist at multiple levels of the biomechanics and motor control involved with running (see Figure 11.1 in the Conclusion section). A study with a comparatively large sample size (483 recreational and competitive runners) attempted to identify kinematic differences between the sexes to assist with improving the understanding of injury pattern differences (3). The authors reported their significant findings in each plane of movement and phase of the gait cycle. In the frontal plane, female runners demonstrated greater maximum and minimum peak hip adduction and knee abduction, greater hip adduction at initial contact, and greater hip adduction and knee abduction at terminal stance compared to males. Female runners also exhibited reduced peak ankle eversion compared to males. In the transverse plane, female runners exhibited greater external rotation of the femur at initial contact and maximum external rotation. In the sagittal plane, female runners exhibited lower minimum peak knee flexion, lower knee flexion at terminal stance, and lower peak ankle dorsiflexion compared to males (3).

Correlations between the sex differences in frontal and transverse motion and kinematics, muscle activation, and timing across various running speeds and inclines have been investigated (4). As with many previous studies, females displayed significantly greater peak hip internal rotation and adduction during stance, as well as hip adduction excursion compared to males. These differences were demonstrated at all walking and running speeds and surface inclinations. Females displayed significantly greater non-sagittal hip and pelvis motion during walking and running across a range of speeds and inclines, whereas sagittal motion at the hip was consistent between sexes.

Significant sex-specific muscle activity differences have been demonstrated. Gluteus maximus activity was consistently greater in females during walking and running. Gluteus maximus activity across the stride cycle in females was approximately twice that of males during all speed-incline conditions. Gluteus medius and vastus lateralis activity also differed in response to speed between sexes. A significant speed by sex interaction was present for gluteus medius and vastus lateralis activity across the stride cycle, particularly during terminal swing to initial loading of running, indicating females increased gluteus medius and vastus lateralis activity with speed to a greater extent than males. Males maintained a fairly consistent level of gluteus medius and vastus lateralis activity across running speeds, whereas females displayed a progressive increase in activity with speed. The sex-specific response of these muscles to changes in speed and incline supports the concept that as task challenge increases, males and females use different neuromuscular strategies. It appears that there are clear sex differences in hip kinematics and muscle activity across a variety of walking and running speeds and surface inclinations. Females display greater peak hip internal rotation and adduction as well as gluteus maximus activity for all walk and run conditions, are likely working at a greater percentage of maximum, and therefore are possibly more susceptible to the effects of fatigue (4,5).

Sex differences with gluteal muscle activation and timing have also been correlated with kinematic and kinetic measurements (4,5). No difference in gluteus medius or gluteus maximus activation *timing* was noted between males and females while running. However, differences were identified in gluteal muscle activation *levels* between male and female during running. Normalized gluteus maximus peak activation level was 40% greater and the average activation level was 53% greater in females compared to males. Associated kinematic differences between males and females were also observed. Females made initial contact with the running surface with 4.0° more hip adduction and 2.8° more knee abduction compared to males. Females also demonstrated 5.1° greater hip adduction at peak vertical ground reaction force. The authors concluded that these results highlight the relative importance of the gluteus maximus compared with the gluteus medius to the sex bias for patellofemoral pain syndrome (PFPS) and related sex-specific pathomechanics. They theorize that greater gluteus maximus activation levels in females during running may lead to the earlier onset of fatigue in females compared to males, thereby reducing their force-generating capacity following exertion. A reduction in gluteus maximus force during prolonged running may promote aberrant hip and knee joint kinematics and greater retropatellar stress. If premature gluteus maximus fatigue is expected among females during a prolonged run, hip extension (gluteus maximus) endurance training may be warranted in efforts to prevent altered hip kinematics (increased hip internal rotation or adduction) that may contribute to increased patellofemoral joint stress and PFPS (4). Conversely, females demonstrated lower levels of fatigue in knee extensors and plantar flexors during ultra-running. It is suggested that this could contribute to the relatively improved performance of females during ultra-running compared to shorter distances (6).

Sex differences have been reported in pelvic and thoracic coupled motions. Female runners demonstrated greater pelvic obliquity and thoracic axial range of motion as well as greater pelvic tilt and anterior lean compared to male runners (7). Relationships between pelvic and thoracic motion and hip strength have also been reported (7). At all running speeds, as hip abductor strength increased, pelvic obliquity motion decreased. As hip extensor strength increased, thoracic axial rotation range of motion (ROM) decreased during all running speeds. The authors discuss clinical implications based on the biomechanical coupling, discussing that it is likely that internal femoral rotation, femoral adduction, pelvic tilt, and thorax axial rotation exhibit some form of coupling during stance. They discuss that during initial ground contact during running, the trunk is near maximum posterior axial rotation on the contralateral side of the stance limb and then undergoes maximum forward rotation near terminal stance. If the sex-prevalent pathomechanics of femoral internal rotation and adduction increases through stance phase, the thorax will have increased rotation at terminal stance to maintain forward-directed motion. This might result in increased thoracic transverse plane rotation with decreased hip strength.

Researchers have identified spatiotemporal sex differences in the three-dimensional angular rotations of the lumbopelvic-hip complex during running (8). Females displayed shorter stance time, swing time, stride time, and stride length and a higher stride rate than males. Females also tended to begin hip flexion immediately before toe-off, whereas males remained in hip extension for a short period during the initial swing. Regarding kinematic differences, there were significant differences throughout the lumbopelvic-hip complex in all planes of movement at various points of the running gait cycle. Females tended to display a greater peak-to-peak oscillation for most of the angular rotations (8). At the hip in the sagittal plane, females tended to have a greater angle of peak hip flexion during the latter third of swing and a greater amplitude of frontal plane hip adduction-abduction than their male counterparts. At the lumbar spine, females displayed significantly greater amplitudes of lumbar spine frontal plane side bending and transverse plane axial rotation. At the pelvis, females demonstrated greater frontal plane anterior-posterior pelvis tilt, frontal plane obliquity, and transverse plane axial rotation. Females statically stood with a greater anterior pelvic angle, ran with a greater sagittal plane pelvic excursion, and ran with a greater average position of anterior pelvic tilt compared to males throughout the entire gait cycle.

Sex-specific kinetic differences have been described. Most specifically, females have demonstrated greater knee loading than males (9). Females have demonstrated greater knee extensor moments, greater patellofemoral forces and loading rates, and increased patellofemoral contact pressures than males (10,11,12). Females have also demonstrated higher initial peak hip adduction moments, lower ankle plantar flexor moments, and lower Achilles tendon loads than males (13,14,15).

COMMON CLINICAL SYNDROMES

Kinematic and kinetic differences have been proposed to contribute to running injuries, most specifically patellofemoral pain syndrome, iliotibial band syndrome, and stress fractures. One of the most widely studied of these injuries is PFPS. Females are twice as likely to experience PFPS compared with males (16). Female U.S Naval Academy recruits were 25% more likely to have a history of PFPS than males, and female recruits were more than twice as likely to subsequently develop PFPS as males (17). Recent studies have suggested that abnormal hip and knee mechanics are associated with PFPS in females (12,18,19,20,21,22). These abnormal mechanics include excessive peak contralateral pelvic drop, peak hip adduction (5,18,23), peak hip internal rotation (14,18,24), decreased peak knee adduction (11,21,22), and increased tibial rotation (11). In combination, these motions result in dynamic valgus of the knee, resulting in lateral patellar tracking and an increase in the loading forces on the lateral aspect of the patellofemoral joint (10,11,19,20,25). Importantly, these abnormal mechanics appear to be present in females with PFPS across a variety of activities, including both running and during a single leg squat (14,18,22,23,24,26). Willy et al. also reported that females with patellofemoral pain performed a single leg squat and ran with greater femoral adduction when compared with the males with patellofemoral pain (22).

The precise kinematics and kinetics behind the incidence of patellofemoral pain in female runners, however, are not consistent across the literature and remain ambiguous. A recent study recognized the discrepancies in the literature and investigated the patellofemoral joint loads produced by female runners in contrast to males in order to gain further insight into the increased incidence of patellofemoral disorders in females (9). The authors used musculoskeletal modeling to calculate patellofemoral joint forces and pressures from healthy males and females to determine sex differences. Their results add to the body of knowledge regarding forces acting on the patellofemoral joint and assist in drawing clinical conclusions to guide sex-specific exercise prescription and gait training. Females exhibited significantly greater peak knee extensor moments compared to males. Females also had greater patellofemoral force and patellofemoral force load rates, significantly increased patellofemoral contact pressures, and significantly increased peak knee abduction moment compared to healthy males.

It is theorized that several mechanisms may serve to explain the increased forces, related moments, and kinematic findings that are fairly consistent across the literature. Female runners have been associated with hip musculature weakness and lack of neuromuscular control at the knee joint during dynamic activities. Related studies examining landing mechanics have also associated weakness of the hip musculature to a compensatory strategy whereby landing mechanics in females relied more heavily on the knee extensor moment to absorb impact forces (15). Female runners have also been shown to exhibit reduced ankle plantar flexor moments and Achilles tendon loads in comparison to males. Enhanced plantar flexion from the ankle joint may be a sex-specific mechanism by which the loads at the knee joint are reduced in male runners (13). Female recreational runners exhibit significantly greater knee loading compared to males. Given the proposed relationship between knee joint loading and patellofemoral pathology, the current investigation does appear to provide some insight into the high incidence of patellofemoral pain in females (9).

Iliotibial band syndrome (ITBS) is another common running injury where frontal and transverse plane pathomechanics have been shown to be related to injury etiology. Female runners with ITBS have exhibited significantly greater peak hip adduction, knee internal rotation angles, and peak rearfoot invertor moment compared with healthy controls (27,28). Transverse plane kinematic differences in male and female runners with ITBS have been described. Female runners with ITBS demonstrated significantly greater hip external rotation angles during 52% to 54% (and meaningful differences during 23% to 60%) of the running gait cycle as compared to male runners with ITBS. A different running kinematic profile was also found for female and male runners with ITBS in comparison to sex-matched healthy controls. Specifically, female ITBS runners exhibited significant differences in transverse plane *hip* kinematic gait patterns while male ITBS runners exhibited significant differences in transverse plane *ankle* kinematic gait patterns as compared with their respective healthy counterparts. The authors therefore conclude that clinicians treating female runners with ITBS should focus on proximal muscle strengthening programs, whereas male runners should focus on distal muscle strengthening programs to prevent ITBS injury (27).

Spatiotemporal sex differences, particularly in the three-dimensional angular rotations of the lumbopelvic-hip complex during running, are felt related to the higher incidence of pelvic and femoral stress fractures in females than males. In one prospective study of high-level track and field athletes, Bennell et al. found pelvic and femoral stress fractures only in female track and field athletes, mostly mid-distance and long-distance runners (29).

Taunton et al. reported similar rates of overuse Achilles tendon injuries in male (8% of running injuries) and female (10% of running injuries) runners (16). Overall, however, males experience a greater number of Achilles tendon injuries compared to females at a rate of 2:1 to 12:1 (13,30,31,32,33).

This discrepancy between the sexes may be related to a greater level of participation in ball sports by males (13,34). Increased Achilles tendon loading in males compared to females may also predispose to Achilles tendon injury (13). Males have demonstrated a greater peak plantar flexion moment and Achilles tendon loading than females during running. Additionally, average and instantaneous Achilles tendon loading rates were significantly greater in male runners (13). The greater Achilles tendon loading and loading rates may contribute to the greater rate of Achilles injury reported in males. Higher stiffness of the plantar flexor muscles and Achilles tendon, evidenced by lower active elasticity, has been reported in men compared with women and has also been theorized to contribute to the higher incidence of Achilles tendon injury in men (35).

CONCLUSION

The results of summarizing the current literature in sex-specific biomechanics in the running athlete demonstrate some common trends as well as some controversies and conflicting results. Overall, there are highlighted differences in how males and females run. Understanding the consistent trends provides the treating clinician with important information to guide a sex-specific running evaluation, develop a management program for injury prevention and treatment, and institute a return to running program.

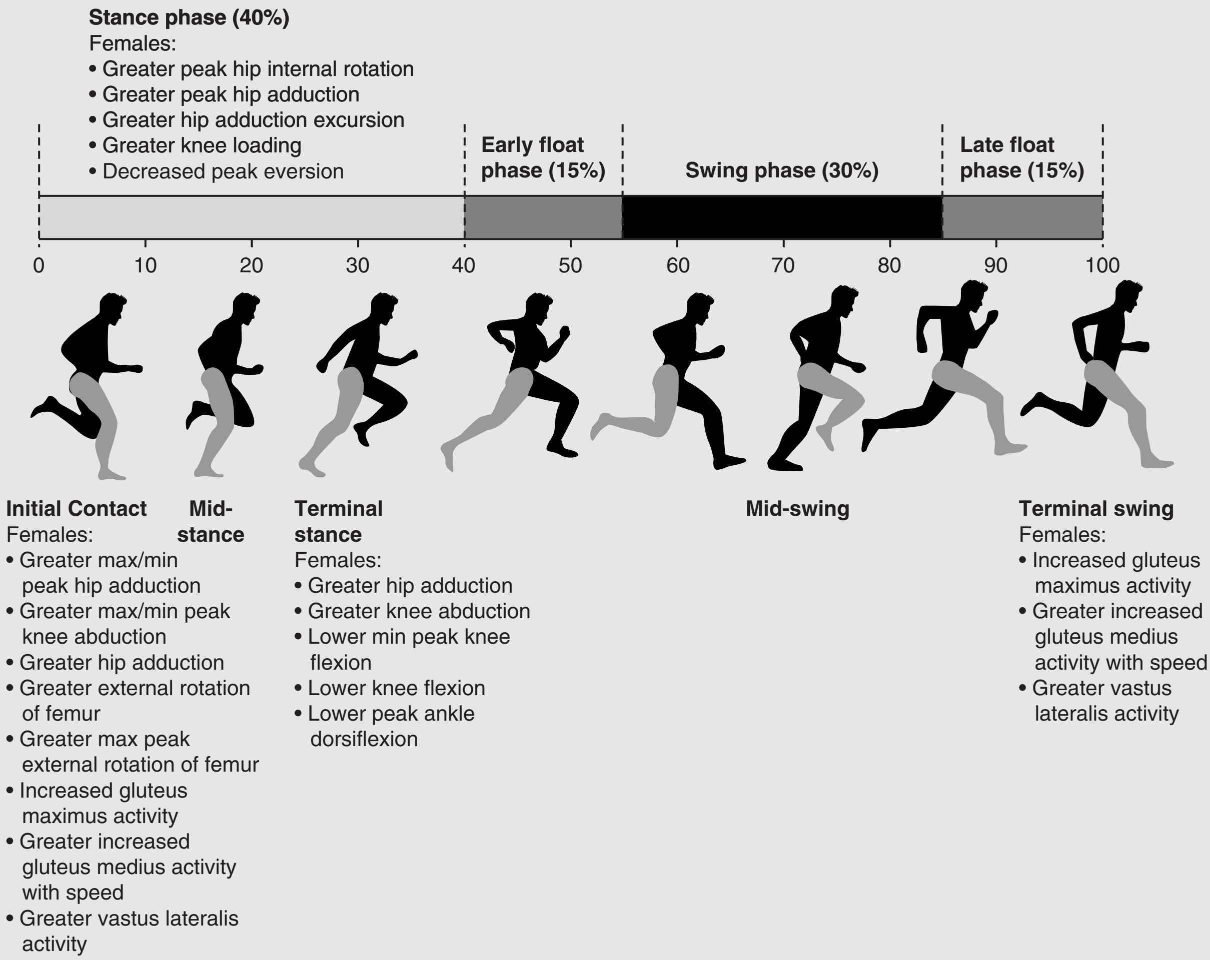

FIGURE 11.1: Running cycle.

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12

BONE

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OVERVIEW

Attaining peak bone mass and strength is an important aspect of overall musculoskeletal health in both female and male athletes. Failure to attain peak bone mass during childhood and adolescence may result in an increased risk for bone stress injuries (BSI) during sports participation and fractures associated with osteoporosis in older adults. In this chapter, we review the biological process of attaining peak bone mass during childhood and adolescence and the influence of sports participation on modulating bone health. Next, we discuss sex-specific clinical syndromes that can impair bone health, including the female athlete triad (Triad). We review sex-specific risk factors for BSI, a common overuse injury in athletes. Finally, we discuss the topic of bone health in older adult athletes.

BONE METABOLISM

Peak Accretion

Childhood and adolescence is a time of growth for the skeleton. Total body bone mineral content (BMC) reaches a plateau on average at ages 18 and 20 in females and males, respectively (1). For both sexes, peak bone mass is reached by the end of the second decade or early third decade of life (1,2). The rate of BMC accrual for both sexes may be greatest in the 4 years surrounding peak height velocity, with approximately 40% of BMC gained in the total body, femur, and lumbar spine during this time (1).

Bone mass is most commonly measured using dual-energy x-ray absorptiometry (DXA), which uses ionizing radiation to measure areal bone mass and determine density and quality of bone expressed as BMC and areal bone mineral density (BMD). Common locations for measurement include the lumbar spine (L1-L4 vertebrae), total body, and proximal femur/hip. In children and adolescents of both sexes, lumbar spine and total body less head (i.e., total body excluding contribution of bone mass from the skull, a non-weight-bearing skeletal site) are locations recommended to measure BMD and content, as the hip is prone to measurement error and variability in skeletal development (3). The DXA values measured for an individual at each site can be standardized to Z-scores and T-scores. In children, men less than 50 years of age, and premenopausal women, Z-scores are recommended to standardize individual results to a reference population standardized to sex, age, and ethnicity normal values (3).

In females who are physically active, including children to premenopausal adults, the American College of Sports Medicine (ACSM) recognizes a BMD or BMC Z-score of less than -1 as low bone mass for age (4). ACSM has not defined a similar criterion in male athletes. The International Society of Clinical Densitometry (ICSD) defines "low bone mass for chronological" age as BMC or areal BMD Z-scores of -2 or less for ages 5 to 19 years in both girls and boys (3). The term osteoporosis in children and adolescence ages 5 to 19 requires both BMD/BMC Z-score of -2 or less with a clinically significant history of fracture defined as one lower extremity long bone fracture, two or more upper extremity long bone fractures, or a vertebral compression fracture (3). Other measures of bone geometry can be derived from DXA measures, including hip structural analysis (HSA) or by using other technologies including peripheral quantitative computed tomography (p-QCT).

Response to Osteogenic Activity

Bone density and geometric properties are influenced by many factors, including extrinsic factors of physical activities that apply stress to the bone. In addition to Wolff's Law (5), the Muscle-Bone Unit theory (6) in children describes that muscle generates the greatest nontraumatic stress on the bone and influences bone health of growth during childhood and adolescence. Other studies have shown that weight-bearing physical activities increase bone mass accrual in children of both sexes (7,8), demonstrating the importance of ground impact forces in influencing bone density and strength.

Sports-specific loading can be categorized into the types of impact loading characteristics. In a review of the influence of sports participation on bone density and geometry in athletes ages 10 to 30 (9), we observed that sports that include activities that generate high impact and multidirectional impact loading (including jumping and ball sports) resulted in greatest BMD/BMC values and bone geometric properties (10–16). Mechanical loading may better explain osteogenic effects of sports participation for improved bone quality rather than high magnitude muscle forces (15). Site-specific loading characteristics influence bone density, as illustrated in racquet sport athletes who have observed greater BMC in the dominant arm compared to the non-dominant arm (14). Furthermore, swimming may result in reduced bone quality compared to sedentary age-matched controls (12) and swimming does not predictably improve bone health with continued participation (17). See Table 12.1 for types of sports and loading characteristics with bone density/geometry comparisons (9).

Jumping programs have been shown to increase BMC in both sexes when performed in early childhood. Gunter and colleagues studied a population of 205 boys and girls of average age 8.6 years old. Schools were randomly assigned to be the control or intervention school. In the intervention school, children performed a jumping program during a physical education program three times per week for 7 months consisting of 100 box jumps. At 7 months, the intervention group had 7.3% to 8.4% greater BMC values than the control group at all sites tested. The benefits of the jumping program reduced over time but remained greater in the intervention group than the control group 3 years after discontinuation of the jumping intervention (18). A subset of children who participated in the larger study (18) were followed for changes of hip BMC over 8 years, and children who participated in the jumping intervention maintained 1.4% greater hip BMC than the control group (19). These findings suggest early jumping activities may be a strategy to optimize future skeletal health in adulthood (20).

Ball sports are a form of high impact, multidirectional loading resulting in high ground reactions forces, similar to jumping. High impact and multidirectional impact sports, including ball sports, appear to confer greatest BMD and bone geometric properties, whereas running does not predictably increase BMD (13). Participation in ball sports has been observed to reduce risk for future fracture in the military and in runners when performed during childhood, particularly in males (21–23). Studies have not shown consistent benefits in fracture reduction in female athletes, and this finding may be explained by triad risk factors that may reduce or potentially eliminate these benefits (22,24,25).

The observation that participating in high impact loading activities including jumping and ball sports during childhood results in improved bone mineral characteristics during later life is supportive of the concept for a critical period to encourage physical activity during early puberty (26). However, discontinuation of sports activities may result in bone loss during adulthood for both former male and female athletes (27–29), suggesting that maintaining impact-loading activities is important to maintain the full benefits of prior sports participation in bone health.

TABLE 12.1: Loading, Bone Density, and Bone Geometry Patterns of Different Types of Sports, Divided by Loading Patterns

	Loading Patterns Influence Bone Health		
	Repetitive Low Impact	Nonimpact	High/Multidirectional (Odd) Impact
Type of Sport	Distance running	Swimming, cycling	Gymnastics, soccer, basketball, volleyball, racquet sports, hurdling, triple jump, high jump, step aerobics
Bone Density and Geometry Patterns	No consistent changes in BMC or BMD; improved geometric properties	No increases in BMC, BMD, or geometric strength	Greater BMC or BMD; increased measures of geometric strength

BMC: bone mineral content; BMD: bone mineral density.

Source: Table 12.1 is a summary of findings from Ref. (9). Tenforde AS, Fredericson M. Influence of sports participation on bone health in the young athlete: a review of the literature. *PMR.* 2011;3(9):861–867.

CLINICAL SYNDROMES

The Female Athlete Triad

The triad is defined as the interrelationship of energy availability, menstrual function, and BMD (30). The condition is considered a spectrum disorder (4) ranging from optimal health to disease for each component:

1. Optimal energy availability to low energy availability with or without an eating disorder
2. Eumenorrhea to functional hypothalamic amenorrhea
3. Optimal bone health to osteoporosis

Low energy availability (defined as the difference of energy intake to estimated energy expenditure standardized to fat-free mass) is considered the primary contributor to the triad and is more common in endurance athletes and in the female sex (31). Both athletes and non-athletes may have one or more component of the triad, although having all three components of the triad is less common (32–34). The effects of the triad appear summative, as female athletes with greater number of triad risk factors are at increased risk for low bone density and BSI (4,23,35,36). Since menstrual status may modulate differences in bone density and geometric properties (37), identification of at-risk female athletes is critical as delayed or "catch-up" bone mass accrual is not ensured (38). The 2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad provides guidelines for cumulative risk assessment of triad in female athletes (30). The Risk Factor Scoring and Medical Risk Stratification are included in Figure 12.1. This is an important advancement in providing evidence-based recommendations and best practices for female athletes with the triad. This information is a powerful tool to assist sports medicine professionals in determining clearance and return to play for female athletes. Additionally, the Female Athlete Triad Coalition provides online resources that are helpful for athletes, physicians, and other sports medicine professionals (www.femaleathletetriad.org). Screening questions for the triad have also been published and are important to include in preparticipation examinations (Figure 12.2) (30).

Risk Factors	Magnitude of Risk Low Risk = 0 points each	 Moderate Risk = 1 point each	 High Risk = 2 points each
Low EA with or without DE/ED	☐ No dietary restriction	☐ Some dietary restriction‡; current/past history of DE;	☐ Meets DSM-V criteria for ED*
Low BMI	☐ BMI ≥ 18.5 **or** ≥ 90% EW** or weight stable	☐ BMI 17.5 < 18.5 **or** < 90% EW **or** 5 to < 10% weight loss/month	☐ BMI ≤ 17.5 **or** < 85% EW **or** ≥ 10% weight loss/month
Delayed Menarche	☐ Menarche < 15 years	☐ Menarche 15 to < 16 years	☐ Menarche ≥ 16 years
Oligomenorrhea and/or Amenorrhea	☐ > 9 menses in 12 months*	☐ 6–9 menses in 12 months*	☐ < 6 menses in 12 months*
Low BMD	☐ Z-score ≥ –1.0	☐ Z-score –1.0***< –2.0	☐ Z-score ≤ –2.0
Stress Reaction/ Fracture	☐ None	☐ 1	☐ ≥ 2; ≥ 1 high risk or of trabecular bone sites†
Cumulative Risk (total each column, then add for total score)	_____ **points** +	_____ **points** +	_____ **points** = _____ **Total Score**

FIGURE 12.1: Female athlete triad: Cumulative risk assessment.

BMD, bone mineral density; BMI, body mass index; DE, disordered eating; EA, energy availability; ED, eating disorder; EW, expected weight.

Source: From Ref. (30). De Souza MJ, Nattiv A, Joy E, et al. Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad: 1st International Conference held in San Francisco, May 2012, and 2nd International Conference held in Indianapolis, May 2013. *Br J Sports Med.* 2014;48(4):289. Used with permission from BMJ Publishing Group Ltd.

- Have you eve had a menstrual period?
- How old were you when you had your first menstrual period?
- When was your most recent menstrual period?
- How many periods have you had in the past 12 months?
- Are you presently taking any female hormones (estrogen, progesterone, birth control pills)?
- Do you worry about your weight?
- Are you trying to or has anyone recommended that you gain or lose weight?
- Are you on a special diet or do you avoid certain types of foods or food groups?
- Have you ever had an eating disorder?
- Have you ever had a stress fracture?
- Have you ever been told you have low bone density (osteopenia or osteoporosis)?

FIGURE 12.2: Triad consensus panel screening questions.

Note: The Triad Consensus Panel recommends asking these screening questions at the time of the sport pre-participation evaluation.

Source: From Ref. (30). De Souza MJ, Nattiv A, Joy E, et al. 2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad: 1st International Conference held in San Francisco, May 2012, and 2nd International Conference held in Indianapolis, May 2013. *Br J Sports Med*. 2014;48(4):289. Used with permission from BMJ Publishing Group Ltd.

The concept of a parallel process of the triad in males has been proposed (39,40). Analogous to the female athlete triad, males may have impaired nutrition and lower sex hormones including testosterone, both of which may negatively influence BMD (40). Our understanding of a similar process in male athletes and health consequences are limited, as research characterizing the female athlete triad is based on greater than two decades of research.

Other Nutrition Considerations: Calcium and Vitamin D

In addition to adequate energy availability, other aspects of nutrition are important to ensure optimal bone mass accrual and prevention of BSI. The Institute of Medicine (IOM) guidelines in 2010 recommend calcium intake of 1,300 mg daily and vitamin D of 600 IU daily for both sexes ages 9 to 18 years old to optimize bone health (41). Table 12.2 is a summary of the recommended daily intake values based on age and sex. Research on target calcium and vitamin D intake for BSI prevention has been primarily performed in young adult female runners and military. Lappe et al. (2008) performed a randomized double-blind, placebo controlled trial in female U.S. Navy recruits; the experimental group supplemented with 2,000 mg of calcium and 800 IU of vitamin D daily benefited from one-fifth reduction in stress fractures compared to the control group over 8 weeks of basic training (42). In a population of competitive female runners ages 18 to 26, Nieves and colleagues demonstrated that higher intake of skim milk, dairy, and calcium reduced risk for stress fracture (43). Additionally, investigators reported that each cup of skim milk per day consumed was associated with 62% reduction in development of a stress fracture (43). A subset analysis within this population (43) found that female runners with daily calcium intake of 800 mg or less were six times more likely to develop a stress fracture compared to those with 1,500 mg or greater daily calcium intake, suggesting that calcium intakes of 1,500 mg daily may be most effective for prevention of BSI in young athletes (44). In a separate investigation, females ages 9 to 15 who consume greater vitamin D were found to have lower rates of stress fracture when performing high levels of high impact activity (45). A report in male military recruits average age 18 found that lower calcium and vitamin D intake values were associated with prospective development of stress fractures during a 4-month course of basic training (46). In summary, meeting intake values for calcium and vitamin D recommended by the IOM is essential during stages of growth and development.

Bone Stress Injuries

BSI represent the failure of bone to withstand submaximal repetitive loading, falling on a spectrum from stress reaction to stress fracture to complete fracture (47). These are a common form of overuse injury in athletes of both sexes. Most research investigations describe incidence of stress fracture injuries in their populations studied. Stress fractures are common and represent up to 20% of injuries seen in sports medicine clinics (48). Both sexes appear more susceptible to BSI at younger ages (49,50). Stress fractures are more common in childhood and adolescent females who participate in greater hours of running, dance/gymnastics, and basketball (51). Other studies have demonstrated that cross-country runners and track and field athletes of both sexes are commonly affected with stress fractures (52,53). High school female athletes are more likely to sustain a stress fracture than males (52), consistent with an earlier review that concluded stress fractures are more common in female athletes and military personnel than males (54).

Sex-specific risk factors for development of BSI have been identified, including the female athlete triad. All female athletes should be screened for risk factors of

TABLE 12.2: Summary of the Recommended Daily Intake Values

Age and Sex	Calcium		Vitamin D	
	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
Infants 0 to 6 months	*	1,000	**	1,000
Infants 6 to 12 months	*	1,500	**	1,500
1–3 years old	700	2,500	600	2,500
4–8 years old	1,000	2,500	600	3,000
9–13 years old	1,300	3,000	600	4,000
14–18 years old	1,300	3,000	600	
19–30 years old	1,000	2,500	600	4,000
31–50 years old	1,000	2,500	600	4,000
51–70 year old males	1,000	2,000	600	4,000
51–70 year old females	1,200	2,000	600	4,000
>70 years old	1,200	2,000	800	4,000
14–18 years old, pregnant/lactating	1,300	3,000	600	4,000
19–50 years old, pregnant/lactating	1,000	2,500	600	4,000

*Adequate Intake for 0 to 6 months of age is 200 mg/day and for 6 to 12 months of age is 260 mg/day.

**Adequate Intake for 0 to 6 months of age is 400 IU/day and for 6 to 12 months of age is 400 IU/day.

Source: From Ref. (41). Institute of Medicine. Dietary reference intakes for calcium and vitamin D. National Academy of Sciences; November 2010, Report Brief.

the triad during preparticipation physical examinations, including completing a full menstrual history (age of menarche, history of menstrual irregularities). It is important to ask about use of oral contraceptive medications or other hormonal therapy, as withdrawal bleeding is not equivalent to eumenorrhea as hormonal therapy does not address the underlying causes of menstrual dysfunction (4). In female high school runners, prior fracture, BMI less than 19 kg/m^2, late menarche (menarche at age 15 and older), and prior participation in dance and gymnastics were each independent risk factors for prospective development of a stress fracture injury (23). Additionally, these risk factors were cumulative, with female runners possessing three of these four risk factors at 40% risk of sustaining a prospective stress fracture during the study (23). Similarly, male runners with history of fracture were more likely to develop a stress fracture (23). A history of fracture has been recognized as a risk factor for future stress fracture in young adult female runners (49). Recently a multicenter investigation of active young women demonstrated the following independent risk factors associated with developing a BSI: participation in 12 hours or more of exercise, BMI less than 21 kg/m^2, and BMD Z-scores below -1 (35). Morphological qualities have been suggested to increase risk for BSI in female track and field athletes. Risk factors include less lean mass in the lower limbs, leg length discrepancy, and decreased calf circumference in females; however, this relationship was not observed in men (55).

MRI is commonly used to grade the severity of BSI. Nattiv et al. (56), Fredericson et al. (57), and Arendt et al. (58) have all proposed grading systems that use MRI to determine severity of BSI on a scale of one to four. To summarize in all three grading systems, the higher grade BSI demonstrate abnormal signal on T2 and T1 (grade 3), with grade 4 defined as evidence of a fracture line. Higher MRI grade BSI, lower BMD values, and trabecular sites (pubic bone, sacrum, and femoral neck) are common risk factors for longer healing time in collegiate track and field athletes of both sexes (56). Additionally, female athletes with oligomenorrhea (commonly defined as menstrual periods greater than 35 days apart) or amenorrhea were more likely to have higher MRI grade BSI (56).

The location of BSI is important for risk factor assessment and clinical management. Injuries in the pelvis, proximal femur, anterior tibia, patella, tarsal navicular, base of fifth metatarsal, great toe sesamoids, talus, and medial malleolus are considered high risk BSI due to multiple factors including increased biomechanical stress, limited vascular supply, and/or potential consequences if healing is not achieved (59). Growth plate injuries are also important to consider in the skeletally immature athletes (60).

For both sexes, management of BSI includes activity modification guided by the athlete being pain-free, which is important to ensure that the bone(s) affected do not continue to be loaded to promote healing. In high-risk fracture locations or if pain persists despite activity modification, initial use of crutches may be required. Walking boots are prescribed to ensure pain-free ambulation for most BSI in the foot and ankle. Athletes of both sexes may usually participate in non-weight-bearing activities, including deep water running, after the initial phase of injury recovery as long as these activities can be performed pain-free.

For an athlete who presents with one or more BSI, it is important to screen for and address risk factors for injury. In both sexes, BMI should be calculated as BMI below 17.5 kg/m^2, which has been suggested as a marker for low energy availability (30) and has been associated with low BMD values in young runners of both sexes (61). Additionally, both female and male athletes should be screened for eating disorders or disordered eating, dietary intake patterns including foods containing calcium and vitamin D, fracture history, personal history of other medical conditions contributing to impaired bone health (including thyroid disease, rheumatologic disease, other inflammatory conditions, food allergies, and malabsorption), and family history of osteoporosis or bone disease. Medications that contribute to impaired bone health include oral steroids, proton pump inhibitors, antidepressants, and anti-epileptic medications. In female athletes who have a positive screen for triad risk factors include menstrual dysfunction, referral to a specialist in the triad can be valuable in aiding a full endocrine workup. Treatment of the triad is patient-centered and may require a multidisciplinary team including sports physician, dietician, coach, athletic trainer, family, and a mental health specialist, if there are comorbid conditions including eating disorders.

Evidence-based guidelines for evaluation and management of male athletes with impaired bone health have not been clearly defined in this population. In our review (40) we outline our current practice in male athletes who sustain high-risk BSI. This includes obtaining a DXA and completing a nutrition evaluation and endocrine workup. Referral to a sports dietician is prudent in male athletes who participate in sports, emphasizing leanness or weight control behaviors. Currently, there are no clear guidelines on the endocrine workup for male athletes who present with BSI or concerns for impaired bone health, although workup may include assessing for vitamin D deficiency, thyroid dysfunction, and low sex steroid hormones including testosterone.

THE AGING ATHLETE

As adults reach older ages and are encouraged to remain active into their later years of life, maintaining optimal bone health is critical to reduce risk for health issues including fragility fractures and overuse BSI as seen in younger athletes. This section addresses bone health in the aging athlete, including hormonal changes affecting bone loss, BMD changes, and the role of exercise in optimizing bone health.

Hormonal Changes in the Aging Athlete

Hormonal changes occur with aging in both sexes, which influences bone health. Sex hormones including both estrogen and testosterone play an important role in bone health throughout life, with estrogen the predominant hormone modulating bone loss for both sexes (62). In females, menopause results in a short period of accelerated bone loss followed by slower ongoing bone loss, whereas aging men have a slow steady decline (62). A review by Khosla (2010) concluded that low estrogen levels remain an important topic to address in postmenopausal women to influence bone health (63). Older men with lowest bioavailable estradiol had greatest rate of BMD loss in the total hip (64). While bioavailable testosterone was not directly correlated with differences in bone loss, the combination of low bioavailable testosterone and estrogen with highest sex hormone binding globulin had the fastest rates of BMD loss (64). While low estrogen places males at increased risk for hip fracture, men at greatest risk for fractures have both low estrogen and low testosterone levels (65).

Changes in Bone Mineral Density With Age

Age-related reductions in BMD observed in both sexes is an important determinant for overall bone health. Osteoporosis may be diagnosed in a male 50 years or older or a postmenopausal female with a T-score less than or equal to −2.5 at the lumbar spine, total hip, or femoral neck (3). Ongoing loss of BMD associated with aging may result in a greater proportion of individuals meeting these criteria. In a prospective population-based study, a menopausal status change from premenopausal/early menopausal transition to late menopausal transition was associated with annual reduction in BMD of 0.7% at the femoral neck and 0.9% at the lumbar spine (66). In this population, reaching postmenopausal status was associated with a decline of BMD of 1.7% at the femoral neck and 2.5% at the lumbar spine (66). Furthermore, greatest BMD loss may begin approximately 1 year before to 2 years following the final menstrual period termed transmenopause (67). The transmenopause stage resulted in a majority of the 10.6% lumbar spine and 9.1% femoral neck cumulative BMD loss observed over a 10-year period surrounding the final menstrual period for a multiethnic population (67). In males 65 years or older, rapid bone loss (defined as greater than or equal to 3% BMD loss per year) and osteoporosis were most common with either estrogen or testosterone deficiency (68).

For both sexes, BMD loss is an independent risk factor for fragility fractures, especially in those with osteopenia (BMD T-score between −1 and −2.5)(69). Low hip BMD is a risk factor for nonvertebral fractures including hip fracture in older men (70). Lower lumbar spine BMD is also associated with fractures, although the relationship is less strong (70). In women before menopause, most bone loss is from the axial skeleton with appendicular bone mass relatively preserved (71). Bone loss at the femoral neck site may be seen in females at their perimenopausal transition (72), and BMD loss then accelerates during menopause (73).

Role of Physical Activity and Exercise on Preserving Bone Mass in Older Adults

Physical activity has numerous benefits for both skeletal and overall health. The 2004 ACSM position statement on physical activity and bone health concludes that activities including both weight-bearing and resistance training may be most appropriate for preserving bone health in adults (74). In addition, moderate walking has been observed to repress bone turnover in postmenopausal women with osteopenia or osteoporosis (75). Similarly for men, one prospective study observed both men and women who maintained their running habits over 5 years had lower rates of lumbar spine bone loss than those who reduced running with older age (76).

Physical activity interventions have been primarily performed in women. A meta-analysis on walking as a singular exercise therapy suggested positive influence on femoral neck and not lumbar spine BMD in postmenopausal women (77). In contrast, high-intensity resistance training may result in increases for lumbar spine BMD (78). Mixed loading exercise programs incorporating both low impact activities (such as jogging) and higher impact/magnitude activities including resistance training may reduce postmenopausal bone loss at both the hip and spine (79). In contrast, insufficient evidence currently exists to recommend specific exercises targeting lumbar spine and femoral neck BMD in men (80).

Practical Applications

Given the clear benefits of physical activity on bone health and overall health and well-being in older adults, it is important to encourage continued physical activity with aging. However, the known bone loss associated with the aging process needs to be considered in evaluation and management of sports injuries. Given that bone loss can be anticipated with the aging process, BSI need to be considered more strongly on the differential diagnosis for an older adult who presents with a sports injury. Both addressing the current sports injury and ensuring the athlete has proper assessment of bone health is important for secondary prevention. Understanding the underlying bone health may be helpful in counseling on relative risks for participation in different forms of sporting activity.

CONCLUSION

Bone develops most during childhood and adolescence, and efforts to optimize bone mass accrual and bone strength are important for lifelong skeletal health. Preserving peak bone mass is important to reduce risk for fracture in both sexes. Efforts should be made during childhood and adolescence to encourage participation in higher impact activities and sports to promote bone health. Screening for risk factors for impaired bone health should be conducted early, including during preparticipation examinations for both sexes. Sex-specific differences for risk factors for BSI need to be included in evaluating injury and providing appropriate management decisions and for secondary injury prevention. A summary of risk factors for impaired bone health and BSI by sex is included in the following table. Efforts should be made throughout life to optimize bone health to ensure an active lifestyle and reduce risk for injury.

Summary of Sex-Specific Differences in Bone Health

	Males	Females
Age total BMC values plateau	20 years of age (1)	18 years of age (1)
Definition of "low bone mass for chronological age" for ages 5 to 19 (3)	BMD or BMC Z-score ≤ –2	BMD or BMC Z-score ≤ –2
Definition of low bone mass for age in athletes	Not defined in males	BMD or BMC Z-score <–1 (4)
Risk factors for BSI	History of fracture (23)	History of fracture (23,49) Female athlete triad[a] (4,23,35) Low BMI (23,35)[b] Late menarche[c] (23) Lower total body BMC (49) BMD Z scores <–1 (35)
Incidence of BSI by sex in athletes (52,54)		Higher in female athletes
Prevention of BSI	Participation in ball sports during youth (21,22,23)	Participation in ball sports during youth[d] (22)
Calcium requirements		Increased daily calcium intake requirements for females ages 51–70 compared to males of similar age

BMC, bone mineral content; BMD, bone mineral density; BSI, bone stress injury; RDA, recommended daily allowance.

[a] Female athletes with greater number of triad risk factors are at increased risk for BSI. A similar process in males is identified, but further research is needed.

[b] Defined as BMI < 19 kg/m^2 in high school runners or < 21 kg/m^2 in active young women.

[c] Defined as menarche at age 15 and older.

[d] Females with menstrual irregularities did not experience benefits of ball sports in stress fracture prevention.

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13

TENDINOPATHY

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INTRODUCTION

While researchers have analyzed sex differences in detail in some musculoskeletal conditions, there are limited studies in the literature directly evaluating the sex differences in tendinopathy. Some studies have described epidemiologic differences of various tendinopathies between males and females. There is a larger body of research that has investigated sex differences in the risk factors associated with tendinopathy, including use of oral contraceptives, hormone replacement therapy (HRT) and other pharmaceuticals, body composition, neuromuscular control, strength, and structural properties of tendons. There are additional studies that have evaluated sex differences in response to various treatments of tendinopathy. This chapter reviews the current literature regarding sex differences in the epidemiology of specific tendinopathies, intrinsic and extrinsic risk factors for tendinopathy, and response to treatment of tendinopathy in the sports medicine population.

EPIDEMIOLOGY

Patellar Tendinopathy

Studies have shown a higher prevalence in males than females for patellar tendinopathy, sometimes referred to as jumper's knee. Lian et al. studied male and female elite athletes in nine different sports. They reported that in male and female handball and soccer players, the prevalence of patellar tendinopathy was higher among male athletes (13.5%; 18 of 133) compared to female athletes (5.6%; 6 of 107) ($P = .042$) (1). Diagnosis of patellar tendinopathy was made by history and physical examination. The training volumes and backgrounds of the male and female handball and soccer players in the study were reported to be similar: 15 to 17 hours/week of total training time and 15 to 18 years of organized training with 5 to 7 years at the elite level (1). Another cross-sectional study of 891 nonelite athletes showed a significantly higher prevalence of patellar tendinopathy in 10.2% of male athletes (51 of 502) and 6.4% of female athletes (25 of 389) ($P = .048$) (2). The authors of both of these studies hypothesize that the sex differences in prevalence of patellar tendinopathy may be related to lower forces on the patellar tendon in females due to lower quadriceps strength (1,2). Another study of 2,224 volleyball and basketball players (1,006 males, 1,218 females) with a mean age of 25.4 ± 4.7 years found a significantly higher prevalence of patellar tendinopathy in males at 25.3% compared to 13.1% in females ($P < .001$) (3). The subjects were classified as having patellar tendinopathy if they indicated pain at the inferior pole of the patella or reported prior diagnosis by a physician or physical therapist on a self-reported survey (3). In a study of 134 active, elite basketball players 14 to 18 years of age (70 males, 64 females), the prevalence of current patellar tendinopathy, diagnosed by history and physical examination, was 11% in males and 2% in females (4).

Additional studies have reported that males are at higher risk of developing patellar tendinopathy than females. In one prospective cohort study of 385 elite and nonelite basketball and volleyball players, male sex was found to be a risk factor for developing patellar tendinopathy, with an odds ratio (OR) of 2.0 (95% confidence interval [CI]: 1.1–3.5) (5). Another prospective cohort study of 141 elite volleyball players ages 16 to 18 years (69 males, 72 females) over a 3 year period reported that males had a three to four times higher risk for developing patellar tendinopathy compared with females (6). Out of the 28 athletes that developed patellar tendinopathy, 22 were males and 6 were females, and the mean annual incidence was 21% per year for males compared to 5.08% for females (6). Patellar tendinopathy was diagnosed by history and physical examination, with a minimum of 12 weeks of symptoms reported by the athlete (6). The authors suggested that possible explanations for a sex difference in patellar tendinopathy include larger muscle mass and ability to jump higher in males (6).

A study of 160 asymptomatic elite athletes in basketball (46 males, 53 females), cricket (6 males, 8 females), netball (25 females), and Australian Rules football (22 males) compared sonographic findings of the patellar tendon to 27 nonathletic controls (7). A sonographic abnormality was defined as a hypoechoic region in the patellar tendon and was more prevalent in athletes compared to controls (22% vs. 4%) and in male athletes compared to female athletes (30% vs. 14%) (7). Previous studies have shown an association between sonographic tendon changes in asymptomatic individuals and the subsequent development of symptomatic tendinopathy (8–10). Analysis of the height and weight of the subjects in this study showed that the athletes were taller and heavier than controls ($P < .001$), and the female athletes and controls were shorter and lighter than their corresponding male athletes and controls ($P < .001$).

Achilles Tendinopathy

There have been limited studies that have analyzed sex differences in the prevalence and incidence of Achilles tendinopathy. A cross-sectional study of more than 57,000 people showed that mid-portion Achilles tendinopathy equally affects males and females, with an incidence of 1.83 per 1,000 persons for males and 1.87 per 1,000 persons for females (11). In a study of 178 master track and field athletes, sex was not found to influence the development of Achilles tendinopathy (12).

Degenerative tendinopathic changes are the most common histological finding in spontaneous tendon rupture (13–15). With regard to Achilles tendon ruptures, the literature has shown a strong male predominance with male-to-female ratios ranging from 1.67:1 to 6.90:1 (16–22). Vosseller et al. performed a retrospective study of 358 patients with acute Achilles tendon ruptures and reported a male-to-female ratio of 5.39:1, similar to prior studies (23). They also compiled the data from prior studies of Achilles tendon ruptures and reported a total male-to-female ratio of 2.81:1 (23). The authors propose that the Achilles tendon is more likely to be ruptured in males because of a greater force of contraction that may exceed the maximum tendon tensile strength more easily than females (23). Male sex has been found in another study to predict a partial rupture of the Achilles tendon with an odds ratio of 3.6 (95% CI 1.3–9.8) (24). The authors discuss that the male predominance in chronic Achilles tendon disorders may be related to higher participation in sports in males compared to females, but state that there is not enough information to determine if the Achilles tendon degeneration that predisposes people to rupture is directly related to being a male (24).

Rotator Cuff Tendon Disorders

The literature on the epidemiology of rotator cuff tendon disorders is very limited, and studies have analyzed shoulder pain and more generalized rotator cuff syndromes as opposed to specific rotator cuff tendinopathy. White et al. performed a population study of more than 3.7 million patient records from 1987 to 2006 and reported an overall incidence of rotator cuff pathology (as identified by diagnostic codes) of 87 per 100,000 person-years (25). The incidence in females was reported to be significantly higher than males (90 per 100,000 person-years; 95% CI: 88–91 versus 83 per 100,000 person-years; 95% CI: 82–85, $P \leq .001$) (25). When comparing the incidence between males and females of different age groups, there was no significant sex difference noted in the peak incidence age group of 55 to 59 years. In the 25- to 34-year-old group, males had a significantly higher incidence of rotator cuff pathology than females ($P < .01$), while females 40 to 54 years old had a significantly higher incidence than males in that age group ($P < .001$) (25). The authors did not discuss any potential explanations for the higher incidence of rotator cuff pathology in males in the lower age group.

This overall higher incidence of rotator cuff disorders in females compared to males is consistent with previous, smaller studies (26–28). Bodin et al. studied the risk factors for shoulder pain and rotator cuff syndrome in 3,710 subjects, including 2,161 males with a mean age 38.5 ± 10.4 years, and 1,549 females with a mean age of 38.9 ± 10.3 years (26). Rotator cuff syndrome was diagnosed based on current symptoms of intermittent pain in the shoulder region and at least one positive shoulder test (resisted shoulder abduction, external or internal rotation, resisted elbow flexion, or painful arc test), and the prevalence was reported to be 8.5% in females and 6.6% in males (26). Roquelaure et al. performed a surveillance study of 2,685 males and females in the working population and reported that the prevalence of rotator cuff syndrome was 9.0% in females and 6.8% in males (27). Walker-Bone et al. studied the prevalence of upper limb musculoskeletal disorders in 6,038 people and estimated the prevalence of rotator cuff "tendinitis" (the study authors' terminology) to be 4.5% in males and 6.1% in females in the general population (28).

Yamamoto et al. performed a population-based study to investigate the prevalence of symptomatic rotator cuff tears. They found that the prevalence of rotator cuff tears in 683 people was 20.7% and reported that rotator cuff tears were more common in males (25%, 114 of 456) than in females (18.6%, 169 of 910) (29). Statistical significance in difference of rotator cuff tear prevalence was not assessed between the males and females in this study.

Overall, the data suggest a higher incidence and prevalence of rotator cuff disorders in females compared to males, although most studies did not evaluate sex differences as a primary outcome variable with regard to rotator cuff tendinopathy. Additional studies looking specifically at sex differences in rotator cuff tendinopathy are needed.

Lateral and Medial Elbow Tendinopathy

No significant sex differences have been reported in the prevalence of lateral and medial elbow tendinopathy. In a population-based study of lateral elbow tendinopathy between 2000 and 2012, there were a total of 5,867 individuals identified with new onset lateral elbow tendinopathy (30). There were 2,769 male and 3,098 female patients, with a slightly lower incidence in male patients (3.3 per 1,000; 95% CI: 3.2–3.5) compared to female patients (3.5 per 1,000; 95% CI: 3.4–3.7) (30). In another population-based study from Finland, there was no significant difference between males and females for the prevalence of lateral elbow tendinopathy (1.2% for males vs. 1.4% for females) or medial elbow tendinopathy (0.4% for males vs. 0.3% for females) (31). Walker-Bone et al. reported an estimated prevalence of lateral elbow tendinopathy in the general population of 1.3% among males and 1.1% among females (28). Other studies have also demonstrated no sex differences in prevalence of medial and lateral elbow tendinopathy (32,33).

RISK FACTORS ASSOCIATED WITH TENDINOPATHY

There have been studies evaluating sex-specific information for factors associated with tendinopathy, including extrinsic risk factors such as use of oral contraceptives, HRT and other pharmaceuticals, and intrinsic risk factors such as body composition, neuromuscular control and strength, and structural properties of tendon. The following sections discuss the current literature describing the relationship between tendinopathy and these factors with a specific focus on sex differences.

Extrinsic Risk Factors

Oral Contraceptive Pills and Hormone Replacement Therapy (Estrogen and Progesterone)

A significant association has been found between Achilles tendinopathy and oral contraceptive use. In a study by Holmes and Lin involving 44 females with symptomatic Achilles tendinopathy, there was a statistically significant greater prevalence for use of either oral contraceptive pills or HRT in females compared to the national averages (34). Of the 15 females younger than age 35 with Achilles tendinopathy, 53% had history of oral contraceptive use compared to a national average of 26.9% ($P < .025$) (34), while 68% of females with Achilles tendinopathy over the age of 50 had a history of HRT, which is statistically significant compared to the national average of 38% ($P < .01$) (34).

Cook et al. studied the effects of HRT and physical activity on Achilles tendons of 85 asymptomatic postmenopausal females, including 53 active females and 32 inactive female controls (35). Ultrasound examination was performed on the Achilles tendons of the participants. Active females on HRT were found to have significantly smaller Achilles tendon diameter (9.6 mm; 95% CI: 8.7–10.5) than active females not on HRT (10.7 mm; 95% CI: 9.9–11.6) ($P < .05$) as well as fewer sonographic tendon abnormalities, defined as a variation in the fiber structure of the tendon evident in both the longitudinal and the transverse scans (35) Increased diameter of tendons may be indicative of pathologic changes in tendons (35,36). There were no significant differences between the groups in terms of height and weight (35). The authors concluded from these results that HRT may have an impact on tendon structure and can potentially reduce tendon abnormalities in active postmenopausal females (35). While this study presents results that appear to contradict previously presented information on the impact of female hormones on tendons, it was limited by a small number of subjects. Another difference is that the Holmes et al. study evaluated symptomatic Achilles tendinopathy while the Cook et al. study evaluated sonographic tendon changes in asymptomatic females.

Hansen et al. studied the effect of oral contraceptives on collagen synthesis of the patellar tendon in young, healthy females. The tendon collagen fractional synthesis rate (FSR), which has been reported to correspond to the synthesis rate of mature collagen (37), was compared between long-term users of oral contraceptives and controls who had never used oral contraceptives (38). The oral contraceptive group had a 57% lower tendon FSR than the control group, which was statistically significant ($P < .05$), and the authors concluded that synthetic female hormones inhibit tendon synthesis in young women (38).

Other Pharmaceuticals

Tendon tears have been associated with anabolic steroid use. There have been reported cases in the literature of tendon ruptures in the setting of anabolic steroid use (39–42). In addition, animal studies have reported that anabolic steroids may change tendon collagen properties, leading to decreased tensile strength (43,44). However, a study on ruptured tendons in four patients, two of whom were anabolic steroid users, concluded that anabolic steroids did not induce any ultrastructural collagen changes that would increase the risk of tendon ruptures (45). If anabolic steroids do not affect the structure of tendon, one suggested mechanism for tendon injury in the setting of anabolic steroid use is a rapid increase in mechanical stress on tendons due to increased training intensity and volume, and failure of the connective tissue to withstand the overload (46). Epidemiologic studies have reported significantly higher rates of anabolic steroid use by males compared to females. In one study, the global lifetime prevalence rate of anabolic steroid use was reported as 6.4% for males compared to 1.6% for females ($P < .001$) (47). Self-reported use of anabolic steroids in adolescents has been shown to range from 5% to 11% in males and between 1.4% and 2.5% in females (48–51). This may explain why males are more likely to have tendon rupture or tendon-related injuries in the setting of anabolic steroid use. It is unknown if endogenous anabolic steroids are associated with an increased risk of tendinopathy.

Fluoroquinolones have been associated with tendon disorders and have been studied primarily in relation to their effects on the Achilles tendon, but fluoroquinolone use has been associated with tendon disorders in other parts of the body (52–57). The average onset of tendinopathy after fluoroquinolone use has been found to be 9 to 17 days, ranging from hours to months (58). Wise et al. performed a large population study of 6.4 million residents in the United Kingdom from 1986 to 2009 and showed that the use of fluoroquinolones had more negative effects on tendons in females than males (58). Fluoroquinolone use was shown to have a significantly larger effect on tendon rupture in females compared to males (OR: 4.0 vs. 1.1, $P = .02$) as well as a stronger association in females for Achilles tendonitis (OR: 5.0 vs. 3.6) (58). A study by Van Der Linden et al. of 50,000 patients in the United Kingdom identified 1,367 patients with Achilles tendon rupture between 1988 and 1998. The authors showed that the effect of fluoroquinolones on the incidence of Achilles tendon rupture was not modified by sex (55). Compared to the study by Wise et al., this study did not assess for the presence of tendinopathy. In addition, the Wise et al. study looked at a much larger database of patients compared to the sample studied by Van Der Linden et al. (55,58).

Intrinsic Risk Factors

Effects of Endogenous Hormones

Endogenous female hormones such as estrogen have been hypothesized to affect tendon structure and contribute to the development of tendinopathy (34,59,60) However, the impact of endogenous female hormones has been studied primarily in the setting of anterior cruciate ligament injuries, with limited studies specifically looking at their impact on tendons. An animal study by Hart et al. showed the presence of messenger RNA (mRNA) for estrogen and progesterone receptors in rabbit tendons (61). The impact of pregnancy on gene expression was different in the Achilles, patellar, flexor digitorum longus, and extensor digitorum tendons (61). The authors hypothesize that tendons therefore may respond to changes in hormone levels. Miller et al. investigated the rate of patellar tendon collagen synthesis in female subjects, taking into account serum estrogen and progesterone concentrations (62). These authors calculated the tendon collagen fractional synthesis rate and found significantly lower tendon collagen FSR in females compared with males both at rest and after exercise (62). At rest, the tendon collagen FSR for females was 55% of the rate of males ($P < .05$), while 72 hours after exercise, the tendon collagen FSR for females was 47% of the rate of males ($P < .05$) (62). The authors concluded that estrogen may play a role in tissue repair, specifically modulating responses of fibroblasts to mechanical loading, and may contribute to a lower rate of repair in females after exercise (62). The lower rate of repair in the tendon may impose a greater risk of injury to females. Additional research is required to determine the relationship between endogenous female hormones and tendons, and whether hormones contribute to sex differences in the development of tendinopathy.

Body Composition

The relationship between body composition and tendinopathy has been investigated. Increased adiposity has been identified as a risk factor for tendinopathy (63). In addition, higher body mass index (BMI) or body weight (64–68), larger waist girth (68), and higher waist-hip ratios (68–70) have also been associated with tendinopathies in various studies. Sex differences have not been studied with regard to these specific anthropometric measures. BMI, waist-hip ratio, and waist circumference have been used to measure general and central obesity and, in turn, to predict the risk of metabolic syndrome (71–76).

Fat distribution has also been studied in relationship to tendinopathy. In the study by Gaida et al. of subjects with asymptomatic Achilles tendon pathology as identified using ultrasound, adipose tissue distribution was measured using dual-energy x-ray absorptiometry (DXA) (70). The 17 males with abnormal Achilles tendons were reported to have higher android/gynoid fat mass ratios (0.616 ± 0.186 vs. 0.519 ± 0.142, $P = .014$) and higher upper-body/lower-body fat mass ratios (2.346 ± 0.630 versus 2.022 ± 0.467, $P = .013$) compared to 110 males with normal Achilles tendons (70). Higher android/gynoid fat mass ratios have been associated with metabolic syndrome and increased metabolic risk (77–79). The eight females with asymptomatic Achilles tendon abnormalities on ultrasound were reported to have lower central/peripheral fat mass ratios than the 163 females with normal Achilles tendons (0.711 ± 0.321 versus 0.922 ± 0.194, $P = .004$) (70). Overall, the study concluded that asymptomatic Achilles tendon pathology is associated with increased peripheral fat distribution in females and increased central fat distribution in males.

There are several hypotheses regarding the relationship between increased adiposity and tendons. There is a proposed direct mechanism where bioactive peptides are released by adipose tissue and directly influence tendon structure (63). Adipose tissue can release free fatty acids and pro-inflammatory cytokines into circulation that may adversely affect tendon function (68). A proposed indirect mechanism involves systemic metabolic changes associated with increased adiposity that could affect tendon structure (63). Another potential explanation is that increased waist girth, which has been demonstrated to correlate with weight, increases mechanical load on tendons, particularly the patellar tendon. Repetitive or excessive loading may lead to failure of tendon remodeling (68).

Strength Differences

Mahieu et al. performed a prospective study of 69 male cadets who underwent 6 weeks of military training (80). Ten of the subjects were found to have Achilles tendon overuse injury as diagnosed by history and physical examination. Decreased plantar flexor strength measured prior to the military training was found to be a significant predictor for later development of Achilles tendon overuse injury (80). Plantar flexor strength less than 50 Nm was identified as a risk factor for developing Achilles tendon overuse injury (80). Females have been shown to have decreased absolute muscle strength when compared to males in prior studies (81,82), which may put females at risk for tendon injury in the lower limb. However, females have also been shown to have equal or greater strength relative to lean body mass or cross-sectional area (CSA) compared to males (83). Nevertheless, the Mahieu et al. study reported absolute ankle plantar flexor strength, and the lower absolute strength of females may place them at a higher risk of developing Achilles tendinopathy than males. Additional studies are required to further evaluate the relationship between strength differences and development of tendinopathy.

Neuromuscular Control and Biomechanics

Neuromuscular control has been studied to evaluate sex differences and relationship to tendon loading (84–87). In a comparison of male and female volleyball players, differences were noted in neuromuscular recruitment strategies of lower limb muscles when landing from a jump (84). The male volleyball players had significantly earlier semitendinosus and biceps femoris muscle onset compared to the females during landing. The males also reached peak semitendinosus activity before the time of peak patellar tendon force, while the females reached peak semitendinosus activity after peak patellar tendon force (84). A higher patellar tendon force loading rate was also shown to correlate significantly with lateral rectus femoris, vastus medialis, and biceps femoris muscle recruitment (84). While these neuromuscular recruitment differences between sexes were reported, no significant association was found among these differences and subsequent patellar tendon force magnitude, relative to body weight, at landing (84).

In terms of the influence of biomechanics on tendinopathy, several studies have evaluated the relationship between jumping characteristics and patellar tendinopathy. Visnes et al. performed a prospective cohort study to evaluate the impact of jumping ability at baseline on future development of patellar tendinopathy in 150 elite volleyball players 16 to 18 years old (68 males, 82 females) (88). Patellar tendinopathy was diagnosed by history and physical examination, with a minimum of 12 weeks of symptoms. The subjects performed the counter movement jump (CMJ) test in which they started at a stationary erect position with full extension of the knees, bent down to as low as 90° of knee flexion, and then jumped to the highest level, which is the end measurement. The authors reported that males who developed symptomatic patellar tendinopathy jumped higher in the CMJ test than males who remained asymptomatic and concluded that higher baseline jumping ability is a risk factor for developing jumper's knee (88). For females, there was no difference in CMJ test at baseline when comparing those that developed patellar tendinopathy to those that did not. No differences were reported between males and females, though assessing sex differences in relation to the development of patellar tendinopathy was not a primary or secondary outcome measure in this study. Cook et al. studied symptomatic and asymptomatic elite junior basketball players and found that females with unilateral or bilateral patellar tendinopathy had a significantly higher vertical jump than those with normal tendons as identified by ultrasound (bilateral 51.0 ± 9.0 cm; unilateral 50.9 ± 6.8 cm; normal 46.1 ± 5.4 cm, $P < .05$) (89). No significant difference in vertical jump height was found in males with patellar tendinopathy compared to those with normal tendons (bilateral 64.4 ± 6.3 cm; unilateral 63.4 ± 6.0 cm; normal 62.0 ± 6.7 cm) (89). The authors concluded that higher vertical jumps are a risk factor for increased abnormal patellar tendon morphology in females, but not in males (89) and report that this difference between the females and males in their study was an unexpected finding, and expressed the need for further research to explain this difference (89).

Jump frequency and rate has also been studied with respect to risk of developing symptomatic patellar tendinopathy. In elite volleyball players ages 16 to 18 years, 12 of 26 males (46.2%) were diagnosed with patellar tendinopathy compared with 1 of 18 females (5.6%). Patellar tendinopathy was diagnosed by history and physical examination. Individual jump counts were compiled based on a review of recorded training sessions and matches. The males jumped 2.6 times more frequently than females in training and 1.5 times more frequently than females during matches (90). Given this potential sex difference in jump frequency, the authors conclude that jump frequency may be a risk factor for developing patellar tendinopathy.

Structural Properties of Tendon

There have been several studies looking at sex differences in the structure and mechanical properties of tendons. One study that measured patellar tendon elongation during isometric contractions in 10 young males and 10 young females showed differences in structural and mechanical properties between sexes (91). Torque was measured with a dynamometer while structure and mechanical properties were studied using ultrasound and co-contraction was estimated using electromyographic (EMG) activity. The authors report significantly different patellar tendon mechanical properties in males and females, including a 26% greater maximum total tendon stress in males compared to females during isometric knee extension (91). Sex differences have also been shown in the viscoelastic properties of tendons. In a study of Achilles tendon properties, females have been shown to have significantly lower stiffness of tendons than males, indicating more compliant tendons in females (92).

Westh et al. studied the effect of exercise and training on the structural and mechanical properties of the Achilles and patellar tendons. They found greater patellar tendon CSA in male runners than female runners ($P < .01$). They also reported greater patellar tendon stiffness in male runners (3528 ± 773 N/mm) compared with female runners and female nonrunners (2069 ± 666 N/mm, 2477 ± 381 N/mm, respectively) ($P < .01$) (60). Male runners were also reported to have greater weight-normalized Achilles tendon CSA compared to female runners ($P < .01$) (60). Andrew and Jonathan performed a study comparing Achilles tendon loading during running in male and female recreational runners. They concluded that males demonstrated a significantly greater Achilles tendon load than females ($P < .05$), and that this finding may help explain the increased incidence of Achilles tendon disorders in males (93).

Knobloch et al. studied 139 patients (average age 49) with symptomatic Achilles tendinopathy, analyzing tendon and paratendon microcirculation using noninvasive laser Doppler and spectrophotometry (59). Overall, females were found to have better tendon and paratendon microcirculation compared to males. Specifically, the symptomatic females were found to have increased Achilles tendon and paratendon oxygen saturation and reduced postcapillary venous filling pressures compared to symptomatic males (59). The authors report that a decrease in tendon oxygen saturation implies downregulation of tendon metabolism (59). While the study did state that 19% of females were taking oral contraceptive drugs, there was no collection of information on endogenous or exogenous hormone concentrations, so it is unclear if either of these variables influences tendon and paratendon microcirculation.

TREATMENT OF TENDINOPATHY

Nonoperative Management

Another study by Knobloch et al. evaluated the response to eccentric training in patients with symptomatic Achilles tendinopathy (94). A total of 75 patients (44 males, 31 females) with a mean BMI of 26 ± 2 were evaluated. Initial pain scores on the visual analogue scale (VAS) were similar between females and males (5.6 ± 2.2 versus 5.4 ± 2.1). The study found that after 12 weeks of eccentric training, females had a significantly higher pain score on VAS (4.4 ± 2.6 versus 3.0 ± 2.1, $P = .023$). The Victorian Institute of Sport Assessment A (VISA-A) scores also improved in males by 27% (63 ± 12 to 86 ± 13), which was significant compared to a 20% improvement in females (60 ± 14 to 75 ± 11) ($P < .05$ for sex difference). Overall, females in this study were found to benefit less than males with symptomatic Achilles tendinopathy from 12 weeks of eccentric training (94). One limitation of the study was that endogenous or exogenous hormone concentrations were not measured and this might influence the females' response to treatment.

Silbernagel et al. evaluated the 5 year outcome of patients with symptomatic Achilles tendinopathy who were treated with exercise (95). The patients consisted of 18 males and 16 females (average age of 51 ± 8.2 years) with Achilles tendinopathy and duration of pain for more than 2 months. The exercise program consisted of progressive Achilles tendon-loading strengthening, mainly eccentric exercises, monitored by a physical therapist for 12 weeks to 6 months. Overall, 80% of the patients treated with this exercise regimen fully recovered in regard to function and symptoms measured by various questionnaires. There were no sex differences in 5 year outcomes for patients with Achilles tendinopathy who were treated with exercise (95).

Operative Management

In terms of operative management of tendinopathy, Maffulli et al. studied the outcomes of 45 males and 41 females who underwent surgery for Achilles tendinopathy (96). The patients had unilateral Achilles tendinopathy, had failed conservative management for 3 to 6 months, including rest from sport or treatment with nonsteroidal anti-inflammatory drugs, physiotherapy, and injections, and had no prior surgeries on the affected tendon. The mean BMI in males (24.1 ± 3.8 kg/m^2) was not significantly different from the mean BMI in females (26.8 ± 4 kg/m^2) (96). However, the body fat percentage was higher in females (26.2) compared to males (18.1) ($P < .01$). The patients underwent surgical management with tenotomies and excision of degenerative areas. The females had more complications (superficial infections of the surgical wound) than the males (19.5% versus 6.7%). Five female patients underwent additional surgery compared with three male patients. Only 24 of 41 female patients (58.5%) reported excellent or good results compared to 39 of 45 males (86.7%), and the female patients took 8.3 months on average to return to activity compared to 4.7 months for the males. Overall, this study found that surgery for Achilles tendinopathy leads to worse results for females compared to males (96). Possible explanations for why females had worse outcomes include longer interval between referral and surgery, time between symptom onset and surgery, and higher body fat compared to males (96).

CONCLUSION

There is a limited body of literature that has specifically investigated sex differences in tendinopathy. In this chapter, we presented the epidemiologic data of various tendinopathies for males and females. We discussed sex-specific data for several extrinsic factors associated with the development of tendinopathy such as use of oral contraceptives, HRT and other pharmaceuticals, as well as intrinsic factors such as endogenous hormones, body composition, differences in strength and neuromuscular control patterns, and structural properties of tendons. Finally, we also presented the literature on sex-specific responses to different treatments for tendinopathy.

Upon review of all of the data in this chapter we have tried to draw some conclusions. Males have been shown to have a higher prevalence and to be at higher risk for developing patellar tendinopathy. This higher prevalence may be related to a higher jump height, increased jump frequency, increased stiffness in the tendon, increased CSA of the tendon, or decreased blood flow around the tendon in males compared to females. While there is a male predominance for prevalence of Achilles tendon rupture, the limited epidemiologic data on Achilles tendinopathy do not show a sex difference. The data for rotator cuff tendon disorders suggest an overall higher incidence and prevalence in females compared to males, but the literature is limited when specifically analyzing the incidence and prevalence of rotator cuff tendinopathy between sexes.

Female oral contraceptive use has been associated with the development of Achilles tendinopathy. However, there are potentially contradictory results regarding the impact of HRT on tendon structure, and additional studies are required to demonstrate the impact of endogenous estrogen as well as exogenous hormones on tendons and the development of tendinopathy. Fluoroquinolones have been shown to have more detrimental effects on tendons in females compared to males.

Regarding body composition, there have been many studies showing the association between increased adiposity and tendinopathy. Increased central fat distribution in males and peripheral fat distribution in females have been shown to be associated with Achilles tendon pathology. While it is a commonly used measurement to estimate adiposity, BMI in athletes may not be an accurate measure of adiposity, and the utility of studying the association between BMI and tendinopathy in this population may be limited (97). Body fat percentage is a better measure of adiposity.

Only one study has evaluated the relationship between muscle strength and tendon injury. While males may have greater absolute muscle strength than females, strength relative to lean body mass should be studied in regard to risk for developing tendinopathy in males and females. From a structural perspective, females have been shown to have superior tendon and paratendon microcirculation compared to males, which may lead to better responses to treatment and recovery. However, this was not seen in a follow-up study showing poorer response to eccentric training for Achilles tendinopathy in females compared to males. Further studies on tendon structure and microcirculation may be warranted to elucidate their impact on healing and response to treatment.

Ultimately, there are limited data on if or how sex predisposes an individual to the development of tendinopathy, so it is difficult to make any broad-reaching clinical associations. However, the current research allows us to begin to determine what relationships may exist between sex and tendinopathy. In order to further investigate and clarify specific sex differences in tendinopathy, additional research is required.

Prevalence

Musculoskeletal Complaint	Sex With Higher Prevalence of Tendinopathy
Patellar tendinopathy	Males
Achilles tendinopathy	Similar between sexes
Achilles tendon rupture	Males
Rotator cuff tendon disorders	Females
Lateral and medial elbow tendinopathy	Similar between sexes

Risk Factors

Risk Factor	Sex With Higher Prevalence of Tendinopathy
Anabolic steroid use	Males
Fluoroquinolone use	Females
Increased central fat distribution	Males
Increased peripheral fat distribution	Females
Higher jump frequency	Males

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14

PAIN

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SEX DIFFERENCES IN PAIN

Do men and women experience pain differently? Understanding and alleviating pain is a universal endeavor that is constantly evolving, revealing new information and new questions. The pain phenomenon incorporates an enormity of contributions that are currently being studied. These include, among many others, a person's age, hormones, culture, medical comorbidities, psychological state, social dynamics and stressors, family structure, and physical environment. As the field of studying pain continues to advance, the complexity of the pain experience becomes more apparent. There have been many new interesting observations made, such as sex-specific changes in hemodynamic and autonomic measures in acute pain (1) and differences in spatial pattern seen in cortical imaging (2–4). Polymorphisms or mutations in certain genes may play a role in sex differences, as well as the influence of past experience of pain (5–8).

Understanding pain is crucial to comprehensive sports medicine. As providers, we strive to diagnose and treat pain in our athletes to maximize their performance and to keep them safe from injury. The idea that there are differences in the pain experience that are specific to a person's sex is well recognized and generally accepted. However, the question of how this contributes to the mosaic of the pain experience remains difficult to delineate in our clinical practice. Perhaps this merely serves to stir our excitement for exploration and a more complete understanding of pain in men and women.

Pain in the General Population

Very few studies have specifically looked at sex differences in athletes with pain. In general, there is evidence that athletes have a higher tolerance for pain than nonathletes, the reasons for which are multifactorial and still being studied (9,10). Pain management in sports medicine is a rapidly growing field, but clear and consistent answers regarding sex differences in pain for athletes still remain as elusive as they do for the general population. For the time being, we will have to derive our understanding of sex differences in pain from this still limited but larger pool of literature addressing the general population of men and women.

Across many studies, pain has been shown to be more prevalent in women than in men. Higher pain prevalence in women is consistently observed, and the pain that women report is more severe, more frequent, more diffuse, and of longer duration than that reported by men. This difference appears to be consistent across nations, race, and culture (11–19). There are some specific pain disorders that are seen more commonly in women than in men. These include fibromyalgia, inflammatory bowel disease, back pain, migraine, tension headaches, neck pain, temporomandibular joint disorders, osteoarthritis, and rheumatoid arthritis (20). Women are also more likely than men to experience multiple pains simultaneously (21–23).

It seems that these sex differences in pain prevalence emerge during adolescence. In boys and girls who have similar experiences in pain, it was found that girls recalled a higher pain intensity of the experience than boys did (24). As girls go through puberty, increasing rates of pain conditions were found in girls. In contrast, the rates of pain conditions in boys remained stable or increased at a slower rate (25).

As people age, these sex differences in the prevalence of pain are found to persist. In the elderly population, there is a higher prevalence of pain in females than in males—similar to the overall prevalence in younger patients (26). Although this overrepresentation of women is consistently seen, it is not well understood. Herein lie the questions that many have attempted to answer over the last few decades. There has been a wealth of research supporting a variety of theories for these sex differences in pain.

Laboratory Studies in Pain

Sport-related pain is more complex than the pain studied in artificial laboratory conditions. The pain that athletes experience usually arises from multiple different stimuli under highly varied environments. For example, a marathon runner could be experiencing lower extremity pain simultaneously from generalized muscle fatigue, hypoxic muscle cramping, tendinopathy, a pressure ulcer, and a sunburn. The pain in any one of these components could be considered a combination of heat/cold pain, ischemic pain, chemical pain, or pressure pain. With many varied factors at hand, it is quite difficult to study the true experience of athletes' pain in controlled, calculated environments. The best data we have come from highly isolated situations yielding results that are limited and vague in application to our targeted population of athletes. The application of available data in clinical practice is subjective and varies by clinician—this must be understood as we review the available data on sex-specific pain differences in the laboratory setting.

Laboratory studies in pain utilize a variety of nociceptive stimuli: cold pain, heat pain, pressure pain, ischemic pain, muscle pain, chemical pain, electrical pain, or visceral pain. In response to one or more of these stimuli, outcome measures include pain threshold, pain tolerance, pain intensity, and pain unpleasantness. Pain threshold is defined as the least experience of pain that can be identified by a subject; pain tolerance is defined as the highest level of pain that a subject is ready to tolerate (27). For example, we can consider the pain threshold of a ballet dancer standing en pointe (on toe). A dancer with a high pain threshold would be able to stand for a longer period of time before beginning to identify pain. In contrast, pain tolerance would be considered the amount of time the dancer continues to stand en pointe while experiencing increasing amounts of pain.

Pain intensity and unpleasantness are subjective scales that can be assessed with validated instruments such as the visual analogue scale (VAS), numerical rating scale (NRS), or verbal rating scale (VRS) (28). Because pain is subjective, standardized scales are difficult to design and remain prone to intersubject variability. For example, in the numerical rating scale, the subject is instructed to consider a 10 the "worse pain you can possible imagine" and 0 as "no pain." One can envision that the "worse pain you can possibly imagine" may actually be quite different from person to person. Perhaps it is even dependent on how big an imagination the person has! Despite this, we can rely on consistency within one subject across successive ratings (29).

Pain tolerance and threshold in athletes has been compared to nonathletes. A meta-analysis of 15 studies found that athletes consistently show a higher pain tolerance than normally active control subjects (30). In contrast, differences in pain threshold were not found to be significant. It appears that athletes actually feel the same initial pain that everyone else does. The difference is that they are able to tolerate it more significantly or continue despite the pain to higher levels of performance. Whereas some people may stop running at the first leg cramp, athletes will "push through" the pain to climb the next hill.

There have been very few, small studies that seem to support male athletes having a higher pain threshold and tolerance than female athletes (31,32). This reflects some of the studies of nonathletes in the general population; some general population studies have shown sex-specific differences in pain, but clear and consistent patterns across studies have not been seen (33,34). Sex differences in response to pain stimuli are variable as a function of the type of stimuli used and the outcome being measured. As mentioned previously, the wide variety of nociceptive stimuli used and the inconsistency of outcomes measured are problematic in drawing general conclusions. A review of 10 years of research suggests that males and females have comparable thresholds for chemical pain and ischemic pain, while pressure pain thresholds were lower in females. In terms of tolerance, there is strong evidence that females tolerate less pressure and thermal pain than males, but tolerance for ischemic pain is comparable between men and women (35). Studies that measured subjective pain intensity and unpleasantness found no sex differences across many different pain stimuli (36–38). Because of the variability of these studies, it is difficult to draw generalized conclusions about gender differences for the pain experience in a laboratory setting. If we were to try and apply these data clinically, would this mean that females were more vulnerable to pain from pressure ulcers? Do they perform more poorly in the hot sun or in snowy conditions? It is difficult to know what data are truly applicable for our patients, and more research is needed for further education.

Animal and Rodent Studies

Pain in animals is measured by observing animals' aversive behavior in response to stimuli. Pain stimuli used in many rodent studies include formalin administration, exposure to complete freund's adjuvant (CFA), injection of carrageenan, and others. Some examples of observed pain behavior include flinching responses, writhing behavior, or licking/shaking of their paws. Different animal models have been developed to mimic human pain syndromes, such as inflammatory pain, temporomandibular disorder pain, and neuropathic pain (39).

Animal and rodent studies have shown differences between the sexes in the pain experience. Compared to human studies, rodent studies have demonstrated more consistent sex differences in pain. Female rats have demonstrated a lower pain threshold by showing increased pain behaviors in response to pain stimuli (39,40). Male mice were also found to have a general higher level of activity in the endogenous analgesic system compared to females, including a stronger analgesic response to mu-opioid receptor agonists. There is some small evidence that female rats have lower levels of stress-induced analgesia (41).

Nociception and Analgesics

Opioids are sometimes considered illegal drugs during competition. However, the role of opioids in athletic performance is more complicated than we think. An interesting simulation was demonstrated in a study by Benedetti, Pollo, and Colloca in 2007 (42). During the precompetition training phase, repeated doses of morphine were administered to subject athletes. On the day of competition, the morphine was replaced with placebo and induced opioid-mediated increase of pain endurance and physical performance. This pharmacologic conditioning may have practical implications and brings to question whether opioid-mediated placebo responses are ethically acceptable in sports competitions.

Commonly known as the "runners' high," it is known that the release of endogenous opioids, or endorphins, in response to exercise is a significant physiologic phenomenon. Elevated levels of endorphins have been linked to changes in pain perception, mood, and hormonal responses (43,44). Nociception refers to the neurobiological receptors and connectivity of the somatosensory nervous system that constitute the pathways of the pain experience (27). Several opioid receptors have been identified and studied as significant components of nociception, the originally classified receptors being the mu-, delta-, and kappa-opioid receptors (45). There may be some sex-specific differences in the activation of these receptors. Sex differences in the opioid, dopaminergic, serotoninergic, and other endogenous pain-related systems have been documented (46–49). The mechanisms that mediate these phenomena are poorly understood and still being studied. Most studies have been performed using animal models or in laboratory settings using healthy human volunteers. The resulting evidence has been mixed, and consistent data to support sex-related differences have not yet been found.

For thousands of years, opioid receptors have been the target for pain treatment and are the most widely used analgesics in clinical practice. One might think that we could further our understanding of the pain experience by studying how opioid medications are utilized and consumed between men and women. However, the results are varied. Overall, there is mixed evidence for differences between men and women in the efficacy and use of morphine and other opioids. When men and women of equal pain scores were compared postoperatively, opioid consumption was found to be higher in men (50). In cancer pain, no significant sex differences were found in analgesic prescriptions or intake of analgesic medications (51). A study with epidural steroid injections showed no sex differences in the magnitude of treatment response (52). There is relatively stronger evidence for greater analgesic efficacy in women of mixed opioid agonist-antagonists (pentazocine, nalbuphine, and butorphanol) (53–63). Women do experience increased adverse reactions to opioid medications as compared to men, particularly nausea and vomiting (64–66).

Opioid Prescription and Aberrant Behavior

There has been concern that athletes are at higher risk for being chronic users of opioid medications. National Football League (NFL) players with injury-related pain are at increased risk for opioid use and misuse, resulting in medical, psychiatric, and social problems. Players who misused opioid medications during their NFL careers were more likely to misuse them after their careers were finished (67). Over 100,000 people have died from prescribed opioids in the United States since the late 1990s. In adults age 35 to 54, these deaths have exceeded mortality from firearms and motor vehicle accidents (68). From 1997 to 2006, the number of fatal overdoses from prescription opioids quadrupled, exceeding those from heroin or cocaine (69,70). In the treatment of chronic pain, providers can be heavily scrutinized in the prescription of scheduled medications, and the fear of addiction or misuse of these medications is an issue that commonly arises.

Among chronic pain patients, some aberrant prescription use behaviors may be sex-specific. Aberrant behaviors that are associated with risk for abuse include lack of adherence to prescription instructions, use via unintended routes (oral versus crushing and snorting), a higher number of prescriptions from the emergency department (ED), multiple or overlapping prescriptions, illegitimate prescriptions, drug dependence disorders, functional impairment, and psychiatric comorbidities (71).

Studies reveal that both men and women have been observed with aberrant behaviors and are at risk for medication abuse. Women are more likely to be regular and long-term opioid users (69,70). More women are prescribed opioids in the ED, have higher dosages prescribed in the ED, and are more likely to have multiple and overlapping prescriptions (72). However, women are more likely than men to use opioids consistent with their prescription instructions, are more likely to use via the intended route of administration, and are more likely than men to have first obtained opioids via legitimate prescriptions (73).

Men acknowledge more misuse of prescription analgesics compared with women (74). Adult men are two to three times more likely than women to have drug dependence disorders, but the rate of escalation of drug use is higher in women (75). Women prone to opioid misuse exhibit greater functional impairment, more psychiatric comorbidities, and higher likelihood of using opioids to cope with psychiatric symptoms and pain than men.

Social and Cultural Influences

Some cultures and societies treat male and female athletes quite differently (76) and create significant differences in athletes' perceptions and expectations (77). Some people postulate that the gender differences in the pain experience are due to the social and cultural expectations that women have versus men. Some people suggest that it is more socially acceptable for women to express or exhibit signs of pain, or that perhaps men are socially discouraged to express or report pain (78,79).

The social interaction between research subjects and investigators has also been studied. Clinicians themselves can have gender-specific stereotypes, whether conscious or unconscious, and it seems that this can influence their treatment decisions for pain (80). One study found that female providers were more likely to recommend psychosocial treatments instead of opioid medications for female pain patients (81). In addition, patients have been observed to report their pain differently with male and female providers. One study found that male and female patients reported higher pain scores to female practitioners than male practitioners (82). Interestingly, another study found that women reported higher levels of pain to their clinician when in the presence of a woman friend. The authors suggest that this higher social support may reinforce pain syndromes in women (83). Alternatively, men were shown to report lower pain intensity with higher social support (84).

Although it has not been studied to date, these social influences on pain reporting raise interesting questions in reference to team versus individual sports. How are team dynamics influential in the experience of pain? Some have suggested that team sports elicit more aggressive behavior than individual sports (85). There are interesting areas for future research: Would male athletes who play team sports be less likely to report pain? Also, would females report more pain if they are involved in team sports or in the presence of fellow female athletes?

Psychiatric Comorbidities

Some people highlight the attribution of anxiety or depression to the pain experience, both of which have shown differences between men and women. It is often clinically difficult to differentiate the cause/effect of pain or anxiety. Is it primarily the anxiety that is making pain worse, or is it pain that is causing feelings of anxiety? Or is it a mutual synergistic effect, breeding a compound suffering of both anxiety and pain? These same questions can be asked of depression or other comorbidities such as insomnia and poor sleep quality (86).

Little is known about mental health disorders in athletes and may be missed in clinical assessments. We know that the prevalence of mental health problems in athletes is high (87,88). In particular, female athletes have been found to have greater odds of experiencing symptoms of depression than male athletes (89,90). Women may be particularly vulnerable psychologically, as compared to men, when faced with acute pain (91). Optimal interventions for anxiety- or depression-related pain are still being studied, but may differ by patient sex (92,93). For example, one study found that higher anxiety was correlated with more pain relief in men but less pain relief in women (94). The authors suggest that this may be due to sex differences in coping strategies. Clearly the relationship between anxiety and pain is quite complex, and how to apply this knowledge clinically in treating our male and female athletes remains to be studied.

Hormonal Influences

Researchers have investigated gonadal hormones as a plausible explanation for sex differences in pain, particularly the role of estrogen. Women have major fluctuations in estrogen and progesterone levels related to their menstrual cycles, as well as significant deficits as they enter menopause. In men, androgens such as testosterone are the predominant gonadal hormones essential for the male reproductive system. Although poorly understood, estrogen, progesterone, and other gonadal hormones have a complex role in inflammatory processes and the pain response (95,96).

Estrogen and Progesterone

Several studies have measured pain during various stages of the menstrual cycle. The average woman's menstrual cycle ranges from 28 to 35 days in length and has a cyclic fluctuation in serum levels of estrogen and progesterone. In the beginning of the cycle, estrogen and progesterone levels are low. Estrogen levels increase during the follicular phase, peak right before ovulation, and then have a smaller peak during the luteal phase. Progesterone levels peak during the luteal phase approximately 6 to 10 days after ovulation. At the end of the luteal phase, both estrogen and progesterone levels decrease (97,98).

As mentioned with previous studies in pain, there are difficulties in drawing generalized conclusions because of variations in pain stimuli modalities and outcomes measured. In addition, studies have been of relatively small magnitude, and there have been methodological inconsistencies in regard to experimental session timing. The timing of measurement across the menstrual cycle was inconsistent; biological markers were not used to specifically track the stages of the cycle. Given these difficulties, measuring pain sensitivity across the menstrual cycle has had minimal or conflicting results (48).

Some studies support a correlation with higher pain occurring during times of low estrogen and lower pain at times of high estrogen. This has been demonstrated in several ways: (a) pain sensitivity is higher during luteal phase (low estrogen); (b) there are increased reports of migraine headaches, temporomandibular pain, and low back pain during luteal phase (low estrogen) as compared to the follicular phase (rising estrogen); (c) higher pain thresholds were found during the follicular phase (rising estrogen); (d) lower pain was reported during late pregnancy (high estrogen) (99–104).

The mechanism for estrogen's influence in pain is poorly understood and still being studied. One study found weaker emotional modulation of pain associated with low estradiol (105). Another interesting study demonstrated that females with low estrogen states showed significantly less regional activation of the endogenous opioid system (106). Rodents have also been observed for pain behavior during menstruation; female rodents have a similar estrous cycle that lasts about 4 days (107). As in human studies, variability in pain stimuli and measured outcomes yielded a range of results, making general comparisons difficult across studies. However, several studies support a significant role for gonadal hormones in pain. Similar to human studies, some studies in rats have supported a correlation between higher estrogen states and less pain (108,109).

Some researchers have studied low estrogen states by comparing women with regular menstrual cycles versus postmenopausal women. If estrogen and progesterone indeed play a role in the pain experience, it would be useful to study pain in the population of postmenopausal women as their endogenous levels of these hormones decline. Women with an oophorectomy are also a comparable population to study as compared to women with regular menses. These studies have produced conflicting results. Some studies have shown increased levels of pain in perimenopausal and postmenopausal women (110). Cranial and orofacial pain conditions were also shown to be more prevalent in these subjects (111). In contrast, however, prevalence rates of joint pain, chronic widespread pain, and fibromyalgia were higher in menstruating women than postmenopausal women. Migraine headaches and temporomandibular disorder pain have also been observed to peak in prevalence during reproductive years (112).

Though not well studied, menstruation in young female athletes has some significance in their sports performance (113). We do know that high-intensity sports combined with inadequate caloric intake can lead to several types of menstrual abnormalities (114). The interrelationship among energy availability, menstrual function, and bone health is called the female athlete triad and has been extensively studied (115). The idea that low estrogen is also associated with higher reported pain makes this syndrome all the more compelling.

If indeed low estrogen levels were associated with higher levels of pain, one would postulate that exogenous estrogen administration might be a possible treatment for said pain. However, results have been mixed or insignificant. When comparing pain in female users versus nonusers of oral contraceptives, many studies did not account for the types of oral contraceptives used, and sample sizes were limited. No correlation was found between oral contraceptive use and chronic widespread pain, and estrogen replacement showed inconsistent results in acute pain assays (116–119).

Testosterone

Testosterone has a significant role in men and women. Biologically normal secretion of testosterone is important for athletic performance (120). Exogenous testosterone administration has been banned from competition because of its performance-enhancing capabilities (121). Although not well understood, there appears to be a relationship between testosterone and the pain experience. There is some evidence that opioid therapy can lower testosterone and cortisol levels (122). Particularly in patients chronically using opioids, long-term testosterone impairment has been observed. In patients with low testosterone, testosterone replacement has produced improvements in pain (123). Whether this provides any insight into sex-related differences in the pain experience remains to be studied.

Cortisol

Cortisol is a steroid hormone secreted by the adrenal gland that is a key component of stress adaptation. Both testosterone and cortisol can enhance changes in muscle growth and performance, especially in resistance training (124). Scientists have noticed that upon repeated exposure to stressful stimuli, a phenomenon of pain suppression occurs. Higher cortisol levels have been associated with this stress-induced analgesia; there is evidence that cortisol influences nociception via peripheral and central nervous system pathways (125). A few small studies have compared male versus female cortisol concentrations related to pain, and some sex differences have been seen. In response to acute pain, women were observed to have a different moderation of their adrenocortical response (126). Males showed an increased cortical reactivity in comparison to females (127). Rodent studies have reflected similar differences. Serum levels of corticosterone were shown to significantly increase after pain stimuli in male rats. Accordingly, stress-induced analgesia was shown to be greater among male rodents than female rodents (128,129).

CONCLUSION

The pain experience is at once both widely universal and uniquely individual. We can understand pain as a common human experience, and yet the precise mechanisms with which this pain is manifested is highly individualized. Amid everything, we accept that sex and gender differences exist in how men and women experience pain, whether it is based on hormones, social influences, nociceptive mechanisms, or other factors. While we believe that differences exist, it is unclear how to utilize the existing data in our clinical practice. There is a large body of research that strives to understand this pain experience, and yet it seems that true and complete understanding is still beyond our grasp. We must continue to strive forward in our studies and research and learn to apply these uncertain concepts to better treat and care for our male and female athletes. The search for answers continues, because the relief of our patients' pain and suffering depends on it.

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CONCUSSION

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INTRODUCTION

Concussion is a common and important injury for a variety of sports participants at every level of play. Whether there are gender differences in the incidence of concussion, the mechanisms of injury, or in the clinical presentation of concussion, as well as the recovery from injury, remain areas of interest. This chapter evaluates the literature that exists exploring the sex and gender differences in sports-related concussion

The Centers for Disease Control and Prevention estimates that between 2001 and 2009, 2.6 million children under the age of 19 were treated for sports-related injuries and 6.5%, or 173,285 of those injuries, were traumatic brain injuries (TBI) (1). Concussion, the most common type of TBI (2), is also the most common head injury occurring in sports, accounting for 8.9% and 5.8% of injuries at the high school and college levels, respectively (3). Certain factors appear to increase the risk for concussion or to delay recovery when a concussion injury occurs, such as a prior history of concussion, migraine or headache disorder, learning disabilities/attention deficit hyperactivity disorder (ADHD), and mood disorders. There are data that suggest that females may have an increased incidence of concussion, and there are also limited data to suggest that there may be differences in the mechanism of injury, the symptoms reported at baseline as well as after injury, and the cognitive and overall recovery from concussion between men and women. This chapter explores the limited research in this area.

INJURY EPIDEMIOLOGY IN WOMEN VERSUS MEN

It can be challenging to compare concussion injury epidemiology due to differences in the definition of concussion, differences in what constitutes an injury (e.g., playing time loss versus injury evaluated by medical staff), the quality of the data, specifically the quality of the denominator in terms of exposures, and finally the reporting system (e.g., whether reported by medical personnel such as an athletic trainer or team physician or self-reported). Though there are data at the college and high school levels, there is a paucity of data at the youth level as well as at the professional level. The Institute of Medicine has recently reviewed the available sport-related concussion data (4).

In 2007, the data from 1998 to 1999 through 2003 to 2004 from the National Collegiate Athletic Association (NCAA) were published and demonstrated that the incidence of concussion was 5.3 compared to 3.9 per 1,000 athlete exposures (AEs) in women compared to men's soccer, respectively, and 4.7 compared to 3.2 per 1,000 AEs in women's compared to men's basketball (5). This same study reported an incidence of concussion in women's softball of 4.3 compared to 2.5 per AEs for baseball. At approximately the same time, another study evaluated 100 high schools and 180 colleges and again demonstrated an increased incidence of concussion in female soccer and basketball players compared to their male counterparts (3). Other studies have also confirmed that for sports using the same rules (e.g., soccer, basketball, and baseball/softball), females report a higher incidence of concussion compared to males (7–12). The most recent data from the NCAA, reviewing the incidence of injury in both game and practices, continue to demonstrate a higher incidence of concussion in sports with the same rules for women compared to men (6). In the same NCAA review, the highest overall incidence of concussion occurred in wrestling, followed by men's football, men's ice hockey, women's field hockey, women's soccer, women's lacrosse, men's lacrosse, men's soccer, women's basketball, men's basketball, softball, women's volleyball, and finally baseball. At the high school level, recent data between 2010 and 2012 reported the incidence of game and practice concussions in girls compared to boys soccer and girls compared to boys basketball was 3.4 and 1.9 and 2.1

and 1.6 per 10,000 AEs, respectively, and 1.6 compared to 0.5 per 10,000 AEs in softball compared to baseball (12). When evaluating the percentage of total injuries in practice and games that are concussions, the recent NCAA data (6) show that for football, 35% of injuries are concussions, followed by women's soccer (12%), women's basketball (10%), men's basketball (8%), men's soccer (6%), wrestling and softball (both 5%), with all other sports less than 5%.

In terms of mechanism of injury, some data exist suggests that in sports with similar rules there may be subtle differences in the mechanism of injury between sexes, with player contact to surface or equipment being more common in females compared to males (7). Dick (7) found that for basketball and soccer, the mechanism of concussion in males was more likely due to impact from other players (81% in males versus 66% in females), whereas the mechanism of concussion in females was more likely due to contact with the ball (8% in males versus 18% in females) or a surface (8% in males versus 13% in females). It is important to understand that there are very few prospective data to evaluate mechanism of concussive injury, and therefore conclusions must be considered preliminary.

The explanation(s) for a potential difference in concussion incidence as well as mechanism of injury is unclear and may be multifactorial. Some of the differences in incidence could be related to a reporting bias, which postulates that females are more likely than males to report symptoms of a concussion to a health provider. Additionally, there may exist a treatment bias where athletic trainers or other health care providers may manage female athletes, especially those of younger age, more conservatively, therefore possibly skewing the data. Other potential explanations for incidence and mechanism of injury include biomechanical differences, such as head-to-neck ratio and strength, and the neuroprotective effect of sex hormones, most notably progesterone. There may also be sex differences in symptom scores and cognitive function at baseline as well as post-concussive injury. There is limited literature exploring sex and gender differences in concussion and more research is needed to answer critical questions regarding concussion, most importantly how injury and complications can be prevented.

COGNITIVE FUNCTION AND SYMPTOMS AT BASELINE VERSUS POST-INJURY

Concussion is characterized as a "subset of traumatic brain injury" and is defined as "a complex pathophysiological process affecting the brain, induced by biomechanics forces" (13). The diagnosis of a concussion can be challenging, without a clear biomarker or diagnostic test, relying instead on a constellation of subjective and objective data. Following a concussion there are typically alterations in function that cover several domains—presence of athlete reported symptoms, physical signs, and behavioral, postural, and cognitive changes. Symptoms and cognitive function are two important components of the multimodal assessment of concussion. Several guidelines for managing concussion have been published (13–19,25), and many of these endorse the concept of "baseline" testing as part of the preseason to assess symptoms and findings that can then be repeated after an injury occurs. The NCAA recently released guidelines stating that every athlete, no matter how minimal the risk for concussion, should have a baseline assessment for concussion (18). There are standardized tools such as the Sideline Assessment of Concussion (SAC) as well as the more recent Sideline Concussion Assessment Tool-3 (SCAT-3), which can be used to assess concussion (20,21). The SCAT-3, which incorporates the SAC, has been shown to be both sensitive and specific to concussion (22). When baseline assessments are available and compared with post-injury assessments, a drop in score of 3.5 points on the SCAT-2 demonstrated a sensitivity and specificity of the SCAT-2 of 96% and 81%, respectively. When a baseline assessment is not available, sensitivity and specificity were 91% and 83% when a cutoff value is used (22,41). Both paper and pencil as well as computerized neuropsychological (NP) testing have been utilized to evaluate concussive injury, and testing can be used for both baseline and post-injury assessments of cognitive function. The utility of NP testing in assessing and tracking recovery after concussion has been reviewed (23,24,26,27). NP testing evaluates brain-behavior relationships and provides objective information regarding speed of information processing, memory recall, attention and concentration, reaction time, scanning and tracking ability, and problem solving. Similar to differences in incidence of injury, research has shown that there are differences between males and females in their baseline reporting of concussion symptoms and measures of cognitive function using NP testing both at baseline as well as after concussive injury (17,28, 29,37). Specifically as it relates to NP testing at baseline, Covassin et al. (28,38,54) found that females scored better on verbal memory with no statistically significant differences in other testing domains. Interestingly, Colvin et al. (29), in their baseline evaluation of soccer players with a history of concussion, found that females had significantly slower reaction times than males. When evaluated after sustaining a concussion, results have shown that females have scored lower on visual memory as compared to males (31,38,53).

The Post Concussion Symptom Score (PCSS) is a subjective measure showing the presence and type of symptom as well as the athlete's perceived severity of that given symptom. There are a total of 22 symptoms, graded 0–6 and covering four domains: physical, cognitive, emotional, and sleep. Severity totals can range from 0 (no symptoms) to 132 (presence of all symptoms rated as most severe). Covassin et al. (28) studied the presence and degree (mild 1–2, moderate 3–4, and severe 5–6) of baseline symptoms, males compared to females. Of the total 1,209 athletes studied, "68% of males and 76% of females" endorsed baseline symptoms with the difference between the sexes reaching statistical significance for "headache, nausea, fatigue, sleep disturbance, drowsiness, sensitivity to light and noise, irritability, sadness, nervousness, feeling more emotional, and difficulty concentrating." For both males and females, fatigue was most prominent at 26% and 29%, respectively. Overwhelmingly, both males and females reported their symptoms as being "mild (1–2 on a 0–6 scale), at 66% and 73%, respectively." These data underscore the importance of an individualized approach to concussion management and the importance of evaluating post-concussion NP testing and PCSS in comparison to baseline values.

Covassin et al. (37) explored how depression affects baseline NP testing and baseline concussion symptoms score. A total of 1,616 collegiate and high school athletes completed Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), PCSS, and the Beck Depression Inventory assessments. Results showed that those with severe depression "scored worse on visual memory" and endorsed presence of symptoms in the "somatic (headache, dizziness), cognitive (memory problems, fogginess), emotional (anxiety, depression), and sleep (more/less sleep, trouble sleeping) domains of the PCSS." At baseline, females overall had more symptoms in the "cognitive, emotional and sleep clusters," but there was no correlation between females and the presence or severity of depression.

In a study of 280 collegiate athletes, Putukian evaluated the SCAT-2 as well as baseline screening assessments of both depression (Patient Health Questionnaire-9 [PHQ-9]) and anxiety (Generalized Anxiety Disorder-7 [GAD-7]), history of loss of consciousness (LOC), migraine, and prior concussion (22,41). The SCAT-2 includes subsets of symptoms, cognitive function (the SAC assessment), and postural stability (modified Balance Error Scoring System). In evaluating for baseline demographics that might explain a difference in SCAT-2 scores, no significant gender differences emerged. In addition, no effect was seen when history of migraine, concussion, or loss of consciousness (LOC) was evaluated. Elevations in both the PHQ-9 and GAD-7 did correlate with SCAT-2 performance, and when this was evaluated further it was found that these scores correlated with increases in symptom score and not the subsets of cognitive function or balance. This study was limited in terms of evaluating the effect of sex or gender on incidence of and outcome from concussion given the small number of concussions during the study period.

After sustaining a concussion, there may be sex differences in the reporting of concussion symptoms. Colvin et al. (29) studied 234 soccer players with a history of previous concussion, which included 93 males and 141 females, ranging from 8 to 24 years old. Results showed that female players reported significantly higher total symptom scores, 25.6 compared to 14.0 reported by males. Conversely, Broshek et al. (30) demonstrated that males and females had a similar mean number of reported symptoms post-concussion, 5.07 compared to 6.66, respectively. However, within these reported symptoms, females self-reported "concentration problems, fatigue, lightheadedness, and seeing fly-specks" more significantly than males. Of note, the most reported symptom by both males and females was headache at approximately 82% and 86%, respectively. Although baseline NP testing reportedly had no differences in the Broshek study, there was no mention or comparison of post-concussion symptoms to baseline symptoms and if a gender difference exists. Several years later Covassin and colleagues (31) studied 79 college athletes, at preseason and at 2 and 8 days post-injury, and noted no sex or gender differences with baseline symptom scores, but they did conclude that males had "significantly higher symptom scores for sadness and vomiting" post-injury. When post-concussion symptoms were evaluated in athletes who played a similar sport, in this case soccer, and controlled for modifiers (ADHD, learning disability, and migraines), Covassin et al. (53) demonstrated that females "reported a greater number of total concussion symptoms at eight days" post-concussion. Specifically the total reported scores for females was 11.9 (±15.70) as compared to 5.3 (±7.40) for males and there were statistically significant gender differences in the "sleep" and "migraine-cognitive-fatigue" clusters. Of note, in the Covassin et al. study, there was no comparison to baseline symptoms, and although the study was controlled for modifiers, it may not be possible to fully conclude that the increased post-concussive symptoms (PCSs) were purely due to sex. Therefore, it appears that females as compared to males will report more symptoms at baseline. However, given that PCSs have not been compared to baseline, we are unable to conclude from these studies whether symptoms post-injury are due to persistent deficits after concussion versus symptoms potentially due to other conditions. Why sex differences might occur in other realms of assessment (e.g., cognitive function and balance) is unclear.

BALANCE/POSTURAL ASSESSMENT AT BASELINE VERSUS POST-INJURY

After sustaining a concussion, there have been reported balance and postural deficits (32). These deficits represent the complex interdependent relationship of the sensory and motor systems that make up our vestibular system that can be tested by vestibulo-ocular reflex (VOR), the vestibulospinal reflex (VSR) and the vestibulocollic reflex (VCR) techniques (32). The VOR helps to maintain vision during head movement, VSR maintains posture and balance, and VCR stabilizes the head. Guskiewicz et al. (33) demonstrated that the Balance Error Scoring System (BESS) is a "practical, valid, and cost-effective method of objectively assessing postural stability" with deficits returning to baseline by "day 3 post-injury." Subsequently, Murray et al. (34) performed a literature search to determine the reliability of postural testing after sustaining a concussion and demonstrated that the BESS has a "moderate test-retest reliability." This was more clearly defined by Finnoff et al. (35) who showed that a change in the total BESS score of greater than 7.3, with the same rater, and greater than 9.3 points, with a different rater, is required to conclude that the difference from baseline is related to changes in postural sway rather the individual completing the test.

Having shown the BESS to be a valid tool to assess postural stability, Zimmer et al. (36) used it with 437 Division II athletes to determine if there is a difference in baseline BESS based on sport and then subsequently based on sex. They looked at a total of seven sports, and when evaluated as a whole, soccer athletes had the least amount of errors at baseline (16.43 errors) and basketball had the most (22.02 errors). When reordered by sex, scores for women's soccer (15.35 errors) were statistically significant as compared to men's basketball (25.04 errors), men's lacrosse (22.52 errors), and football (22.22 errors). It seems logical that soccer players would have better BESS results at baseline given the need to perform a majority of the sport-specific skills on one leg. Therefore, this further underscores the importance of baseline testing or at a minimum having sport-specific normative data that can be used in the evaluation and management of athletes after sustaining a concussion.

In another study using the BESS, athletes who had sustained a concussion were evaluated to see if there were any correlations with sex or age (38). A total of 222 athletes were tested: 157 male and 65 female, of which 150 were from high school and 72 from college. The athletes were analyzed at days 1, 2, and 3 post-concussion. Although not statistically significant, the results showed that college females had a mean of 21 errors compared to 13 for college males after sustaining a concussion. However, the results were opposite at the high school level, with females having 17 errors and males having 19 errors. Of note, the statistically significant finding from this study was the gradual improvement in total BESS of all participants from day 1 to 3.

A recent retrospective chart review of 206 patients, age 6 and over, with a concussion diagnosis (80 that were sport-related, ages 10–65) was completed to determine if there was any significant correlation among age, gender, BESS, SAC, and King-Devic (K-D) testing. The results showed no sex effect on SAC, BESS, and K-D; however, there was a significant correlation between female sex, older age, and a higher symptom score. Similarly, there was a correlation, as expected, between older age and higher BESS errors. Limitations of this study include the inclusion of concussions that were not sport-related as well as a better stratification of BESS performance by age (39). In reviewing the current literature available on sex differences and BESS testing, what is apparently missing are prospective longitudinal data. Zimmer et al. (36) showed a sex difference in baseline BESS, but there was no correlation to post-concussion data in the subjects that were studied. Similarly, Covassin et al. (38) demonstrated a sex difference in post-concussion BESS with college females scoring the worst, but there was no baseline BESS for these subjects. Therefore, more research is needed to evaluate the changes from baseline to post-concussion across the currently established measures used (i.e., BESS and NP testing) to evaluate for any differences based on sex.

LENGTH OF RECOVERY

The decision to begin a return to play (RTP) progression should be done on an individual basis and in a stepwise progression. Several position statements agree with this concept (13–19,25) and recommend a RTP protocol that begins with light aerobic activity (to maintain a heart rate greater than 70% of maximum) and, if tolerated, progresses over a 24-hour period to sport-specific exercises, noncontact drills, and finally sport-specific activity and full contact. Of note, although widely accepted, this stepwise progression is not an evidence-based approach. Therefore, it is important to understand that each concussion is different and that individualized management is necessary. While the overwhelming literature supports the concept that the large majority of concussions will resolve in 7 to 10 days (13,40), more recent published data demonstrates a more conservative approach with RTP taking 14 to 21 days (22). Additionally, one must consider "modifiers" that may prolong recovery, such as female sex, younger age, history of previous concussions, or history of ADHD, learning disability, depression, or migraines (13,16). A recent meta-analysis has found that symptoms persisted for 15 days in high school athletes compared to 6 days in college athletes, though NP testing deficits were similar in both groups (52).

Bazarian et al. (42) evaluated 1,425 individuals that sustained a mild traumatic brain injury (MTBI) to determine correlation between sex, PCS, and return to baseline (determined as the length of time to return to normal activities and the amount of work days missed). Close to half of the study subjects were female, and the results showed that females were more likely to have PCS scores greater than 16 and to miss more than 7 days of normal activities. Of the three parameters, the only one that was statistically significant was the correlation between female sex and PCS score. At 3 months post-injury, the mean PCS score for males was 4.0 compared to 7.0 for females and was most apparent between ages 14 and 56. Similarly, King (43) found a significant correlation between female sex and prolonged PCS, defined as symptoms being present 12 to 18 months post-injury, with a mean age of 35.9 years. In the adolescent population (ages 11 to 18), 67.7% of females took 1 month or more to return to baseline and 41.2% took more than 2 months (44). Though more research is needed, there appears to be evidence that female gender increases the risk for having prolonged PCS.

WHAT EXPLAINS THE DIFFERENCE?

Although research has shown an increased incidence of concussion in females compared to males participating in sports with the same rules, and there appear to be differences in both baseline and post-injury assessments of symptoms, cognitive function, and postural stability, there remains an unclear understanding as to the etiology of these differences. Possible explanations include reporting bias, treatment bias, the effect of fluctuating sex hormones across the menstrual cycle, and biomechanical differences.

One possibility that has been eluded to is that females may be more likely to report symptoms, both at baseline as well as post-injury. This can be a challenging argument and certainly deserves further attention. The possibility of sex hormones as reason for sex disparity has also been an area of research. Animal studies have demonstrated that progesterone has “anti-apoptotic” and protective effects when administered serially to adult male rats after sustaining a “contusion of the frontal cortex” (45). The significance and reproducibility of these findings in humans has been questioned. Wunderle and colleagues (46) studied what they termed the “withdrawal hypothesis.” They postulated that the downregulation of progesterone production after sustaining an MTBI would lead to worse outcomes. They evaluated 144 patients between ages 16 and 60 and stratified them into three groups—those taking synthetic progestin (SP), those in the luteal phase (LP) of their menstrual cycle (as determined by serum progesterone concentration), and those in the follicular phase (FP) of the menstrual cycle. Those in the LP group had statistically significant lower scores on the Quality of Life (QoL) general health rating and QoL index score as compared to the SP group. The authors hypothesized that the lower scores in the LP group might be due to a drop in progesterone just after the time of injury as progesterone levels fall toward the end of the LP. The LP group had worse Riverbed Post Concussion Questionnaire (RPCQ) scores as compared to the SP and FP groups, but they were not statistically significant. The differences between the LP and FP groups, across all three measures, however, was not statistically significant. Mihalik et al. (47) evaluated if baseline neurocognitive function, postural stability, and symptoms scores were affected by being in the LP or FP of the menstrual cycle. Thirty-six females were tested using ImPACT, the Sensory Organization Test (SOT), and PCSS in both their follicular and luteal phases and there was no statistically significant difference between the menstrual phases across all three tests. Therefore baseline tests done at any phase in the menstrual cycle are valid and any deviations noted can be assumed to be secondary to the concussion. However, these results should be considered with the knowledge that cycle phase was determined with the calendar, which is far less reliable than using urinary or serum markers. Thus, additional research is needed to evaluate the role of sex hormone levels and menstrual cycle phase as an explanation for the sex differences seen in concussion.

Another area that warrants exploration is the biomechanical differences between the sexes, specifically head-to-neck ratio, which effects head stabilization and acceleration during contact. Tierney et al. (48) examined 40 physically active individuals, 20 female and 20 male, to assess gender differences in head-neck stiffness, mass, and acceleration. Males were found to have longer head-neck length, greater head-neck mass, and greater neck girth, but only the difference in mass and girth were statistically significant, with females having 43% less head-neck mass and 30% less neck girth. Although females activated their cervical stabilizing muscles faster, sternocleidomastoid (SCM) 29% faster, and trapezius 7% faster, and generated 79% more muscle activity, they had up to 70% more acceleration and 39% more displacement than males. These differences in head acceleration and displacement may increase the risk of concussion. Whether neck mass and girth can be modified and whether this translates to a decrease in head acceleration and displacement is unclear. Schmidt et al. (55) found that greater cervical stiffness and less angular displacement after perturbation, and not isometric muscle strength or size, was associated with mitigating head impact severity in high school and college football players. More research evaluating head impact biomechanics and if and how they relate to concussive injury is needed, as well as research specifically addressing gender differences in head impact biomechanics.

Mansell et al. (49) followed 36 college soccer players (17 males and 19 females) to see if an 8-week cervical resistance training program would improve dynamic stabilization when force application was known or unknown, and then evaluated for sex differences. Although females demonstrated increased extensor strength by 22.5% and increased girth by 4.5%, there was no reduction in acceleration whether the force application was known or unknown. Conversely, Eckner et al. (50) demonstrated that if the force is known, subsequent cervical muscle activation led to reductions in linear and angular velocity. These reductions held true across both sexes and in both the pediatric and adult groups. Intuitively it makes sense that if one sees the impact coming the acceleration force that the head sees is diminished. Applying Newton's second law, where mass equals force times acceleration, if the cervical muscles are held rigid, the mass is now the body and the head (instead of just the head alone) and one would expect a decrease in the acceleration seen by the head. More research is needed in this area.

Collins et al. (51) measured neck strength in 6,662 male and female high school athletes and subsequently compared strength to concussion incidence. They found that across both sexes and all sports, with the exception of soccer, weaker neck strength consistently correlated with those athletes that had sustained a concussion. They also extrapolate that "for every one pound increase in neck strength, odds of concussion decrease by 5%." This research supports the concept that concussion may be prevented by measures to increase strength of the neck musculature.

CONCLUSION

There appears to be evidence to support that in sports with the same rules, the reported incidence of concussion is higher in females compared to males. There are limited data to demonstrate a potential difference in mechanism of concussive injury in males versus females, with males more likely to sustain contact injuries with another player and females more likely to sustain a concussion from impact with a ball or stick. In addition, in several studies, females endorse more symptoms at baseline and post-injury when compared to males, and in some studies their recovery is delayed. The explanation for these sex and gender differences is likely multifactorial, with reporting bias, hormonal differences, and biomechanical differences as important considerations. Potential interventions to consider include programs to improve biomechanics and/or cervical spine strength or stiffness.

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16

THE YOUNG ATHLETE

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SPORTS PARTICIPATION

Sports participation is common among youth in the United States with 60 million children participating in organized sports each year (1). Total sports participation in both male and female youth athletes has been increasing steadily over the past few decades (1,2). Among high school students in particular, the number of students participating in sports increased from around 4 million in the early 1970s to 7.8 million, according to the 2014 National Federation of State High School Associations (NFHS) participation survey (2). The Centers for Disease Control and Prevention (CDC) 2013 data showed that just over half (54%) of all high school students played team sports (3). Data regarding sports participation in younger age groups are less prevalent; however, Physical Activity Council data from 2014 showed that 62% of Generation Z (born in 2000 or later) ages 6 through 14 played outdoor sports and 57% played team sports (4). A nationwide survey conducted by the Women's Sports Foundation on kids in third through twelfth grade found even greater participation with 84% of kids surveyed indicating they played organized or team sports (5).

Despite the popularity of youth sports among both males and females today, sex disparities regarding sports participation have long existed, with historically more males participating in organized sports compared to females. According to the NFHS, approximately 3.7 million boys and only 294,000 girls participated in high school sports in 1971 (2). In the past few decades the gap between male and female youth sports participation has been closing. In 2013, the NFHS found that 4.5 million boys and 3.3 million girls participated in high school sports (2). Reasons are likely multifactorial, but largely influenced by increased access to female sports since the passage of Title IX. Title IX of the Education Amendments of 1972 prohibited sex discrimination in all federally funded education programs and activities, resulting in increased opportunities for athletic participation by females (6). The trend toward more female youth sports participation has continued to increase well beyond the 1970s when Title IX was first passed. A 2008 sports participation report of the National Council of Youth Sports (NCYS) found that, compared to its 1997 report, girls were participating in organized sports at a younger age, and compared to the 2000 report, more girls in the 16 to 18 age group were participating in sports (1).

Great strides have been made to increase female sports participation; however, still slightly more males than females participate in youth sports overall. CDC data from 2013 showed that 59.6% of male high school students were involved in team sports compared to 48.5% of female students (3). This difference may be less prevalent in younger athletes, as the NCYS 2008 sports participation report found greater sex equity in sports participation in younger age groups compared to older athletes (1).

A chart review of sports medicine clinic data from 2000 to 2009 by Stracciolini et al. suggested that boys participate in more types of sports compared to girls, with an average of 2.5 sports played by each boy and an average of 2.2 sports played by each girl (7,8). In addition to differences in overall sports participation, this study found sex disparities between the types of sports played by males and females. Compared to girls, a significantly greater percentage of boys played team sports and contact/collision sports that are associated with more acute/traumatic injuries than overuse injuries. High school sports participation data have shown similar sex differences in the types of sports played by boys and girls. The NFHS reported in 2014 that the most popular high school sports played by males, in descending order, were football, track and field, and basketball, and the most popular sports for girls were track and field, basketball, and volleyball (Table 16.1) (1,2).

TABLE 16.1: Most Popular High School Sports Based on Participation

Male	Number of Participants	Female	Number of Participants
1. Football	1,093,234	1. Track and Field	478,885
2. Track and Field	580,321	2. Basketball	433,344
3. Basketball	541,054	3. Volleyball	429,634
4. Baseball	482,629	4. Soccer	374,564
5. Soccer	417,419	5. Softball	364,297
6. Wrestling	269,514	6. Cross-Country	218,121
7. Cross-Country	252,547	7. Tennis	184,080
8. Tennis	160,545	8. Swimming and Diving	165,779
9. Golf	152,647	9. Competitive Spirit Squad	120,593
10. Swimming and Diving	138,373	10. Lacrosse	81,969

Source: Adapted from Ref. (2). 2013–2014 High School Athletics Participation Survey. National Federation of State High School Associations. http://www.nfhs.org/ParticipationStatics/PDF/2013-14_Participation_Survey_PDF.pdf

SPORTS INJURIES

Sex disparities in sports injury type, location, and severity exist and may be due to several factors, including differences in sports participation, anatomy, and biomechanics. A study reviewing injuries in 1,614 patients presenting to a pediatric sports medicine clinic found a significantly greater percentage of spine, hip/pelvis, and lower extremity injuries in girls and a significantly greater percentage of head, upper extremity, and chest injuries in boys (7,8). Another study of 1,421 musculoskeletal injuries presenting to an emergency department showed similar results, finding more sprains, contusions, and ankle and back injuries in girls and more fractures and hand injuries in boys (Table 16.2) (9).

High-risk sports for sustaining an injury vary by sex. One study found that football accounted for the highest percentage of sports-related injuries in boys, while soccer was responsible for the highest percentage of injuries in girls (10). When examining injury patterns in sex-comparable sports (Table 16.3), location and type of injuries differ between girls and boys. In soccer, high school girls sustain more severe knee injuries and more ligament sprains, while high school boys sustain more fractures (11). Similarly, in basketball, high school girls sustain more severe knee injuries and complete ligament sprains, while boys sustain more severe foot injuries and fractures (11). Sex disparities in sports injuries can be further discussed in the context of traumatic injuries versus overuse injuries, with different patterns seen in males compared to females.

Traumatic Injuries

Boys sustain more sports-related traumatic injuries and more severe injuries compared to girls, in part due to differences in the types of sports in which they participate, since males are more likely to play in contact and collision sports compared to females (7,10,11). Studies examining the incidence of pediatric musculoskeletal and/or sports-related injuries presenting to an emergency department or trauma center found that 62% to 84% of sports-related injuries presented in males (9,12,13). An epidemiologic study that examined the rate of severe injuries incurred by high school athletes in a convenience sample of 100 high schools in the United States found that the severe injury rate per 1,000 athletic exposures in all-boys sports was significantly higher than in all-girls sports (0.45 versus 0.26, respectively) (11). This difference was primarily due to the high injury rates seen in boys wrestling and football. However, for sex-comparable sports such as soccer, basketball, and baseball/softball, the severe injury rate was significantly higher in girls compared to boys (0.29 versus 0.23, respectively) (11). Both boys and girls were found to have a significantly higher injury rate during competition

TABLE 16.2: Sex Differences in Injury Incidence, by Injury Location

Study	Setting and Study Population (dates of data collection)	Total Number of Injuries and Injury Type (M = male injuries, F = female injuries)	Injury Location	Injury Incidence*	
				Male	Female
Schroeder et al., 2015	• U.S. National High School Sports-Related Injury Surveillance System, High School Reporting Information Online (RIO) database • High school athletes from representative sample of 100 high schools (2006–2012)	2,834 overuse injuries (M = 1450, F = 1384)	Shoulder	11.7%	11.4%
			Elbow	3.5%	2.1%
			Lower back/spine/pelvis	12.6%	8.7%
			Hip	7.6%	7.1%
			Thigh/upper leg	10.4%	7.3%
			Knee	14.7%	17.2%
			Lower leg	17.5%	26.2%
			Ankle	3.9%	4.6%
			Foot	12.3%	10.3%
			Other/unknown	5.8%	5.0%
Stracciolini et al., 2014	• Pediatric sports medicine clinic • Patients age 5 to 17 (2000–2009)	2,133 sports injuries (M = 982, F = 1151)	Head	2.6%	0.5%
			Chest	2.1%	0.6%
			Upper Extremity	29.8%	15.1%
			Lower Extremity	53.7%	65.8%
			Hip/pelvis	3.7%	6.7%
			Spine/back	8.2%	11.3%
Darrow et al., 2009	• U.S. High School RIO database • High school athletes from representative sample of 100 high schools (2005–2007)	1,378 severe injuries** (M = 1067, F = 311)	Knee	22.2%	43.8%
			Ankle	9.2%	19.1%
			Shoulder	14.4%	3.4%
			Hand/finger	9.2%	4.9%
			Head/face	6.7%	7.0%
			Lower leg	6.4%	6.2%
			Foot/toe	4.4%	5.9%
			Wrist	5.2%	2.3%
			Other	22.3%	7.4%
Damore et al., 2003	• Emergency department • Patients age 5 to 21 (October 1999 & April 2000***)	1,421 sports injuries in 1275 subjects	Hand	21%	16%
			Ankle	20%	26%
			Back	4%	7%

*Percentages represent percentages of a particular body part injury compared to all injuries for that sex.

**Severe injury defined as any injury resulting in loss of more than 21 days of sports participation (11).

***Random sampling of patients presenting to an emergency department over 2 months corresponding to Fall and Spring sports seasons.

Source: From Refs. 7, 9, 11, 21.

compared to practice, and ligament sprains and fractures were the most common types of severe injuries (11).

When examining fracture incidence in particular, several epidemiological studies have found a sex disparity in pediatric fracture risk, with boys sustaining significantly more fractures than girls (7,14–17). In a study of 204 pediatric hand fractures (subjects age 17 or younger) presenting to a tertiary care center in Singapore, the male-to-female ratio of fractures was 3.2:1, and sports participation was the most common cause of injury (14). A similar Austrian study of 3,421 pediatric fractures presenting to a level 1 trauma center found a 3:2 ratio of male-to-female fractures, with a more pronounced sex difference in fracture occurrence in adolescents compared to younger children (17). Valerio et al. found that as children got older, the male-to-female ratio of time participating in sports increased and that this was likely contributing to the sex difference in fracture incidence with age (15).

TABLE 16.3: Sex-Comparable Sports

Darrow et al., 2009 (11)	Yang et al., 2012 (20)	Schroeder et al., 2015 (21)	Changstrom et al., 2015 (25)
Basketball	Baseball/softball	Basketball	Baseball/softball
Baseball/softball	Basketball	Baseball/softball	Basketball
Soccer	Cross-country	Lacrosse	Cross-country
	Gymnastics	Soccer	Soccer
	Swimming/diving	Swimming/diving	Swimming/diving
	Track and field	Track and field	Track and field
		Volleyball	Volleyball

Note: Sex-comparable sports are sports played by males and females with similar rules and equipment.

Source: From Refs. 11, 20, 21, 25.

Overuse Injuries

Overuse injuries are injuries that occur with an insidious onset, without a clear preceding traumatic event, and are due to repetitive microtrauma (18). Studies have shown a higher overall rate of overuse injuries in female compared to male youth athletes (7,18–21). A study on sports injuries using data from High School Reporting Information Online (RIO), a national sports injury surveillance database, found that overuse injuries represented 13.3% of all girls' and 5.5% of all boys' sports injuries. Girls were at 1.5 times increased risk of developing overuse injuries compared to boys and for sex-comparable sports (Table 16.3), girls had a 1.45 times increased risk of developing overuse injuries compared to boys (21). Other research showed that in collegiate athletes females had a significantly higher proportion of overuse injuries overall, but this pattern was no longer significantly different when comparing sex-comparable sports (Table 16.3) (20).

Patellofemoral pain syndrome, a type of overuse injury to the knee, is more common in females compared to males (7,8,22–24). Rates of patellofemoral dysfunction are higher in female compared to male youth, with one study finding 7.3% of female basketball players had patellofemoral pain syndrome compared to 1.2% of male basketball players (23). Patellofemoral pain syndrome was three times more common in girls than boys presenting to a sports medicine clinic, representing 14% of female youth clinic visits compared to 4% of male youth clinic visits (7,8,23).

Stress fractures are also more common in female youth athletes compared to males. A study using High School RIO data from academic years 2005 through 2013 showed that females accounted for 54% of stress fractures across all sports. In sex-comparable sports (Table 16.3), rates of stress fractures per athletic exposure were significantly higher in female compared to male adolescents (2.22 versus 1.27 injuries per 100,000 athletic exposures) (25).

Intensity of physical activity plays an important role in bone health. One study found that preadolescent and adolescent girls who participated in at least 16 hours of weekly exercise had a 1.88 times greater odds of stress fracture compared to girls who participated in less than 4 hours of weekly exercise (26). Other studies have shown that high impact physical activity provides benefit to young athletes by increasing bone mass (27). Optimal bone health in both sexes likely involves a balance between participating in enough weight-bearing physical activity to improve bone mass and avoiding excess activity that may lead to increased stress fracture risk.

Sex disparities regarding incidence and type of overuse injuries are likely multifactorial. Females are more likely than males to play sports associated with overuse injuries, such as track and field, dance, swimming, tennis, gymnastics, and cheerleading (8). Differences in anatomy, biomechanics, joint laxity, muscle strength, neuromuscular control, hormones, training, and coaching may also play a role (18–20). Furthermore, some authors postulate that females may be more likely to report injuries and seek medical care compared to males (18).

Concussion

Concussion has become of increasing interest in youth sports over the past decade due to enhanced awareness of associated adverse physical, cognitive, and psychosocial effects on the athlete. According to the International Conference on Concussion in Sport held in Zurich in 2012, concussion "is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces" (28). While much is still unknown about the pathophysiology of concussion, there is evidence that differences exist between boys and girls regarding risk of sustaining a sports concussion, symptoms, and recovery (Table 16.4).

TABLE 16.4: Summary of Sex Differences in Concussion

Prevalence
- Males sustain more concussions per athletic exposure
- Females sustain more concussions in sex-comparable sports

Mechanism of Injury
- Males sustain more injuries via player-player contact
- Females sustain more injuries via player-playing surface and player-equipment contact

Symptoms
- Females display more objective impairments in cognitive function
- Females report more subjective symptoms

Recovery
- Females more likely to experience prolonged recovery
- Females may require more treatment interventions

Risk Factors for Concussion
- Anatomic/biomechanical: Females have smaller head-neck mass
- Hormonal: Estrogen is possibly neuroprotective
- Cultural: Males less likely to recognize or report a concussion

Epidemiological studies have found that overall boys have a greater rate of concussion per athletic exposure compared to girls (29–31). A study of pediatric patients under the age of 19 presenting to emergency departments in the United States found that 69% of patients with concussion were male. A similar study of children between the ages of 6 and 16 found that males accounted for 71.6% of concussions presenting to the emergency department (30,31). Children above the age of 10 and 11 are most likely to sustain a concussion during sports activity (30,31). In the United States, the highest-risk sports for sustaining a concussion are football and soccer for boys and soccer and basketball for girls (29,32,33). Some studies include boys, wrestling and boys and girls lacrosse as high-risk sports as well (29,32). Outside the United States, other popular high-risk sports include ice hockey in Canada and rugby in the United Kingdom, Australia, and South Africa (34,35).

The higher incidence of concussion in boys is likely due to their greater participation in high-risk sports. However, in directly comparable sports, high school girls sustain nearly twice as many concussions as boys, and a greater proportion of total number of sports injuries in females compared to males are due to concussion (29,32,36–38). Female athletes may also be at increased risk of recurrent concussions compared to boys (32). The mechanism of injury, whether from contact with a playing apparatus, another player, or the ground, differs between sexes depending on the sport (32,36). A study by Marar et al. comparing concussion incidence among 20 high school sports found that in directly comparable sports, girls sustained a greater proportion of concussions from player-playing surface and player-equipment contact compared to boys, who suffered more injuries from player-player contact (32).

In addition to differences in concussion incidence, there are also sex differences in symptom and recovery patterns. Female athletes experience more objective impairments in cognitive function and report more subjective symptoms post-concussion compared to males (34,39–42). A study of high school- and college-aged athletes in non-helmeted sports showed females were more than twice as likely as males to demonstrate cognitive dysfunction on neuropsychological testing post-concussion (57% versus 28%, respectively) (42). Another study showed college females were more likely than males to demonstrate poor performance on visual memory tasks post-concussion (43). Sex disparities also exist with regard to post-concussive symptoms. Several studies have shown that female athletes experience more total concussion symptoms compared to males; however, data on whether specific types of symptoms vary between males and females have been variable (40,43,44).

Sex differences are seen with concussion recovery. Female adolescent athletes may have a more prolonged recovery from a concussion compared to males. In a study of 266 adolescent athletes presenting to an outpatient sports medicine concussion clinic, 41.2% of females took more than 60 days to recover from their symptoms while half as many males, 20.7%, had a prolonged recovery of more than 60 days (33). Conversely, a study examining post-concussive symptoms in subjects 3 months after sustaining a sports-related concussion found that among athletes under 18 years of age females had similar symptom scores to males; however, for subjects age 18 and older, females had higher symptom scores than males (45). Thus, recovery patterns may vary based on age group and patient population. Female athletes have also been found to require more treatment interventions in addition to physical and cognitive rest, such as academic accommodations, vestibular therapy, or medications, to augment their recovery compared to male athletes (33).

The higher incidence of sports concussion in females, increased symptoms, and neurocognitive deficits post-concussion are likely due to a combination of anatomic, hormonal, biomechanical, and cultural risk factors (37,46). Anatomic risk factors include differences between male and female head and neck sizes (46,47). In a study of male and female collegiate soccer players, head-neck segment length was 7% shorter and head-neck segment mass was 20% lighter in females compared to males (46). In a similar study of physically active young adults, women had 30%

shorter neck girth and 43% lighter head mass compared to men (47). These anatomic differences may cause alterations in biomechanics that place females at a higher risk of sustaining a sports concussion; however, data to support this remain inconsistent. Tierney et al. found that women had more head-neck segment angular acceleration, angular displacement, and muscle activity in response to force application and less head-neck stiffness and isometric neck muscle strength compared to men (47). In another study of high school soccer athletes, females sustained significantly more concussions via player-ball contact through heading compared to males. These studies lend support to the theory that biomechanical factors involving the head and neck play a role in the sex disparity in concussion incidence (32). In contrast, Mansell et al. found no difference in head-neck kinematics, neck stiffness, and electromyography (EMG) neck muscle activity between male and female subjects (46). Mansell et al. speculated that their cohort of soccer players had better neuromuscular adaptations to handle head-neck loads as part of their soccer training compared to a general population of physically active young adults in the Tierney et al. study, and that this could account for the difference in their findings (46).

Hormonal factors may also contribute. Rat studies have shown that estrogen in females may be neuroprotective and may result in superior outcomes in female rats following brain injury (48). However, human studies exploring the effects of hormonal differences between males and females on concussion are lacking.

Psychosocial differences appear to play a significant role, as males may be more likely to underreport their symptoms. A survey of over 1,500 male high school varsity football players showed that only 47.3% of respondents who admitted to having a concussion post-season reported their symptoms during the season (49). The most common reason for underreporting was thinking the injury was not serious enough to report, followed by (in descending order of frequency) not wanting to leave the game, not knowing their symptoms could be a concussion, and not wanting to let their teammates down (49). A study of high school athletes across multiple sports showed that females had a better knowledge of how to identify a concussion and were more willing to report concussion symptoms or stop play due to symptoms compared to males (50). High school males are also more likely than females to be noncompliant with return-to-play guidelines and resume sports prior to full recovery (38). Additionally, female athletes may be treated with more sympathy by coaches and adults, while male athletes may feel more pressure to "tough it out." In a study regarding youth and parents' perceptions of concussions, mothers were more likely than fathers to think concussion was a critical issue, and boys were more likely than girls to report that their friends would think they were "dumb" for caring about concussions (51).

SEX DIFFERENCES IN RULES OF SPORT

Rules of play are similar between boys and girls in many popular youth sports including tennis, soccer, and basketball; however, there are a handful of youth sports with rules that are considerably different between males and females, leading to different injury rates and patterns. The next sections are brief discussions of popular sports that differ between sexes, including lacrosse, ice hockey, softball, and baseball.

Lacrosse

Lacrosse is a team sport of increasing popularity with nearly 400,000 youth participants and slightly more male participation (65%) than female, according to the 2013 U.S. Lacrosse Participation Survey (52). Rules and equipment differ substantially between girls and boys lacrosse (Figure 16.1). Required protective equipment for male youth field players consists of a helmet, mouth guard, shoulder and arm pads, gloves, and a protective cup. Rib pads are optional (53). Female youth field players required protective equipment is less extensive and includes a mouth guard and goggles, with optional gloves and optional soft headgear (54). In boys' lacrosse the field stick can vary in length depending on the position and has a deeper pocket, while in girls' lacrosse the stick length remains constant among players and has a shallower pocket. The design of the boys' field stick requires more aggressive play to dislodge the ball from the deeper pocket compared to the girls' field stick.

The differences in protective gear and playing equipment are due to sex differences in rules of play. Boys' lacrosse is considered a full-contact sport allowing for intentional stick checking at all levels and body checking in participants older than 11 years of age. For girls, body checking is prohibited, modified stick checking is allowed in girls age 10 to 12, and full stick checking is allowed in girls older than 12 (55).

The differences in rules and equipment result in different injury patterns. A study of high school lacrosse players showed injury rates were 1.5 times higher in males than females (56). Males are more likely than females to be injured during player-player contact, while females are more likely to be injured during contact with a playing apparatus or due to overuse (56,57). The most common

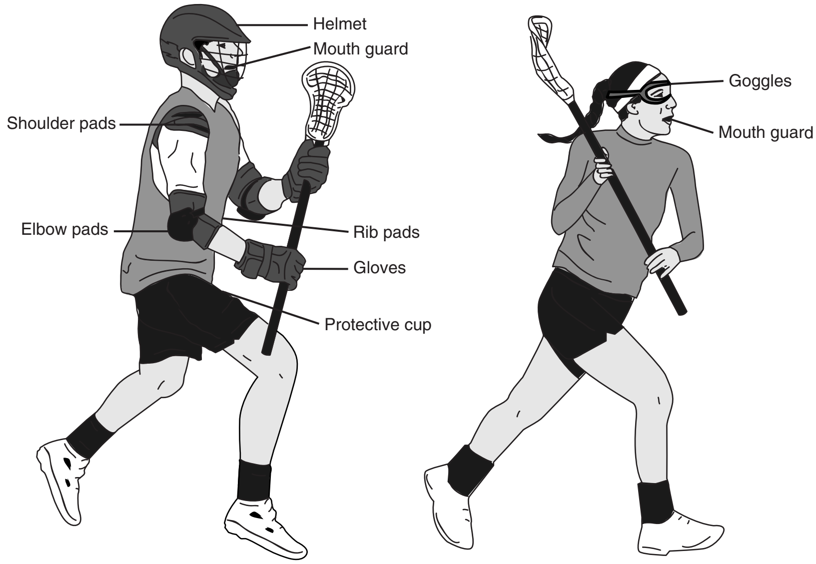

FIGURE 16.1: Male versus female youth lacrosse equipment.

injuries in both sexes are sprains/strains, followed by contusion or concussion (56,57). High school boys playing lacrosse are more likely to sustain a concussion compared to girls, and this increased risk is more prevalent in players aged 11 to 14, where body checking is allowed (29,56–58). Boys' lacrosse is a full contact sport, which leads to more sports injuries compared to girls, despite the increased protective equipment worn by boys.

Ice Hockey

Ice hockey is played by over 350,000 youth in the United States, 85% of whom are male (59). Female youth participation is similar in Canada, where ice hockey is considered a national pastime, with females estimated to be about 14% of youth ice hockey players (60). The primary rule difference between female and male ice hockey is that females are not allowed to body check, while body checking is allowed in males older than 13 years of age in the United States and Canada.

Approximately 90% of ice hockey injuries presenting to U.S. emergency departments are in males; however, the proportion of injuries in females increased from 5% of all ice hockey injuries in the 1990s to 9% from 2000 to 2006 (61). In a Canadian study of youth ice hockey players, females had significantly more soft tissues injuries, sprains/strains, and injuries due to falls while males sustained more fractures, upper extremity injuries, and injuries due to body checking (60). In both sexes, adolescent athletes are at highest risk of injury (60). A study of ice hockey injuries presenting to U.S. emergency departments showed that females accounted for a higher proportion of the head injuries and concussions while males accounted for more facial injuries and fractures (61). Although female hockey players have a higher incidence of concussion compared to males, a study by Brainard et al. found that collegiate female ice hockey players sustained significantly fewer head impacts per season compared to males (62).

The overall injury rate is nearly twice as high for males compared to females (approximately 4 versus 2 injuries per 1,000 athlete exposures (AEs), respectively) (63). Body checking allowed in male leagues likely plays a large role. Body checking has been found to increase the risk of all injuries in male ice hockey players twofold to fourfold, as well as increase the risk of concussion (63,64). Due to the high risk of injury with body checking, the American Academy of Pediatrics issued a policy statement in 2014 recommending expansion of nonchecking leagues for boys older than age 15, no checking in games prior to age 15, and restricting body checking to the highest competition levels (64).

Softball and Baseball

Baseball and softball are popular sports in youth athletics with relatively low risk of injury compared to other sports (65,66). Males primarily play baseball, while softball is a female-dominated sport. Although the objective of each game is similar, key differences exist (Table 16.5). In high school, the baseball field is larger than the softball field and the mounds are farther apart. A baseball is smaller, with a higher coefficient of restitution than a softball, and is made of leather, whereas a softball may have a synthetic covering (67). In terms of protective equipment, players of both sports wear gloves and a batting helmet. Softball players are required to have a face mask attached to their helmet, while this is optional in baseball players (67). Rules for batting and fielding are similar between the sports; however, the pitching mechanics and average pitch counts differ considerably in baseball and softball. The baseball pitch is overhand and is performed from an elevated mound 60.5 feet from home plate, while the softball pitch is an underhand windmill pitch delivered from a flat pitching circle 40.0 feet from home plate (68). Despite these differences, joint loads at the shoulder are similar in youth softball and baseball pitchers (68). However, softball players are less regulated in their pitch counts, with a high school softball player often pitching 1,200 to 1,500 windmill pitches in a 3 day period compared to 100 to 150 pitches made by a baseball pitcher in the same time period (68).

Much of the data regarding sex differences in baseball and softball injuries are focused on high school athletes. Rates of severe injuries are similar in boys' baseball and girls' softball (0.19 versus 0.18 per 1000 AEs, respectively) (11). Female softball players sustain significantly more knee injuries, ligament sprains, and dislocations than male baseball players (11). Males are more likely to be injured during pitching, while females are more likely to be injured while batting or being hit by a pitch (11). Concussion injury data have been mixed. One study showed female softball players had a higher rate of concussion than male baseball players (1.6 versus 0.5 per 10,000 AEs, respectively), while another study showed similar concussion rates between the sports but a greater proportion of total softball injuries due to concussion (32,36).

Upper extremity injuries involving the shoulder and elbow are common in both baseball and softball. One study found that the incidence of shoulder injuries was significantly higher for boys' baseball than for girls' softball (1.72 versus 1.00 injuries per 10,000 AEs) (69). Muscle strains and incomplete muscle tears were the most common shoulder injuries in both sexes and occurred more frequently during practice. Female softball players were more likely to be injured during throwing while males were more likely to be injured during pitching (69). Pitching injuries were more likely to require surgical treatment in both sexes; however, baseball pitchers were twice as likely to sustain a shoulder injury compared to softball pitchers (69). This is likely because the baseball pitching motion, combined with faster pitching speed, generates more force at the shoulder and elbow than the softball pitching motion (69).

Little league elbow is a common overuse injury unique to young (skeletally immature) throwing athletes,

TABLE 16.5: Summary of Select High School Baseball and Softball Rule Differences

Rule	Baseball (Male)	Softball (Female)
Base path distance (feet)	90	60
Pitching distance (feet)	60.5	43
Pitch delivery	May or may not be underhand	Must be underhand
Ball weight (ounces)	5–5.25	6.25–7
Ball circumference (inches)	9–9.25	11.88–12.25
Batting helmet face mask	Optional	Mandatory
Headwear	Caps required	Caps, visors, and headbands optional
Diving	Illegal	Legal

Source: Adapted from Ref. (67). Pecora A. 2015 Baseball Softball Rules Differences. Indianapolis: National Federation of State High School Associations (NFHS); 2015. https://www.nfhs.org/media/727147/2015baseballsoftballrulesdifferences.pdf particularly pitchers. It is caused by a traction apophysitis on the medial epicondyle of the humerus at the origin of the common flexor tendon. A similar overuse injury can occur at the proximal humeral epiphysis, called little leaguer's shoulder. In an attempt to decrease the risk of overuse injuries, youth baseball leagues limit pitching counts per week and per day based on the age of the athlete; however, similar regulations are lacking in youth softball leagues (66). More research is needed regarding whether restricting pitching counts in youth softball players could help decrease risk of injury.

PUBERTY, JUMPING MECHANICS, AND NEUROMUSCULAR CONTROL

Anthropometric Changes in Puberty

Puberty is defined as the process through which a child biologically becomes an adult and includes development of adult height, secondary sex characteristics, and the capacity for reproduction. Sexual maturity can be evaluated using the Tanner staging system, which uses secondary sex characteristics to differentiate stages of puberty (Table 16.6). The onset of pubertal changes occurs earlier in females compared to males. In females the mean onset of puberty is between 8 and 12 years of age and is marked by the development of breast buds. Menstruation occurs approximately 2 to 2.5 years later at a median age of 12 (range: 9 to 16 years of age). In males, the mean onset of puberty is between 11 and 13 years of age and is marked by testicular enlargement (70,71).

Accelerated growth occurs early in puberty for boys and girls; however, males demonstrate a longer prepubertal growth period and greater growth velocity compared to females (72). Boys reach their peak growth velocities 2 to 3 years after girls and typically continue to grow 2 to 3 years after girls have stopped growing (70). Average mature male height is taller than average mature female height (69.4 versus 63.8 inches, respectively) (73). This difference is primarily due to leg length as opposed to trunk length. Boys develop a significantly greater increase in leg length compared to females due to the longer prepubertal growth period (72,74).

Prior to puberty, girls and boys are similar in terms of their body composition. There is a significant divergence in body composition, including lean muscle mass, fat mass, and bone mass, between females and males during puberty. This is due to differences in gonadal hormones and other endocrine factors (74,75). Prepubertal muscle mass, also referred to as lean mass or fat-free mass, is fairly similar between males and females. During puberty, boys gain significantly more muscle mass and strength compared to girls (76–86). At age 12 to 14, female muscle mass plateaus and male muscle mass continues to increase at an accelerated rate due to a rise in testosterone (75,87). The distribution of muscle mass also differs, with males developing significantly more upper body muscle mass and strength compared to females (74,82,87,88).

TABLE 16.6: Tanner Staging/Sexual Maturity Rating

Tanner Stage	Male	Female
1	Preadolescent stage before onset of physical changes of puberty.	Preadolescent stage before onset of physical changes of puberty.
2	Pubic hair present but sparse. Penis and testes start to increase in size.	Pubic hair present but sparse. Breast buds start to develop.
3	Pubic hair still sparse but starts to curl and darken. Penis and testes continue to increase in size.	Pubic hair still sparse but starts to curl and darken. Breasts continue to develop without separation of contour of the breasts and areolae.
4	Pubic hair becomes more coarse and curly. Penis and testes continue to increase in size.	Pubic hair becomes more coarse and curly. Secondary mound formation by areolae and papillae.
5	Pubic hair, testes, and penis in adult form.	Pubic hair and breasts in adult form.

Source: Adapted from Ref. (70). Kliegman R, Nelson WE. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia, PA: Elsevier/Saunders;2011:lxvii, which was adapted from Tanner JM. *Growth at Adolescence*. 2nd ed. Oxford: Blackwell Scientific;1962.

Females have a slightly greater percentage of body fat compared to males as young as infancy, a difference that becomes more pronounced during puberty (74,75). Girls' percentage of body fat increases significantly with puberty, while the percentage of body fat declines in boys (76–86). This divergence results in an average percentage of body fat of 10% to 15% in adult males compared to 20% to 30% in adult females (74,75). The distribution of body fat also varies between males and females. Females gain more fat around the hips and thighs and males gain more fat around the abdomen, resulting in the typical gynoid and android body shapes in females and males, respectively (Figure 16.2) (74,75).

Female bone development is largely influenced by the effects of estrogen and primarily results in an increase in cortical thickness during puberty. Males experience an increase in not only cortical thickness, but also an increase in bone and medullary diameter, creating larger and stronger bones compared to females (74,75,86,89). Further changes in bone structure during puberty result in differences in pelvic shape and lower extremity alignment between females and males. The mature female pelvis has a larger pelvic outlet to allow for the process of childbirth, compared to the mature male pelvis (90,91).

The quadriceps angle (Q angle), a measure of lower extremity alignment, differs in postpubertal females and males. The Q angle is created by the intersection between a line from the anterior superior iliac spine (ASIS) to the center of the patella and a line from the center of the patella to the tibial tuberosity (92–96). The Q angle is typically slightly greater in females compared to males (92–100). While often thought to be due to the wider female pelvis, data suggests that sex disparities in the Q angle are primarily due to height differences, with decreased Q angles found in taller individuals and increased Q angles in shorter individuals (92,101). Increased Q angle may be a risk factor for knee injuries by increasing medial stress on the knee and promoting patellar maltracking; however, studies supporting this theory have had mixed results (102–109).

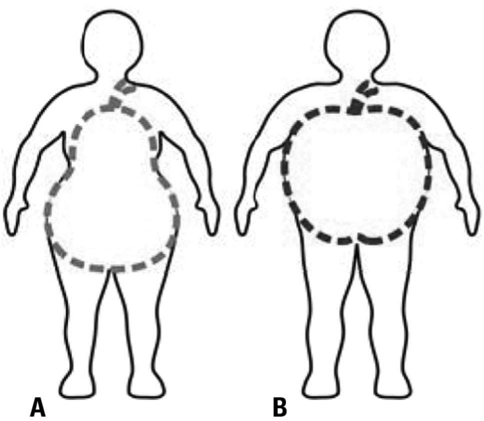

FIGURE 16.2: (A) Pear-shaped gynoid body type typically seen in postpubertal females. (B) Apple-shaped android body type typically seen in postpubertal males.
Image by Ryan Connaughton, PhD.

Ligamentous laxity, which can be measured clinically using the Beighton score (Figure 16.3), is greater in pubertal and postpubertal females compared to males (110–113). This increase in joint laxity is due, in part, to differences in sex hormones and their effects on the mechanical properties of ligaments (114). Ligamentous laxity is thought to decrease joint stability, particularly about the knee, and increase the likelihood of musculoskeletal injuries (102,106,115–118).

There are limited data regarding the impact of intense athletic training on pubertal growth in males and females and whether sex disparities exist. This topic has been most studied in youth gymnasts. In 2013, a committee organized by the Scientific Commission of the International Gymnastics Federation published a review of the literature regarding the impact of gymnastics on growth and pubertal maturation. They concluded that current evidence suggests that gymnastics training does not negatively impact adult height in male and female gymnasts, nor is there evidence to suggest that gymnastics training has a negative impact on pubertal growth and pubertal maturation (119). Rather, the observed shorter stature and delayed puberty among elite female gymnasts compared to their nongymnast peers is likely due to the fact that success in gymnastics requires a small, compact body type. Thus, the sport naturally selects for girls who are genetically programmed to be shorter and/or start puberty later, as it has been noted male and female gymnasts have shorter parents than other athletes (119–125). Further research is needed on the effects of other types of intense training on pubertal growth and whether sex disparities exist (119).

Jumping Mechanics and Neuromuscular Control

Changes in anthropometric measures during puberty correspond with differences in jumping mechanics and athletic performance. Before the age of 11, girls and boys are similar in terms of jumping performance (83). After age 11, boys have significantly greater jumping height and power

FIGURE 16.3: Beighton criteria for determining hypermobility. Total scoring ranges from 0 to 9, with higher scores representing greater ligamentous laxity. One point is scored for each fifth digit that extends past 90°, each thumb that can touch the forearm, each elbow that extends 10° past neutral, and each knee that extends 10° past neutral. One point is scored for touching the ground with the palms of the hands with knees in full extension. Clinicians typically use a score of at least 4 or 6 out of 9 to define hypermobility.

Source: Adapted from Ref. (113). Beighton PH, Grahame R, Bird H. *Hypermobility of Joints*. 4th ed. London: Springer; 2012. Photo by Ryan Connaughton, PhD.

(83). When taking off for a jump, girls' ground reaction force decreases with pubertal development, while boys' ground reaction force remains constant (126). The maintenance of takeoff force allows boys to generate an increase in jumping height. Both sexes increase lower extremity muscle strength, measured through knee flexion and extension peak torque, similarly until age 14, when boys begin to gain significantly more muscle strength (127). The increase in lower extremity muscle strength with age in boys is nearly double that of girls, even when controlling for body weight (127). Concordantly, boys' vertical jump height increases through each Tanner stage of pubertal development, whereas girls' jump height remains constant (126,128).

When landing from a jump, boys' ground reaction force decreases significantly with development while girls' ground reaction force remains constant; boys' greater lower extremity muscle strength likely contributes to this finding by absorbing the force (126). This results in a reduction in impact forces when landing in postpubertal males that is lacking in females. In addition to an increase in impact forces, postpubertal females have been shown to develop more detrimental landing mechanics compared to males (Figure 16.4). Females tend to be more "ligament dominant," meaning they use passive ligament structures rather than dynamic musculature to absorb ground reaction forces during physical activity (129). As the ligament dominant athlete lands from a jump, the external ground reaction force vector pushes the knee medially (129). After puberty, females have significantly more medial knee motion compared to males when landing from a jump (130–133). Postpubertal males are more "muscle dominant" compared to females. Males increase their hamstring and quadriceps peak torque postpuberty while girls' torques remain the same (130). The co-contraction of the hamstring and

FIGURE 16.4: Typical female jumping mechanics demonstrating asymmetric lower extremity alignment, knee valgus, and decreased hip flexion when landing from a vertical jump.

quadriceps muscles protect the knee joint by decreasing forces across the ligaments, which likely makes the male knee less susceptible to injury (134).

Females are more likely to be “quadriceps dominant” compared to males, meaning they preferentially recruit the quadriceps muscle over the hamstring muscle, increasing the knee extensor moment during sporting maneuvers (129). Females land more erect compared to males during vertical jump trials, again resulting in increased torque across the joints of the lower extremity, which may predispose the female knee to injury (130–132).

Females have also demonstrated more “leg dominance” compared to males (130–132). Leg dominance refers to imbalances in strength and coordination between the right and left lower extremities (129). Ford et al. found that female high school athletes had a significant difference in the knee valgus angle between their dominant and nondominant lower extremities, a difference that was not seen in male athletes (133). Leg dominance puts both the dominant and nondominanties limbs at increased risk of injury by placing excessive forces on the dominant limb and affording the nondominant limb decreased ability to handle average joint forces (133).

Differences in jumping performance and mechanics are a result of a neuromuscular spurt during pubertal development in boys, defined as an increase in power, strength, and coordination, which is lacking in pubescent girls (129). For boys, this spurt results in enhanced neuromuscular control that provides dynamic knee stability and decreases joint forces that place a strain across the static stabilizing ligaments of the knee (129). This sex disparity in neuromuscular control puts postpubertal females at increased risk of knee injuries compared to males; anterior cruciate ligament (ACL) injuries in particular are four to six times more likely in females compared to males (129,135,136). Neuromuscular training programs have been developed to teach athletes safer movement patterns during cutting and landing maneuvers and have been shown to decrease lower extremity injury risk during sports participation (134). These programs may also improve athletic performance, a finding that can help encourage coaches and athletes to adopt such programs (137). A complete discussion on sex disparities with ACL tears and other knee injuries can be found in Chapters 8 and 9 of this book.

CONDITIONS UNIQUE TO THE SKELETALLY IMMATURE ATHLETE

Osteochondritis Dissecans

Osteochondritis dissecans (OCD) is an idiopathic subchondral bone lesion that can progress to involve the articular cartilage and is a potential cause of joint pain in the adolescent athlete. The etiology is unknown but is thought to be due to repetitive microtrauma causing a disruption of blood flow to the epiphysis during growth. OCD occurs most commonly in the knee at the lateral aspect of the medial femoral condyle (Figure 16.5), followed by the ankle at the talus and the elbow at the capitellum (138). OCD is most prevalent during adolescence (139). The mean age at diagnosis is decreasing over time, especially in females, likely due to increased participation in competitive sports at a younger age (140). Males are at two to three times greater risk than females for developing OCD overall (7,138,139,141). However, with ankle OCD in particular, some studies have shown a female predominance (142,143). Treatment is usually conservative with activity modification, including avoidance of running and jumping, bracing, and/or casting. Unstable OCD lesions that do not respond to conservative measures can be treated surgically with debridement, reduction, internal fixation, and/or transarticular drilling.

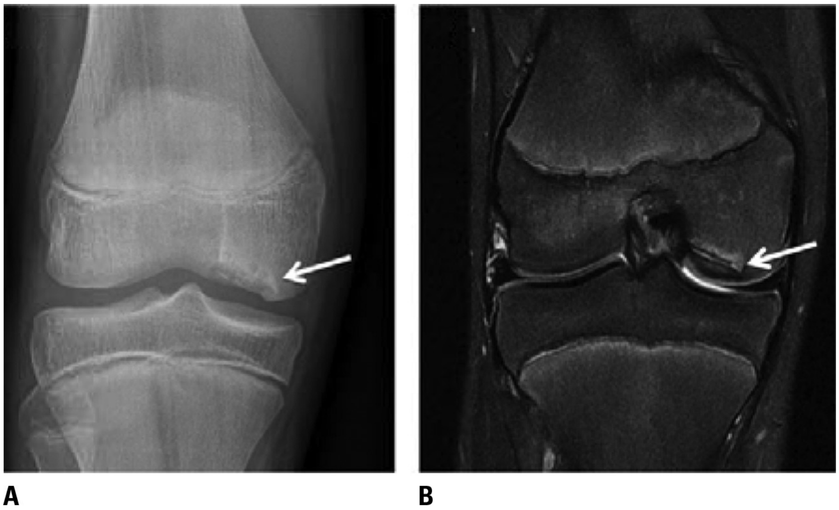

FIGURE 16.5: Knee osteochondral lesion. (A) Radiograph of knee depicting an abnormal lucency in the lateral aspect of the medial femoral condyle. (B) Coronal T2-weighted fat-saturated MRI of the same knee showing unstable osteochondritis dissecans (OCD) lesion with surrounding bone marrow edema.

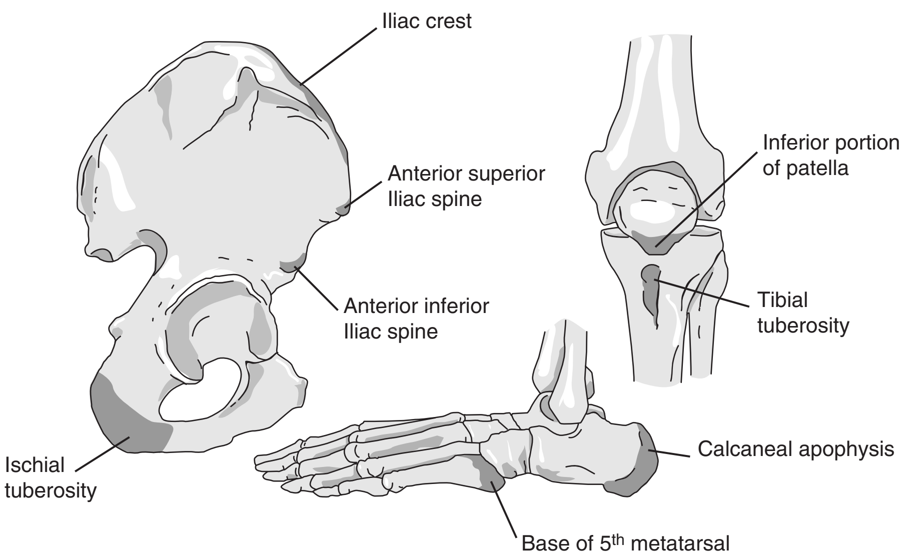

FIGURE 16.6: Diagram showing common locations of apophysitis.

Limited data suggest that females may have increased morbidity compared to males with regard to OCD treatment and outcomes. One study found that females were more likely to undergo surgery and had lower postsurgical functional outcomes compared to males (143). In another study, females were found to have a higher incidence of residual pain compared to males following surgical management of patellofemoral OCD (141).

Apophysitis

Apophysitis is defined as irritation of an accessory ossification center at the tendon attachment site, commonly due to overuse or repetitive microtrauma, but it may also be caused by direct trauma (144). Typical sites for apophysitis in the lower extremities are the iliac crest, ischial tuberosity, tibial tubercle, distal pole of the patella, calcaneus, and base of the fifth metatarsal (Figure 16.6). In the upper extremity, medial epicondyle apophysitis is most common. The limited data available regarding sex differences in apophysitis show that the overall prevalence is greater in males compared to females, likely due to differences in patterns of sports participation (145,146).

The age of presentation depends on the location of the apophysitis, but for any given location, the average age of onset is younger for females compared to males due to the earlier growth spurt in females (Table 16.7). Treatment of apophysitis is often conservative and includes activity modification, bracing, and/or use of shoe orthoses. Whether sex differences exist with regard to treatment and outcomes, including return to play, is unknown.

TABLE 16.7: Common Locations of Apophysitis and Age of Presentation

Apophysitis	Age of Presentation (years)	
	Female	Male
Calcaneus (Sever's disease)	8–12	9–15
5th metatarsal (Iselin disease)	9–12	11–15
Tibial tubercle (Osgood-Schlatter disease)	8–12	12–15
Iliac crest	13	15

Source: From Refs. 145–150.

CONCLUSION

Sports participation is common among American youth. Although in the past there were more males than females participating in sports, this gap is closing. The differences in the rules of the game exist between the sexes with many youth sports. Male youth tend to play more contact sports than female youth, lending to differences in injury patterns. Differences in anatomy, biomechanics, joint laxity, muscle strength, neuromuscular control, hormones, training, and coaching may also play a role. In general, males sustain more traumatic injuries and females sustain more overuse injuries. Males have a greater rate of concussions than females; however, in sex-comparable sports, females have a greater risk of concussions than males. While the field of sports medicine has gained a good deal of knowledge on injuries in youth sport, there is still much to learn about sex differences in pediatric and adolescent sports injuries.

Summary of Sex Differences in Pediatric/Adolescent Sports Injuries

Musculoskeletal Complaint	Sex With Higher Prevalence
Traumatic musculoskeletal injuries	Males (7,9–13)
Overuse musculoskeletal injuries	Females (7,18–21)
Concussion	Males have a greater rate overall, but in sex-comparable sports, females have a greater risk (29–32,36–38)
Fracture	Males (7,14–17)
Patellofemoral pain syndrome	Females (7,23,24)
Stress fracture	Females (25)
Osteochondritis dissecans	Males have a greater rate overall, but some studies have shown a greater rate of osteochondritis dissecans of the ankle in females (7,138,139,141–143)
Apophysitis	Males (145,146)

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17

THE AGING ATHLETE

Prakash Jayabalan

SEX DIFFERENCES IN THE AGING ATHLETE

Currently people over age 65 account for 12% to 13% of the total population, and by 2030 it is estimated that they will comprise 20% (1). With this aging population comes the increasing societal burden of musculoskeletal diseases. The majority of these degenerative disorders are characterized by patients presenting with increased pain, decreased range of motion, and functional deficits, which together can cause a significant reduction in quality of life. Age-associated decline in physical function and physiological decline lead to an increase in morbidity and mortality rates. Sex differences have been shown to potentially play a role in both etiology and treatment outcome for these diseases and this chapter outlines the differences seen. This chapter focuses on common issues related to sex-specific responses to training in the aging athlete and two of the most common disorders associated with aging: sarcopenia and osteoarthritis (OA). Osteoporosis, although a common problem in the aging athlete, is featured in Chapter 12 on bone health.

SEX SPECIFIC RESPONSES WITH AGING

Physiological Decline With Aging and Sedentary Behavior

Aging is associated with physiological declines in bone mineral density (BMD) and lean body mass with an increase in body fat and central adiposity. In women, the onset of menopause likely also augments this decline in activity. Wang et al. compared almost 400 women in the early postmenopausal period to women who were premenopausal and found higher levels of abdominal and total body fat in postmenopausal women (2). However, there was also correlation between age and fat distribution. They did note that a decrease in lean muscle mass after menopause appeared to be independent of age and could be more attributed to menopause. Douchi et al. compared body composition variables between pre- and postmenopausal women (3). They also demonstrated a significant increase in percentage of body fat, trunk fat mass, and trunk-leg fat ratio with aging. Baker et al. found that in addition to a decline in BMD in postmenopausal women compared to men of a similar age, these women also had a higher incidence of metabolic syndrome, with associated cardiovascular risk factors, including obesity, high levels of low density lipoprotein (LDL) cholesterol, hypertension, and high fasting blood glucose levels (4). These metabolic changes were attributed to both changes in body composition and decreased physical activity. A longitudinal study of 77,000 women aged 34 to 59 years, done over 24 years, found that lower levels of physical activity (less than 30 minutes a day of moderate-intensity to vigorous activity) was associated with a higher risk of cardiovascular disease and all-cause mortality (5). Furthermore, Sisson et al. found higher levels of sedentary behavior (more than 4 hours a day) associated with a 54% increased risk in development of cardiovascular disease (6).

Sex Differences in Fat Metabolism With Aging

Women in general have lower rates of resting fat oxidation compared with men (7,8). A lower rate of fat utilization has been shown to increase subsequent weight gain (8). This difference may explain the higher amount of adipose tissue in women compared to men. The fat oxidation that occurs during exercise is from adipose-derived free fatty acids through lipolysis. Lipolysis is regulated by the sympathetic nervous system through stimulation of alpha- and beta-adrenergic receptors (9). Differences in fat mobilization via the sympathetic nervous system activation have been postulated to explain variations in bodily fat content between men and women. In keeping with prior findings, Toth et al. showed that older men (over 65 years of age) oxidize fat more than women at rest (10). However the differences they observed in resting fat oxidation could not be explained by variations in noradrenergic activity, free fatty acid availability, body composition, or aerobic capacity. They also found that there was no difference in rate of lipolysis or fat oxidation during submaximal exercise. Furthermore, despite higher plasma noradrenaline concentrations, no sex differences in the rate of appearance of free fatty acids or fat oxidation were found during submaximal exercise.

Sex Differences in Response/ Reaction Times

Reaction times are defined as the elapsed time between the presentation of a sensory stimulus and subsequent behavioral response. They are a vital part of an athlete's performance and have been shown to vary with both age and gender. It has been shown that reaction times shorten from individuals in their late 20s and then increase slowly from individuals in their 50s into their 70s, with more variability with aging. Variability in reaction times in older adults has been associated with impaired recognition of stimuli and has been suggested to be a potential measure of neural integrity (11). Individuals over age 50 have been shown to be better at reacting to targets by visual distraction because they look for known features of the targets (12). Myerson et al. (13) found that older adults were as proficient as younger people at assimilating information. In general, the majority of studies have shown that in almost every age group, men have faster reaction times than women. The slower reaction times in women are not reduced by practice to the levels of their male counterparts. Spierer et al. reported that when male soccer players were compared to female lacrosse players, the men were able to respond faster to both visual and auditory stimuli (14). Botwinick and Thompson postulated that the difference between sexes was accounted for by the lag between the presentation of the stimulus and the start of muscle contraction (15). The duration of muscle contraction to perform the task was similar, however. Interestingly, a 2005 study found that gradual dehydration, with the average loss of 2.6% of body weight over a 7-day period, caused females to have lengthened choice reaction time (two stimuli with two potential responses), but males to have shortened choice reaction times (16). Barral and Debû tested men and women's ability to aim at a target and found that men were faster than women initially in aiming; however, the women were more accurate (17). A study with rats found similar results: When rats were given a choice reaction task with distractions, males tended to make premature responses and female rats were more likely to miss the valid stimuli (18). Of note, it has been reported that the typical male advantage in visual reaction time is getting smaller, particularly outside the United States. A potential explanation could be that compared to these early studies, women now participate in fast-action sports that require faster reaction times (19).

SARCOPENIA

Sarcopenia has been commonly defined as the age-related loss of muscle mass. However, over recent years, this term has evolved to also include loss in strength and function. A consensus statement on sarcopenia proposed the inclusion of functional measures such as gait speed in the diagnostic evaluation of the condition (20).

Epidemiology of Sarcopenia

Sarcopenia has varying reported prevalence between men and women. Baumgartner et al. measured appendicular muscle mass in the New Mexico elderly study cohort (population based survey of 883 elderly Hispanic and non-Hispanic white men and women living in New Mexico from 1993–1995) (21). They reported that 15% of males and 24% of females aged 65 to 70 had sarcopenia measured by relative muscle mass (RMM) on dual-energy x-ray absorptiometry (DXA) scanning. They also found higher rates of disability in sarcopenic men (4.1 times higher) and women (3.6 times higher) compared with those with muscle mass in the normal range. The prevalence of sarcopenia was higher for men over age 75 (58%) than women (45%). Iannuzzi-Sucich et al., studying a community-dwelling cohort in Connecticut of 195 women and 142 men, reported a prevalence of sarcopenia of 53% in men and 31% in women in a sub-cohort aged greater than 80 (22). Using data from the third National Health and Nutrition Exam Survey (NHANES III), Janssen and colleagues reported 50% of men and 72% of women over the age of 80 met criteria for sarcopenia using the skeletal muscle index (23). Generally, the reported prevalence of sarcopenia has been lower for both sexes in non-U.S. populations. For example Tankó et al. reported a prevalence of 12% in a population of Danish women over age 70 who had sarcopenia, while in a Taiwanese population, Chien and colleagues found a prevalence of 20% in all subjects over 80 years of age (24,25).

Longitudinal observational studies have reported a progressive decline in skeletal muscle mass beginning in the third decade that becomes clinically significant in the fifth decade (26). For both sexes, the loss of muscle mass was greater in the lower body. Furthermore, Candow and Chilibeck reported that the loss of muscle strength with aging was greater in the lower body in men and women (27). This finding may reflect decreased activity or altered patterns of activity of the lower extremity muscles with aging.

Sex-Related Pathophysiology of Sarcopenia

Several interrelated factors have been postulated to cause the development and progression of sarcopenia. Nutritional, hormonal, metabolic, and immunological factors likely contribute in varying degrees to age-related losses of muscle mass, strength, muscle quality, and function. The loss of muscle mass appears to be the most important etiological process, with studies incorporating muscle biopsies showing diminished type II fiber size (20%–50% reduction), with type I fibers (1%–25%) being less affected (28). In addition to age, a number of demographic factors influence the progression of skeletal muscle decline seen in sarcopenia. The initial muscle mass represents a pivotal factor that determines the development of clinically evident sarcopenia and represents the hypothetical threshold that distinguishes a normal from an abnormal decline. This means that the larger the starting mass, the longer it will take for the threshold of clinically evident sarcopenia to develop (28). Therefore, men have a larger total muscle mass and strength compared to women that in part may explain some of the sex differences seen with sarcopenia.

Patterns of Skeletal Muscle Decline

The pattern of skeletal muscle loss varies between the sexes. Using a cross-sectional design Vandervoort and McComas examined young, middle-aged, and elderly men and women (29). Maximal voluntary and electrically evoked twitch forces were determined for the ankle plantar flexor and dorsiflexor muscles. Women generated lower forces than men at all ages, and significant declines in force were observed for both groups with progressive age. Strength losses were relatively similar for men and women, and decline rates were similar for evoked and voluntary contractions over time for both sexes. Over a 4-year period, Bassey and Harris reported a 3% loss of grip strength in men and 5% for women (30). The age-related decline in skeletal muscle may be greater in men compared to women and the differences in body composition could significantly affect muscle function in men and women. For example, low muscle mass is more strongly associated with poor muscle strength in men, whereas in women higher levels of adipose tissue may act to impair function (31). Sex-specific confounders such as different patterns of activity and hormonal differences were not investigated in these studies and could have a significant effect on the susceptibility to loss of muscle mass and strength.

Sex Differences in Muscle Quality With Aging

Muscle quality (MQ) refers to muscle strength per unit of cross-sectional area (CSA) and is suggested to be a more beneficial indicator of muscle function rather than strength alone. Sex differences in MQ have been demonstrated with aging. Lynch et al. examined differences in MQ between arm and leg muscles (32). They measured concentric and eccentric strength and determined muscle mass using whole body DXA scanning, with estimation of arm and leg muscle mass. Age-associated decline in MQ was greater for men than women, whereas leg muscle quality declined similarly between the sexes. It is important to note that arm MQ was higher than leg MQ for all age groups and both sexes. However in men, the decline in MQ was at the same rate for the arm and leg, whereas in women the decline in MQ was greater in leg musculature than arm MQ. These differing patterns of age-related changes in MQ were postulated by the authors to be related to increased connective tissue and changes in neural connections, though muscle biopsies were not performed. Frontera et al. tested whole muscle strength, whole muscle cross-sectional area (WMCSA), and contractile properties of segments from single fibers of the vastus lateralis in young men, older men, and women. Although age-related differences were eliminated after controlling for WMCSA, sex-related differences were not. Type I and type IIA fibers from older men were stronger than similar fibers from older women (28).

Hormones, Aging, and Sarcopenia

Sex hormones such as estrogen and testosterone have been shown to have anabolic effects on skeletal muscle. In rat models, gonadectomy causes a dramatic decline in spontaneous physical activity (33). The suppression of ovarian function in young women may trigger a decline in muscle mass and the withdrawal of estrogens in menopausal women appears to accelerate the loss of muscle mass (i.e., muscle quantity) and the decline in specific muscle force (i.e., muscle quality) (34). To date, the exact mechanisms by which hormones regulate skeletal muscle metabolism have not been fully elucidated. Furthermore, it is not clear whether age-related changes in gonadal function regulate physical activity in humans.

Estrogen

Gonadal function is a mediator of the sexual dimorphism that occurs in hypertrophy of skeletal muscles mass during puberty. It has been postulated that the loss of gonadal function with aging likely contributes to the development of sarcopenia in adults. Estrogen has been postulated to act against the development of sarcopenia by inhibiting the release of inflammatory procatabolic cytokines such as tumor necrosis factor alpha (TNF-alpha) and interleukin (IL-1 and IL-6). IL-6 has been shown to have a biological link to the anabolic cytokine insulin-like growth factor 1 (IGF-1), levels of which have been found to be low in the postmenopausal period (35,36). Cappola et al. showed that women with IGF-1 levels in the lowest quartile or IL-6 levels in the highest quartile had a significantly greater limitation in walking and activities of daily living. IL-6 levels have also been shown to be a significant predictor of the development of sarcopenia (37).

The onset of menopause is associated with decreased levels of circulating 17-beta-estradiol concentrations in middle-aged and elderly women. Studies have shown that at menopause onset, women lose fat-free, lean muscle mass and instead gain fat mass such as adipose tissue (38). In addition, muscle strength also declines at this time; however, a major limitation in the literature is that few studies have correlated these findings to estrogen concentrations. The use of estrogen replacement therapy (ERT) has also not been shown to prevent the changes in body composition that occur with menopause such as loss of skeletal muscle mass (39). Kenny et al. showed that there was no significant difference in the rate of sarcopenia between nonobese, long-term ERT users and those not using ERT (40). In addition, ERT did not augment the increases in fat-free mass or leg strength in postmenopausal women age 60 to 72. However, a study of women in the early postmenopausal period who had ERT together with a prescribed resistance training program reported improvement in lower extremity muscle CSA and power compared to controls who did not receive ERT (41). This suggests that ERT may have a potentially beneficial effect on muscle mass early in the postmenopausal period when taken together with resistance exercise. Further studies are required to elucidate the role of ERT in maintaining muscle mass and function.

Testosterone

In males, serum levels of testosterone decreased approximately 1% a year with age. As women age, testosterone levels also decrease to a variable extent, particularly in the postmenopausal years. Epidemiological studies have suggested that there is a relationship between decline in muscle mass, strength, and function with decreasing testosterone levels (42). Testosterone replacement has been shown to increase muscle mass and strength in hypogonadal men (43) and women (42) and also increase muscle protein synthesis. In a randomized placebo-controlled trial, Ferrando et al. reported that following 6 months of testosterone replacement, male subjects had increased total lean body mass and leg and arm strength, which was associated with an increased expression of IGF-1 (44). Studies have also shown that low levels of testosterone are associated with increases in IL-6 concentration. Increased levels of IL-6 have been shown to decrease satellite cell density and proliferative capacity. Satellite cells have been described as myofiber stem cells that give rise to new myofibers. Importantly, they are activated and proliferate in response to muscle injury. They have been suggested to be a vital target for androgen-associated hypertrophy as they express androgen receptors (45). Benjamin and colleagues investigated myoblasts transfected with wild-type or mutant androgen receptors and showed that testosterone caused a variable rate of cellular differentiation and proliferation (46). Although testosterone replacement appears to be a potential future treatment option in hypogonadal aging individuals, further research is required to delineate the optimal dosing regimen for improving function and the risks of long-term use.

The steroid hormone dehydroepiandrosterone (DHEA) has been shown to decline with age in males and females, and exogenous administration of the hormone in elderly subjects has been shown to increase biologically active IGF-1 (47,48). Morales et al. gave elderly patients exogenous DHEA for 6 months, which led to reduced body fat mass and increased muscle strength at the knee and lumbar paraspinal musculature in men only, not in women (49).

Of note, levels of growth hormone and IGF-1 decline with increasing age, and increasing serum levels through exogenous administration has been postulated to be of therapeutic benefit for sarcopenia. In general it has been shown that growth hormone administration increases muscle mass but not strength. Yarasheski et al. showed that 1 month of growth hormone or IGF-1 increased nitrogen balance protein turnover and muscle protein synthesis, but in response to a 16-week resistance training program, growth hormone did not increase strength or protein synthesis compared to no hormone administration. At present there is insufficient evidence to recommend these treatments (50).

ATHLETIC TRAINING IN THE AGING ATHLETE

Sex Differences in Response to Aerobic Exercise

The American Heart Association currently suggests at least 150 minutes per week of moderate exercise or 75 minutes per week of vigorous exercise for general health (51). Multiple cross-sectional and interventional studies have reported that endurance-type training can have significant beneficial effects on cardiovascular (CV) risk factors, including blood pressure, lipid profiles, body fat, and insulin sensitivity (52,53). In addition, maximum oxygen consumption (VO_{2max}) typically decreases 5% to 15% on average per decade after the age of 25, and aerobic exercise has been shown to increase this parameter (54). These physiological responses to aerobic exercise result in a number of beneficial physiological changes that include increased mitochondrial density, capillary density, and myoglobin content, and decreased blood pressure and heart rate with improved ability to deliver glucose as well as oxygen to working muscles (55). A recent longitudinal study of 23,747 men and women attempted to investigate the level of activity that may protect against CV mortality (56). The subjects did not have a history of CV disease at baseline, and their level of physical activity was tracked over a period of 7 to 10 years. The investigators found that a minimum of two sessions of moderate to vigorous physical activity per week was associated with a reduced risk of CV disease and all-cause mortality in both men and women. Inactive individuals had an elevated risk of CV disease and all-cause mortality (hazard ratio [HR]: 1.50 versus active individuals with HR: 1.11). Multiple studies in older men and women have supported these findings, demonstrating that walking or jogging for 30 to 60 minutes 2 to 5 days per week can have beneficial effects on BMD, VO_{2max}, and body weight (57–59).

Ogawa et al. investigated the mechanisms by which aging, gender, and physical training affect CV responses to exercise (60). They quantified VO_{2max}, cardiac output, and heart rate during submaximal and maximal treadmill exercise in men and women of both young age (average 27 ± 3 years) and older individuals (age 63 ± 3 years) who were both sedentary and physically trained. They found that physically trained subjects who were in the older age group had a 25% to 32% higher VO_{2max} compared to sedentary individuals. For physically trained subjects, maximal cardiac output and stroke volume normalized to fat-free mass were greater in men than women. This difference appears to be related to the greater percentage of body fat in women than men.

Sex Differences in Response to Resistance Exercise/Strength Training

Resistance training (RT) has been shown to have benefits on body composition, mobility, and functional capacity. It has been shown that regular RT can help maintain or increase BMD and total body mineral content as patient's age (61). Despite the benefits of RT being well documented, there remains some disparity in regard to ideal training volume for a patient in terms of the loads used, number of repetitions that should be performed, and comparative individualized regimens for men and women (62).

In one of the few sex comparative studies, Bamman et al. tested whether older men (n = 9, 69 ± 2 years) would experience greater resistance-training-induced myofiber hypertrophy than older women (n = 5, 66 ± 1 years) following knee extensor training 3 days per week at 65% to 80% of one-repetition maximum (1RM) for 26 weeks (63). Vastus lateralis biopsies were analyzed for myofiber areas, myosin heavy chain isoform distribution, and levels of messenger RNA (mRNA) for anabolic proteins such as IGF-1 and myogenin. For all three primary fiber types, there was enhanced 1RM strength gain in men compared to women. This was not found to be related to circulating IGF-1, myogenin, or expression of the myogenic transcripts they examined. Lemmer et al. examined a cohort of young (n = 18, 20–30 years old) and older (n = 23, 65–75) men and women for their 1RM and isokinetic strength before and after a 9-week unilateral knee extension strength training and detraining regimen (64). They found that changes in 1RM strength due to a strength training and detraining regimen were determined by age. Strength training induced increases in muscular strength that were maintained significantly above baseline for all groups except older women after 31 weeks of detraining. Studies that did not compare sexes and were performed singularly with older men or women have also suggested differences in the hypertrophic response to strength/resistance training. For example, hypertrophy of types I (34%) and II (28%) muscle fibers has been shown following resistance training, with greater increases after 12 weeks in sedentary males of varying ages. Older women, however, are potentially more resistant to myofiber hypertrophy in response to this type of training regimen (28). Charette et al. reported that CSA of type II muscle fibers increases 20% after 12 weeks of resistance training in older women with no change in type I fiber size (65). However, a year of resistance training in older women only causes modest increases in type I CSA (10%–28%) and no significant changes in type II CSA (66). Häkkinen et al. did show hypertrophy in all three primary myofiber types (22%–36%) following 21 weeks of resistance training in older women (67). The resistance training program used in this study was different in that it was spread across 21 weeks with higher loading volume during the final 8 weeks of the study, which may have influenced their results. In another elderly female cohort, low volume training (one set per exercise) compared to high volume training (three sets per exercise) performed twice a week for 13 weeks induced significant improvements in maximal dynamic strength for knee extensors and elbow flexion, muscular activation of the vastus medialis, biceps brachii, and muscle thickness for the knee extensors and elbow flexors. This suggests that during the initial months of training, elderly women can increase upper and lower body strength through low volume training. This level of activity may also improve adherence to exercise regimens prescribed.

OSTEOARTHRITIS

OA is the most common cause of disability in patients over age 65, and it is estimated that by 2030, 20% of the U.S. population will be at risk for the disease (1). In 2004, the estimated cost of treating patients with this condition was $849 billion, the equivalent of 7.7% of the gross domestic product (GDP). Patients with OA commonly present with pain, decreased range of motion, and functional deficits, which have a significant impact on quality of life. Men and women vary in the prevalence, location, and severity of OA. In large population-based studies, women in general have more multiple joint involvement of OA, particularly of the knees, ankles, and feet, whereas men have a greater prevalence of OA of the hips, wrist, and spine (1,68). More recent studies in non-Caucasian populations have further suggested that female sex is a major predisposing factor for knee OA, and that in general women have more severe clinical symptoms. A study using the NHANES III, a U.S.-based study cohort, in individuals with knee OA (radiographic definition of Kellgren-Lawrence [K-L] grade greater than or equal to 2) over 60 years of age were more likely to be female and African American (69). A study of Korean community residents (n = 660) who were age 65 to 91 found that women had more severe radiographic OA than men. Women also had worse Western Ontario and McMaster Universities Arthritis Index (WOMAC) and short form health survey (SF-36) scores (suggesting worse physical function and quality of life) compared to men for the same K-L grading of OA (70). In a similar epidemiologic study of Japanese patients age 60 to 69, the prevalence of knee OA on radiographs was 35% in men and 57% in women (68).

Sex-Related Structural Risk Factors for the Development of OA

Joint Alignment

Abnormal loading mechanics of the joint that can occur with changes in joint alignment can potentially increase the risk of developing cartilage damage. The majority of studies that have investigated sex differences in joint alignment and associations with the development of OA have been of the knee. Estimates of the contact stresses at the articular surface of the knee joint during a static standing position have been shown to predict the development of symptomatic and radiographic knee OA 15 months after a baseline evaluation (71). At the knee, varus alignment, for example, increases the stress on articular cartilage in the medial compartment and, conversely, valgus alignment increases the stress in the lateral compartment. Varus alignment has been commonly associated with knee OA, with the finding of an almost twofold increased risk of development of the disease compared to neutral or valgus alignment (72). However, the prevalence of varus alignment in this particular study was not influenced by the sex of the participants. When individuals have radiographic evidence of knee OA at baseline there is also evidence that both varus and valgus limb alignment increase the risk of progression of the disease (73). Although there is likely a role of limb alignment in the development and progression of knee OA in particular, there is limited evidence of sex differences influencing limb alignment and subsequently affecting the incidence of knee OA (74). The main issue from epidemiological studies is that there are a large number of etiological factors that also play a role in the development of OA. These include biomechanical and biochemical changes that occur during dynamic actions such as walking and changes that occur naturally with age irrespective of sex.

Studies have shown differences in the structure of the knee joint that may contribute to differences in the prevalence of OA. For example, the female femur has been shown to be narrower than the male femur. Women also have a thinner patella, with a larger quadriceps angle (Q angle), with a proportionately smaller lateral tibial condyle compared to the medial tibial condyle (75). The distal femur as a whole in women is smaller, with generally a proportionately narrower medial-lateral diameter compared to the anterior-posterior distance.

Cartilage Thickness

There are differences in the thickness of the knee articular cartilage between men and women. The cartilage of the distal femur is thinner both in adolescence and adulthood in females compared to males. Adult men also have significantly larger patellar and femoral cartilage volume than women, independent of body and bone size (76). Using three-dimensional MRI, Faber et al. demonstrated that women have smaller cartilage volumes than men with percentage differences ranging from 19.9% at the patella to 46.6% in the medial tibia (77). Sex differences of the cartilage thickness were smaller at the femoral trochlea (2.0% difference), medial tibia (13.3%), and medial femoral condyle (4.3%). Cartilage surface areas were on average lower in females by 21% at the femur and 33.4% at the lateral tibia. Sex differences in cartilage volume and surface area in men and women could contribute to the increased risk in women of developing OA, though this is yet to be elucidated. A longitudinal study of an Australian cohort (135 men, 190 women, aged 26–61, mean age 45 years) showed that women have a proportionately higher cartilage volume loss compared to men with time, with these changes seen as early as age 40 (78). Over an average of 2.3 years, women had a higher annual rate of cartilage volume loss compared to men in all knee compartments, but only tibial cartilage loss was statistically significant.

Kumar et al. evaluated the differences in cartilage MR relaxation times (which have been shown to predict future progression of OA) and static and dynamic measures of knee joint loading between men and women in three groups: young healthy (under age 35), middle-aged healthy (35 years or older), and OA populations (79). Of note, higher $T_1\rho$ (MRI relaxation time) indicates worsened cartilage composition with lower proteoglycan content They showed that compared to men, middle-aged women with knee OA have higher MR relaxation times in the lateral and patellofemoral compartments and lower second peak adduction moment. The women also had lower static and dynamic varus in the middle-aged and OA groups and lower varus and more valgus alignment during walking in all groups. This suggests that the women with OA in this study had greater loading over the lateral compartment during walking. Women in the OA group had higher articular cartilage $T_1\rho$ readings in the lateral compartment compared to men.

Muscle Strength and the Progression of OA

Cross-sectional studies have suggested that weakness of knee extensor muscles precedes the development of knee OA (80,81). The contribution of muscle function to the stresses experienced during joint loading has been investigated during dynamic patterns of movement such as walking (82). The Multicenter Osteoarthritis Study (MOST) is a large prospective study of risk factors for knee OA. A subcohort of participants (1,617) without radiographic knee OA were grouped into tertiles of quadriceps strength (82). The study found that subjects within the highest third of quadriceps strength had significantly less development of symptomatic knee OA at 30 months follow-up. Approximately 10% percent of the knees in women and 8% of those in men had incident symptomatic knee OA 30 months from baseline. Together with the previous findings, this large longitudinal study demonstrated that weak quadriceps strength was predictive of incident symptomatic but not radiographic OA progression in both sexes.

Resisted knee extension exercises are commonly incorporated in the rehabilitation regimen of patients diagnosed with knee OA. Although they have been shown to have a functional benefit for patients, improvement in knee extension strength has not been shown to have a significant effect on the structural progression of the disease at the tibiofemoral joint. Regardless of limb alignment, Amin et al. found that there was no association of quadriceps strength with tibiofemoral joint cartilage loss for either sex. They did, however, find that there was an association with decreased cartilage loss in the lateral aspect of the patellofemoral joint on MRI, but there were no differences between sexes (83).

During dynamic activities such as walking there are different patterns of muscle activity in OA between men and women. In a subgroup of the MOST study, 60 subjects from this cohort, who had an average age of 64.2 (33 women, 27 men) and had developed radiographic and symptomatic knee OA, were evaluated in terms of their muscle strength and gait characteristics while performing a 400-meter walk (84). The variability in walking speed for male subjects was explained to a mild extent by the power in the sagittal plane produced by muscles that span the hip and ankle joints when walking at a moderate speed (0.89 meters per second). In addition, the 400-meter walk times for men had a strong correlation with isokinetic strength of the knee flexors and extensors. In women, however, isokinetic strength for the knee and hip muscles was not associated with the 400-meter walk time. In contrast, their walk time had a significant correlation with the torque and power about the hip in the frontal plane and knee joint in the sagittal plane when walking at a moderate speed. Interestingly, in subjects with symptomatic knee OA, the speed of a 400-meter walk decreased with age for men, whereas with women, it decreased with self-reported pain score (the WOMAC pain score). In men, the torque and power produced around the knee during walking did not differ with the level of functional mobility and was similar to men without symptomatic knee OA. However, women who were higher functioning had larger hip and ankle muscle activity during walking than those that were less mobile. These findings suggest that men and women with knee OA and who are higher functioning rely more on an ankle strategy than a hip strategy when walking. Men with less mobility decrease the ankle strategy and women with less mobility decrease their hip strategy. A study that incorporated gait analysis in an Israeli population of patients with knee OA reported that both men and women walked at the same speed, cadence, and step length but found differences in the phases of the gait cycle. Women walked with a longer stance phase and double limb support but had a smaller swing and single limb support compared to men. They also had a smaller toe-out angle compared to men (85).

Hip Dysplasia as a Risk Factor for OA

It is well known that severe developmental dysplasia of the hip is a risk factor for the development of hip OA and has a preponderance toward women (86). Studies have attempted to compare the differences in risk for the development of OA in individuals with mild developmental dysplasia of the hip between the sexes. Using a prospective cohort design over 8 years, acetabula dysplasia was associated with only a small increased risk for incident hip OA in a study of elderly white women (87). In the Rotterdam study of adults aged 55 or older who had no radiographic evidence of OA at baseline, acetabula dysplasia was a strong determinant of the development of OA at a mean of 6.6 years follow-up (88). Although women with acetabula dysplasia developed joint space narrowing more often during the follow-up period, the overall association between dysplasia and OA was independent of age, gender, and body mass index (BMI). A similar study cohort, the Copenhagen Osteoarthritis Study, found that the risk for hip OA in men and women was influenced by hip dysplasia in men and hip dysplasia and age in women (89). A smaller study on Turkish men and women found that acetabula hip dysplasia was more common in men (13%) than in women (3.7%), though this was not a significant factor in the development of hip OA (90).

A number of issues still remain in examining the impact of structural factors of the joint that could influence sex differences seen in OA. Due to a lack of long-term longitudinal studies investigating the impact of rehabilitation regimens, it remains unknown whether strength training can significantly alter the structural progression of knee OA and whether there is a difference in response between the sexes. Also, during walking exercise, the differences in the loading magnitudes on articular cartilage between men and women require elucidation. This could allow the creation of more efficacious regimens that are individualized to patient's sex and potentially limit structural progression of the disease.

SYSTEMIC RISK FACTORS FOR THE DEVELOPMENT OF OA

Inflammation and Obesity

Multiple observational studies have shown that obesity is a significant risk factor for the development of OA, with an increased risk in women. BMI is a known independent predictor of the onset and progression of knee OA, with a stronger effect in women than men (91,92) The Framingham study reported a relative risk of OA in overweight individuals was 2.07 times greater for women and 1.51 times greater for men compared to those individuals with the lowest body weights (91). The Genetics of Osteoarthritis and Lifestyle (GOAL) case-control study identified BMI as a factor that increased the likelihood of developing knee OA, the odds ratio (OR) being 2.68, with the risk for knee OA being greater for women (OR: 3.23) compared to men (OR: 2.20) (92). The waist-to-hip ratio, which is a measure of body shape and health, has been shown to be independently associated with an increased risk of hip and not knee OA in women, whereas there is no such association in men (93). In a study of 387 patients with meniscal tears, radial tears of the medial meniscus (which has been shown to cause a

25% increase in cartilage contact pressure) were associated with older age, female sex, and obesity (94). However, another study by Laberge et al. showed that in 137 obese individuals with OA aged 45 to 55, 64% had meniscal tear with a significantly higher prevalence in men (36%) compared to women (13%) (95).

Historically OA has been described as a "wear and tear" disease, with association of the disease with excessive joint loads. Obesity has often been thought to be an etiological factor for the development of OA due to the likely increased loads placed on the joint with increased body weight. However, recent epidemiological studies have revealed that the risk of OA in non-weight bearing joints such as the hand is twofold higher in obese individuals compared to those with a normal BMI (96). A potential reason for this is that obesity has been shown to be a chronic inflammatory state as evidenced by increased production of systemic cytokines and inflammatory mediators such as IL-6 and IL-8, and interferon-γ in these patients (97). Adipokines are cytokines specifically secreted by white adipose tissue and are involved in the inflammatory process and matrix degradation. Women have been shown to have higher concentrations of adipokines in their synovial fluid compared to men (98). This is likely due to differences in body fat content compared to men particularly in the postmenopausal period. In vitro studies have shown that these proteins upregulate matrix metalloproteinases (MMPs) and induce collagen release from cartilage by working in synergy with other procatabolic cytokines such as IL-1beta (99). Leptin is the most well investigated adipokines and patients with OA have been shown to have higher concentrations in their synovial fluid, which correlated strongly to BMI (100). For example, Hooshmand et al. found increased levels of leptin together with IGF-1 in knee joint synovial fluid in women with knee OA, but not in men (101). There are a lack of studies that have investigated whether the different levels of these inflammatory cytokines in men and women contribute to the differences in incidence of OA between genders.

Hormones and OA

Most epidemiological studies have shown that OA is more prevalent in men than women before the age of 50, but after menopause, the incidence in women increases significantly and is associated with a higher severity of symptoms (102,103). It has therefore been suggested that there is potentially a link between OA and concentrations of sex hormones, particularly serum estradiol. However, this hypothesis is controversial and is discussed in great detail in Chapter 1 on the influence of sex hormones on the musculoskeletal system.

CLINICAL PRESENTATION AND TREATMENT OF OA

There are limited studies reporting differences in the clinical presentation for OA between men and women. Women tend to report knee pain more frequently than men and seek care from physicians for hip and knee problems more often than men (104). A study using the Framingham cohort showed that 64% of older women and 52% of older men reported musculoskeletal pain (105). The factors associated with the pain in women were BMI, systolic blood pressure, and depressive symptoms and not radiographic OA. In men the pain was associated with polyarticular radiographic OA. A study using a Swedish population registry of people aged 55 to 74 found that women had significantly more knee-related complaints on the Knee OA Outcome Score (KOOS), including pain, symptoms, and ability to perform activities of daily living compared to age-matched men. In men, worsened sports and recreation functioning was seen in the 75- to 84-year-old age group, but in women, this was observed in the 55- to 74-year-old age group.

The majority of studies pertaining to rehabilitation regimens have focused on resistance exercises on the quadriceps, with minimal differences in outcome between men and women. For end-stage OA, women tend to delay surgery and generally wait until their symptoms are more severe compared to men. In terms of surgical outcomes, the best outcomes occur in nonobese women over age 60 (implant survival was 99.4%,); whereas the worst results were in obese men less than 60 years (survival rate of 35.7%) (106). Overall this study found that men tended to have a higher surgical revision rate than women (10.2% and 8%, respectively). Similar trends were seen in a report on 134,799 primary total knee replacements from the Australian Joint Registry (107). A statistically significant difference was noted in the cumulative 5-year revision rate of the replacement, 4% for men and 3.3% for women. In contrast, a report from the Swedish Arthroplasty Registry (35,857 unicompartmental and total knee arthroplasties) did not find any differences between genders in revision rates (108). Of note, women are also less likely to undergo surgery, which explains their higher use of prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) (104). Conventionally, patients undergoing total knee replacement have been treated with the same prostheses irrespective of gender.

However, as outlined previously, sex differences in the anatomy of the knees have led to the introduction of gender-specific prostheses in recent years. These include the NexGen Gender Solutions prostheses (Zimmer Biomet, Warsaw, Indiana) and the Triathlon Knee System (Stryker Orthopaedics, Mahwah, New Jersey). The NexGen gender-specific prosthesis, for example, was designed specifically for the female anatomy with a narrower medial to lateral dimension to prevent against overhang of the component and limiting potential soft-tissue irritation and pain. In addition, the thickness of the anterior flange is reduced to accommodate the reduced height of the femoral condyles in women and the angle of the trochlear groove is increased by 3° to match the larger Q angle in women. Theoretically these gender-specific prostheses are thought to result in a better anatomic fit, but there is little evidence of improved surgical outcomes including patient function or satisfaction (109–111). The majority of studies in this domain have examined total knee replacements.

Similar investigations in total hip replacements are inconsistent. For example, Röder et al. (112) reported that women had lower early acetabular cup failure than men independent of cup fixation. Conversely, Howard et al. (113) reported a protective association of male sex and the risk of cup revision. A study using a Scandinavian registry did not find significant sex differences in total hip arthroplasty (THA) revision rates. Potential reasons for the conflicting findings between these studies could be attributed to the different definitions of revision, follow-up times, statistical analyses, and different outcome measures used (112–114). Inacio et al. investigated the association between the risk of implant failure and sex in 35,140 THAs performed between 2001 and 2010. In their study women had a 29% higher risk of short-term implant failure, after considering for the specific surgeon, surgeon-volume, and implant-specific risk factors compared to men. Of note, these investigators also observed that among those who received smaller femoral head sizes, women continued to have a 19% higher risk of revision compared to men (115). The varying findings of studies investigating outcome of THA and the influence of patient sex have limited the need for development of gender-specific hip joint prostheses.

CONCLUSION

Despite the growing aging population in the United States, there are limited studies that have investigated how gender influences the musculoskeletal system in older adults. Sarcopenia and osteoarthritis are the most studied disorders in this realm. In sarcopenia, men in general have a higher percentage loss of muscle mass than women and a larger response to resistance training with increased hypertrophy of type I and II fibers. Hormonal differences between men and women likely play a large role on this difference. In OA, the most studied joint by far is the knee. Multiple studies have shown that women have a higher incidence of knee OA compared to men, with thinner femoral and patellar cartilage and increased annual cartilage loss. Women overall present earlier with knee pain, but are less likely to undergo surgery and have a higher amount of NSAID use. Structural anatomic differences between the sexes have led to the development of joint prostheses that are gender-specific. However, there is limited evidence of benefit of these prostheses compared to conventional arthroplasty surgeries that use nongender-specific components.

In conclusion, differences between the sexes in terms of the epidemiology and morbidity secondary to OA have been described, but few studies have looked at the development of treatments that take into account these gender-related differences. This innovative individualized approach may provide more efficacious individualized treatments for this debilitating disease. With the proliferation of nonoperative regenerative medicine procedures, sex-based differences in the biology of the joint will need to be further clarified

Summary of Sex Differences in Musculoskeletal Properties/Disorders in the Aging Athlete

Musculoskeletal Property/Disorder	Sex Differences
Bone mineral density	Decrease highest in postmenopausal women
Fat oxidation rate	Higher in men
Reaction times	Faster overall in men

(*continued*)

Summary of Sex Differences in Musculoskeletal Properties/Disorders in the Aging Athlete (*continued*)

Musculoskeletal Property/Disorder	Sex Differences
SARCOPENIA	Similar prevalence but generally men have a larger percentage loss of muscle mass
• Type I and type IIA fibers	• Fibers from older men stronger than older women
• Estrogen	• Variable effect of ERT in women, potentially beneficial in early postmenopausal period with resistance training
• Testosterone	• Increases muscle mass and strength in hypogonadal men and women
• DHEA	• Exogenous administration increases muscle strength in men
Exercise: Response to aerobic exercise	Moderate to vigorous physical activity reduces risk of cardiovascular disease in both sexes
Exercise: Response to resistance training	Hypertrophy of type I and II fibers higher in males
OSTEOARTHRITIS	
Structural factors:	Higher prevalence of OA in women after age 50
• Cartilage thickness	• Distal femoral and patellar cartilage thinner in women • Higher annual cartilage loss in women
• Quadriceps strength	• Decreased strength predictive of worsening functional progression in both sexes
• Gait cycle	• Women walk with a longer stance phase and double limb support
• Hip dysplasia	• Risk in both sexes for hip OA
Systemic factors:	
• Obesity	• Stronger predictor of onset and progression in women than men
Clinical presentation and treatment:	
• Time to presentation	• Women present earlier with knee pain but are less likely to undergo surgery and more likely to use NSAIDs
• Surgical outcomes	• Similar outcomes with total knee replacements

DHEA, dihydroepiandrosterone; ERT, estrogen replacement therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis.

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18

SPORTS CARDIOLOGY

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INTRODUCTION

Exercise can be viewed as the process whereby an individual does mechanical work on the environment to move the environment (weightlifting), move oneself through the environment (swimming), or a combination of both (cycling). In an exercising individual the cardiovascular system plays three important roles: the delivery of oxygen and nutrients to exercising muscle, the removal of waste by-products from exercising muscle, and the dissipation of generated heat through convection.

While a sequential and organized program of exercise can train the cardiovascular system to function more efficiently, vigorous physical activity can also exacerbate or make manifest cardiovascular disease. Thus, within the field of sports cardiology, there are two major clinical concerns: identifying athletes with life-threatening cardiovascular disease before competition, and prescribing safe limits on level of exercise intensity for those individuals with known cardiovascular disease.

Important sex differences exist in both the realm of exercise physiology and cardiovascular pathology. Therefore, this chapter is divided into two sections: sex differences in cardiovascular physiology, and sex differences in cardiovascular disease. The first section begins with a primer on cardiovascular physiology; the second section begins with important considerations when evaluating the athlete with known or suspected cardiovascular disease.

Primer in Exercise Physiology

The body makes acute and chronic adaptations to accommodate the increased metabolic demand of exercise. The cardiovascular system, pulmonary system, musculoskeletal system, central and peripheral nervous systems, and hematologic system all make crucial changes during exercise to preserve cellular oxygenation and acid-base homeostasis. Here we examine the body's adaptive mechanisms to exercise, with a particular focus on the cardiovascular system, and articulate the gender and sex differences in exercise physiology and cardiovascular disease.

Energy Production

The body's response to exercise is complex and requires many short- and long-term adaptations. The mechanical work done by muscles during exercise requires energy—energy derived from the high-energy chemical bonds present in adenosine triphosphate (ATP). A variety of machineries exist to regenerate ATP, and different types of exercise use different metabolic mechanisms to generate ATP. Aerobic activity, such as swimming, long-distance running, and cross-country skiing, is characterized by low-intensity, long duration exercise. This type of exercise is supported primarily by aerobic metabolism, which requires oxygen to be present for the generation of energy from sources such as glucose, glycogen, and fat. This process, called oxidative phosphorylation, occurs in the mitochondria of muscle cells. In aerobic metabolism, the cardiopulmonary system must replenish oxygen in working muscles.

In contrast, high-intensity activities such as sprinting, heavy weightlifting, and interval training are supported primarily by anaerobic metabolism. In anaerobic metabolism, anaerobic glycolysis rapidly generates ATP from the breakdown of glucose without requiring oxygen. This process is less efficient than oxidative phosphorylation and cannot be sustained due to the production of lactic acid, which inhibits further glycolysis. Anaerobic glycolysis occurs in the cytosol of muscle cells, in contrast to aerobic respiration that occurs in mitochondria. High-intensity exercise can also utilize an additional metabolic pathway, the creatine kinase reaction, to facilitate rapid production of ATP (1).

Aerobic Respiration

The utilization of oxygen by working tissue is a process that involves three distinct steps—oxygenation, oxygen delivery, and oxygen consumption (Figure 18.1). Inspired oxygen diffuses across the alveolar-capillary membrane from the lungs into the blood (oxygenation). Red blood cells then transport hemoglobin-bound oxygen throughout the body (oxygen delivery) and tissues extract oxygen for use in aerobic respiration (oxygen consumption). Thus, the delivery of oxygen to working tissue is dependent on the function of the lungs, the cardiovascular system, and red blood cells in order to meet the metabolic demands of the body (2). Here we briefly describe each of these key steps and describe some of the short- and long-term adaptations the body's organ systems make during activity.

Oxygenation. Oxygenation occurs when inspired oxygen diffuses across the alveoli into the pulmonary capillaries. This oxygen becomes predominantly bound to hemoglobin in red blood cells, although some oxygen dissolves in the arterial plasma. The driving force for diffusion of oxygen across the alveolar-capillary membrane can best be understood by the alveolar gas equation. Mathematically, the alveolar gas equation is defined as $PAO_2 = PiO_2 - (PACO_2/RER)$, where PAO_2 is the alveolar partial pressure of oxygen, PiO_2 is the partial pressure of inspired oxygen, $PACO_2$ is the alveolar partial pressure of carbon dioxide, and RER is the respiratory exchange ratio, or the ratio between the amount of oxygen consumed (VO_2) and carbon dioxide produced (VCO_2) in each breath (VO_2/VCO_2). PAO_2 is preserved during exercise by several mechanisms. The minute ventilation is the amount of air that is inhaled or exhaled in 1 minute. Minute ventilation increases incrementally with increased metabolic demand, primarily due to increased tidal volume, or the volume of air inhaled (or exhaled) with each breath (3). With increased minute ventilation, the alveolar ventilation (V_A), the component of tidal volume that participates in gas exchange, also increases. Furthermore, the lung bases—areas that typically have low ventilation/perfusion indices—become better ventilated during exercise due to larger tidal volumes. Additionally, the blood flow to the pulmonary capillaries is increased, which increases

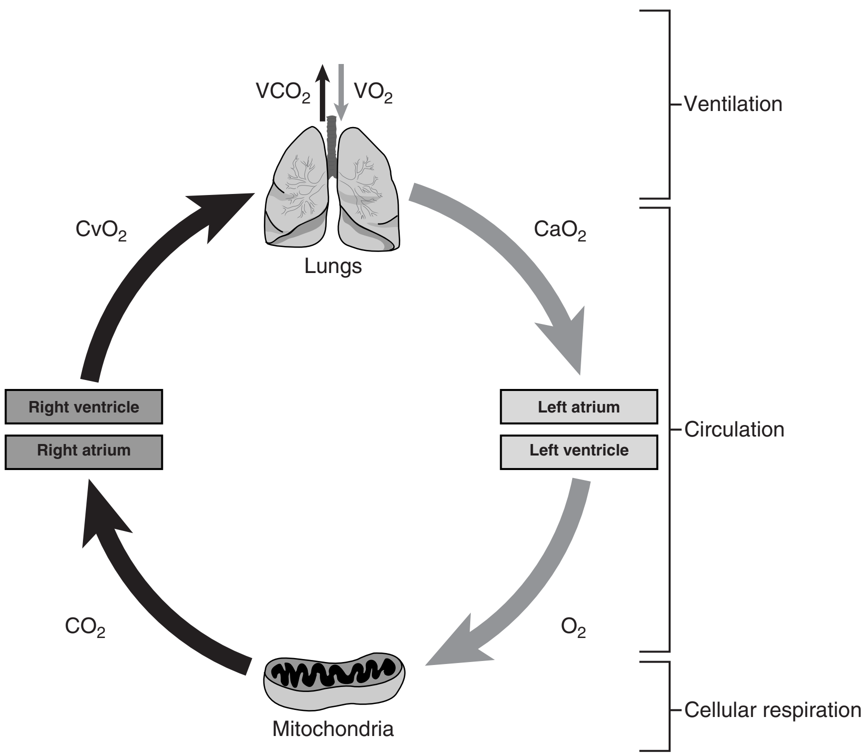

FIGURE 18.1: Gas transport.

the amount of surface area for oxygen to diffuse across. The net result of these adaptations is preservation of the PAO_2 despite increased metabolic demand (4).

Oxygen Delivery. Oxygen delivery, or DO_2, is the rate at which oxygen is transported from the lungs into the peripheral tissue. DO_2 equals the product of the cardiac output and the arterial oxygen content (C_aO_2). Cardiac output in turn is equal to the heart rate in beats per minute multiplied by the stroke volume, or the amount of blood ejected by the heart during each beat. Arterial oxygen content is defined as the amount of oxygen bound to hemoglobin plus the amount of oxygen dissolved in arterial blood. Since most oxygen is bound to hemoglobin, with only a small contribution from oxygen dissolved in arterial blood, oxygen content is mostly dependent on the hemoglobin concentration and the oxyhemoglobin saturation. DO_2 is augmented during activity primarily through increases in cardiac output.

The Frank-Starling mechanism is an important model for understanding the heart's ability to augment its forces of contraction, and therefore stroke volume, in the setting of increased workload. The Frank-Starling mechanism states that contractility increases when end-diastolic volume (EDV), or the heart's preload, increases (5). This can best be understood on the level of the myocardial cells. As the heart fills with more blood, the nature of the actin and myosin filament interaction changes in a manner that results in increased contractility. It is believed that during exercise, left ventricular (LV) filling is increased due to greater negative intrathoracic pressure and the pumping action exhibited by exercising limbs (6). As a result, the left ventricular-end-diastolic volume (LVEDV) increases, augmenting the contractility and thus stroke volume.

The systemic circulation also makes key adaptations that enhance oxygen delivery. Blood flow is preferentially redirected to working muscles and away from less metabolically active organs, such as the gastrointestinal system and the kidneys. Although systolic blood pressure increases with activity, diastolic blood pressure changes little. Furthermore, the rise in mean systemic blood pressure is less than expected given the increase in cardiac output, indicating a decrease in systemic vascular resistance (SVR) (7). Exercise performance has been correlated with the ability to decrease SVR (8).

Oxygen Consumption. Once oxygen is delivered to working muscles, it must be extracted for use in aerobic respiration. Oxygen consumption, or VO_2, is defined as the rate at which oxygen is taken up by working tissues. The Fick equation is useful for calculating VO_2. The Fick equation defines VO_2 as the cardiac output multiplied by the amount of oxygen muscles are able to extract from the blood passing through them, quantified by the arteriovenous oxygen content difference, $(a\text{-}v)O_2$. During exercise, VO_2 increases due to elevated cardiac output and increased $(a\text{-}v)O_2$. The $(a\text{-}v)O_2$ is expected to increase during times of strenuous exercise, as working muscles are extracting more oxygen. This is facilitated by changes in the oxyhemoglobin dissociation curve (9). Local lactic acidosis during strenuous activity causes a rightward shift in this curve, decreasing affinity between hemoglobin and oxygen and increasing the availability of unbound oxygen for working muscles (10).

Anaerobic Threshold. The anaerobic threshold (AT) is the point at which aerobic metabolism transitions to anaerobic metabolism. This occurs at the exercise intensity when the partial pressure of oxygen is no longer sufficient for a given VO_2. At this point, several physiological responses occur. Muscle cells use anaerobic glycolysis to generate ATP for energy use. Lactic acid is produced as a result, leading to increased metabolic acidosis, increased ventilatory drive, and increased fatigue. The anaerobic threshold varies dependent on the fitness level of the athlete, with higher-level athletes being able to meet a higher VO_2 before entering anaerobic metabolism. Several mechanisms have been proposed to explain how AT can be increased, including enhanced oxygen delivery to working skeletal muscle fibers, increased rate of lactate clearance during exercise, and biochemical alterations within skeletal muscle that reduce lactate formation (11). AT can be increased by high-intensity interval training and moderate-intensity continuous training.

Long-Term Adaptations of Exercise Training

Exercise training confers long-term adaptations throughout many of the body's organ systems. The cardiovascular system, pulmonary system, and musculoskeletal system all exhibit adaptive responses that improve efficiency of energy utilization during exercise. Cardiac hypertrophy, or "athlete's heart," is a physiological adaptation to increased workload. In contrast to pathological hypertrophy, physiological hypertrophy is associated with normal or augmented contractility (12). The type of physiological hypertrophy is dependent on the type of exercise. Endurance training is associated with LV eccentric hypertrophy, where both left ventricular cavity and wall thickness are increased from the volume overload produced during exercise. Strength training, on the other hand, is associated with left ventricular concentric hypertrophy in response to increased afterload during isometric exercise, where there is increased wall thickness but no change in cavity size (13).

Endurance training improves stroke volume, cardiac output, and maximal oxygen uptake (VO_{2max}), defined as oxygen consumption at maximal heart rate. VO_{2max} is the fastest rate at which the body can utilize oxygen during activity and is widely accepted as the best indicator of overall cardiopulmonary fitness and functional aerobic capacity. During the first stage of aerobic exercise intensity, from rest to approximately 40% VO_{2max}, cardiac output is augmented primarily by increased stroke volume, with a moderate increase in heart rate. Cardiovascular response differs between trained and untrained individuals at the second stage of aerobic exercise intensity, from 40% VO_{2max} to 90% VO_{2max}. In untrained individuals, peak contractility is reached at 40% VO_{2max}. Thus, any increase in cardiac output after this threshold is reached is a result of increased heart rate. Well-trained individuals, on the other hand, are able to augment stroke volume up to VO_{2max}. During the third and final stage of aerobic exercise, from 90% VO_{2max} to VO_{2max}, cardiac output increases due to a sharp increase in heart rate. This increased heart rate reduces left ventricular filling time, so stroke volume becomes slightly decreased. During this final stage of aerobic exercise, untrained individuals rely primarily on anaerobic metabolism (14).

The lungs and skeletal muscle also undergo important adaptations in response to endurance training. In skeletal muscle, endurance training confers an increase in mitochondrial size, muscular capillary density, and muscle myoglobin levels. All of these adaptations improve the muscle's ability to extract oxygen during exercise (15). In the lungs, ventilation (VE) at maximal aerobic exercise increases with training experience (16). Untrained individuals primarily augment VE by increasing respiratory rate. The trained individual, on the other hand, can increase both tidal volume and respiratory rate. The augmentation of VE exceeds the amount of blood that circulates through the lungs at exercise and thus is usually not the limiting factor during maximal aerobic metabolism.

Sex Differences in Exercise Physiology

The cardiovascular system, pulmonary system, hematologic system, and metabolic system exhibit sex-specific differences in function and morphology in response to activity.

Sex Differences in Cardiovascular Physiology

There are several important sex-related differences in cardiovascular physiology. Males and females have different cardiac structure and hemodynamic response to exercise. Cain et al. used cardiac MRI to measure left ventricular dimensions in healthy volunteers. Compared to adult females, adult males had higher body surface area (BSA)-adjusted end-diastolic volumes (EDV) and end-systolic volumes (ESV) with similar stroke volumes and ejection fractions (EF) (17). No sex differences were seen in the younger (11–15 years old) age group, suggesting that the difference in left ventricular dimensions may be due to differences in sex hormone profiles between the sexes. Another study evaluated echocardiographic parameters in males and females at rest and at peak VO_2 (18). In males and females with equal peak VO_2, males were found to achieve higher exercise workload while females were able to reach higher heart rate. The two groups had similar left ventricular stroke volumes and cardiac outputs when indexed for BSA. While indexed EDV and ESV were smaller in females, females had higher early diastolic velocity, suggesting enhanced lusitropy, or relaxation function of the heart. Indexed stroke volume was the sole multivariable predictor of peak VO_2 in men. Markers of increased left atrial pressure—such as raised early diastolic velocity and short diastolic filling time—were predictions of peak VO_2 in women. These findings suggest that the cause of exhaustion in the athlete differs according to gender. While stroke volume is the main limiting factor in males, raised left atrial pressure—and subsequent pulmonary venous hypertension—may be the main cause of fatigue in females. This pulmonary venous hypertension may be exacerbated during endurance exercise in females, which may result in LV hypertrophy, a decrease in LV cavity size, and further increase in left atrial pressure. This could partially explain the differences in endurance exercise athletic performance between the sexes.

In addition, males and females exhibit differences in the heart's adaptation to progressive overload. Cardiac remodeling (meaning the change in heart size and wall thickness) is more pronounced among male athletes. When compared to male athletes of similar age and training regimen, females were found to have 23% less left ventricular wall thickness and 11% smaller left ventricular size (19). Data from various animal studies also demonstrate sex-specific regulation of physiological hypertrophy in response to exercise. In these studies, females were shown to have an increased hypertrophic response to training load compared to males. It was hypothesized that sex hormones, particularly estrogen and testosterone, were important in modulating the development and progression of physiological cardiac hypertrophy (20). It has also been postulated that substrate utilization of myocardial cells may impact the sexual dimorphism of physiological cardiac hypertrophy. Animal studies have shown increased plasma free fatty acid levels and augmented lipolysis in females after training when compared to males, indicative of preferential fatty acid utilization (21). Fatty acid utilization as the primary fuel source during sustained activity has been suggested as one of the important mechanisms distinguishing physiological from pathological cardiac hypertrophy (22).

Females have a lower VO_{2max} when compared to males. Astrand (23) reported a 17% lower VO_{2max} for 18 female students when compared to 17 male students of comparable stature, while Bruce et al. (24) determined that females had 23% lower VO_{2max} when compared to male counterparts. The gender-related difference in VO_{2max} is probably related to differences in left ventricular dimensions. Sex differences in VO_{2max}, however, are reduced to about 10% when comparing elite athletes. And if VO_{2max} is adjusted for fat-free mass, the differences disappear in some studies (25). Nonetheless, studies have consistently shown increased endurance performance in athletic competition in men compared to women. This is thought to be due to greater VO_{2max}, lower body fat percentage, and higher hemoglobin count (26) in men.

Sex-related cardiovascular differences are also demonstrated during anaerobic exercise. The peak Wingate anaerobic test is used to measure anaerobic capacity and peak anaerobic power. At peak Wingate anaerobic test, Sagiv et al. (27) showed that males had significantly higher values of cardiac output and stroke volume, while $(a\text{-}v)O_2$, VO_2, and $\%VO_2$ out of total energy utilized were significantly lower when compared to females. Males also had a significantly lower resting heart rate. The data suggest that women had a significant increase in oxygen extraction during anaerobic activity, which partially compensated for lower cardiac output. Another study demonstrated that although males had higher absolute values in anaerobic capacity and power, statistical significance diminished when indexed with fat-free body mass (28).

Sex Differences in Pulmonary Physiology

In addition to the cardiovascular system, there are also several sex-specific differences in pulmonary function during exercise, which are largely a product of hormonal and morphological differences between males and females. Sex hormones play a key role in the pulmonary response to exercise. The reproductive hormones progesterone and estrogen can influence vascular volume dynamics, ventilation, substrate metabolism, and thermoregulation (29). Increased estrogen levels can increase fluid retention and therefore blood volume, which could potentially affect gas exchange in the lung (30). With the exception of possible improvement in endurance during the luteal phase, there do not seem to be conclusive data on the effect of the menstrual cycle on athletic performance (26).

Structural pulmonary differences have also been noted between males and females. Height-matched men have larger diameter airways (31), larger lung volumes, and increased diffusion surface areas compared with postpubertal women (32). It has been hypothesized that gender differences in diffusing capacity of the lung can be explained by these differences in surface area and airway diameter. Studies indicate that during heavy exercise, women experience increased work of breathing and greater expiratory flow limitation compared to men. It is plausible that respiratory muscle fatigue could adversely impact aerobic capacity and exercise tolerance in women compared to men, consistent with differences in airway diameter. These findings suggest that respiratory limitation to oxygenation may play a greater role in determining exercise tolerance in women compared to men (29).

Some studies (33,34) indicate that women experience exercise-induced arterial hypoxemia (EIAH) more frequently than males. Harms et al. (34) found that women developed EIAH, defined as greater than 10 mmHg decrease in PaO_2 from rest to exercise, across all levels of aerobic fitness and exercise intensity. The etiology of EIAH is thought to be multifactorial. Oxygen diffusion limitation, inadequate hyperventilation, and ventilation-perfusion inequality are thought to contribute to the incidence of EIAH (33). It was hypothesized that EIAH was also due to smaller lung volumes and airway diameters with resultant mechanical constraints (e.g., expiratory flow limitation) during exercise. This study demonstrated that reversing these mechanical restraints with heliox gas partially reversed EIAH in females who developed expiratory flow limitation. An additional study demonstrated that even a small amount of EIAH had a significant detrimental effect on VO_{2max} in well-trained female athletes (35). Furthermore, VO_{2max} improved when the exercise-induced hypoxemia was corrected with increased fraction of inspired oxygen (FiO_2).

Sex Differences in Hematologic Physiology

The hematologic system, critical for the transportation of oxygen to working tissues, is also influenced by sex. On average, men have mean hemoglobin levels approximately

12% greater than women. The sex difference in hemoglobin levels is thought to be a result of the activity of sex hormones in erythropoiesis. Androgens stimulate erythropoietin production in the kidney and have a direct stimulatory effect in association with erythropoietin in the bone marrow. Estrogen in females, on the other hand, has been shown to have an inhibitory effect on erythropoiesis (36). As a result of higher mean hemoglobin levels, men have a higher oxygen-carrying capacity compared to women, which allows for greater aerobic capacity.

At the center of the heme moiety in hemoglobin is elemental iron, responsible for the binding of oxygen and allowing for its transport. Athletes may have low iron stores through a variety of mechanisms. Iron-deficiency anemia has been observed in athletes after endurance exercise due to hemolysis and iron losses from gastrointestinal bleeding. Furthermore, iron absorption can be impaired due to the release of inflammatory cytokines in response to physical activity (37). Premenopausal females are at increased risk of iron-deficiency anemia compared to men due to blood losses from menstruation, which represent a significant source of iron excretion. Anemia is believed to affect over 40% of pregnant women and 30% of nonpregnant women as a result (38). Ostojic and Ahmetovic (39) found a high prevalence of iron deficiency anemia among female athletes from across different sports, with similar incidence in individuals independent of their training volume. Anemia in the athlete can impair tissue oxygenation, which can in turn lead to a decrease in endurance, a decrease in aerobic adaptation and metabolic responses, and increased muscle fatigue (40).

The oxygen-binding characteristics of red blood cells are also sex-dependent. Humpeler et al. (41) found that P_{50} values (the partial pressure of oxygen at 50% oxygen saturation of hemoglobin) were significantly higher in sexually mature women than in men, indicating less affinity between hemoglobin and oxygen. This was due to a significantly elevated level of 2,3-diphosphoglycerate (2,3-DPG) observed in women. A rightward shift in the oxyhemoglobin-dissociation curve is induced by 2,3-DPG, favoring the deoxygenated state of hemoglobin and increasing availability of oxygen for utilization in peripheral tissues. Interestingly, no difference in oxygen affinity was found before puberty and post-maturity in females. This suggests a sex hormone and maturation-induced influence in the development of the oxygen transport system, with estrogens favoring a decrease in oxygen affinity of hemoglobin. The physiological consequences of the gender-related difference in oxygen affinity are unclear, though they may be beneficial as an adaptation to tissue hypoxia or in cardiovascular disease (41).

Sex Differences in Metabolism

It is believed that men have greater reliance on anaerobic glycolysis when compared to women. Men have greater muscular force of contraction with an associated greater metabolic demand. This force of contraction may cause local compression of the vascular bed, reducing the availability of oxygen and increasing the utilization of anaerobic metabolism to generate energy (42). Interestingly, greater reliance on anaerobic glycolysis by men has been observed under similar oxidative conditions as compared to women. Multiple studies have demonstrated that women exhibit greater resistance to fatigue than men when engaging in submaximal, isometric exercise. It was hypothesized that this difference in fatigue was related to difference in utilization of metabolic pathways. Russ and Kent-Braun (42) tested this hypothesis by having healthy young males and females perform 4 minutes of intermittent muscular contraction under free-flow and ischemic conditions. Females exhibited less fatigue under free-flow conditions, but comparable fatigue during ischemia. This suggests that women may have what is known as an “oxidative advantage” compared to men, whereby they are more effective in utilizing oxidative phosphorylation during muscular activity (43).

SEX DIFFERENCES IN CARDIOVASCULAR DISEASE

General Considerations in the Cardiac Evaluation of the Athlete

The Symptomatic Athlete

Exercise has numerous health benefits, including reducing insulin resistance (44), coronary heart disease (45), cardiovascular events (46), and all-cause mortality (47). Despite the long-term health benefits associated with regular activity, cardiovascular events such as arrhythmia, myocardial infarction, and sudden cardiac death can occur during or immediately after exercise. Cardiovascular disease can also present as a functional limitation of the athlete, with a reduction in exercise tolerance and athletic performance. This functional limitation can also manifest clinically as progressive fatigue, dyspnea on exertion, chest pain, presyncope/syncope, and palpitations. As these are relatively nonspecific symptoms, the astute clinician must have a high index of suspicion when evaluating an athlete with exercise-related symptoms and perform a careful history, physical examination, and diagnostic evaluation in order to exclude potentially life-threatening cardiovascular disease processes.

Sudden Cardiac Death

Of the negative outcomes associated with cardiovascular disease in the athletic population, sudden cardiac death (SCD) is the most dreaded. Thus, much of the evaluation of the symptomatic athlete focuses on assessing risk of SCD in addition to understanding any functional limitations imposed by cardiovascular disease. Exercise-related SCD is defined as death occurring within 1 hour of participation of sports, and it is estimated to occur in one to five cases per 1 million athletes per year (48). It is the leading cause of death among athletes (49). The most common sequence of events leading to SCD is thought to be degeneration of ventricular tachycardia (VT) into ventricular fibrillation (VF), during which disorganized ventricular contractions fail to pump blood effectively, causing a pulseless state (50). The underlying cause of SCD differs depending on the age of the athlete. SCD in "masters athletes" older than 35 is most often related to coronary heart disease with myocardial infarction, while SCD in younger athletes is primarily due to hereditary cardiovascular disorders (51). The incidence of SCD is much higher in men than in women, with men accounting for an estimated 75% of all SCD. Men also have a 50% higher age-adjusted rate of SCD (52). This is due to multiple different factors, including difference in sex hormones as well as rates of participation in different sports.

Return-to-Play Guidelines

The presence of cardiovascular disease elevates the risk of SCD. Many cardiovascular diseases limit or may even preclude participation in various sports. Clinicians are often confronted with the decision of whether to advise athletes to return to play (RTP) after a cardiovascular condition is discovered, either by medical history, routine pre-participation screening, or after a cardiac event has occurred. In the United States, the 36th Bethesda Conference Eligibility Recommendations for Competitive Athletes with Cardiovascular Abnormalities are the most often-used guidelines to make this determination.

Sex Differences in Specific Cardiovascular Diseases

Cardiovascular Disease in Athletes

Broadly, cardiovascular diseases that affect athletes can be grouped into three different categories: arrhythmogenic disorders, structural heart disease, and coronary heart disease (Figure 18.2). In this section we discuss various cardiac disorders that can affect athletes by affecting athletic performance or by putting them at risk for SCD. We then discuss important known sex and gender differences in these various cardiovascular disorders and point out areas where literature is lacking. In general, we restrict our discussion to disorders with known gender and sex differences in either prevalence or outcomes, unless the disorder is common.

Arrhythmogenic Disorders

Arrhythmogenic disorders with important gender-related differences include arrhythmogenic right ventricular cardiomyopathy, long QT syndrome, Brugada syndrome, catecholaminergic polyventricular tachycardia, Wolff-Parkinson-White syndrome, and supraventricular tachycardias.

Arrhythmogenic Right Ventricular Cardiomyopathy. Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an autosomal dominant genetic disorder characterized by right ventricular enlargement and dysfunction as well as life-threatening ventricular arrhythmias. The pathologic hallmark of ARVC is fibrofatty infiltration of the myocardium. ARVC is the leading cause of SCD in athletes in the Veneto region of Italy, accounting for approximately one fourth of events. The incidence of SCD in athletes with ARVC is estimated to be 0.5/100,000 persons/year (53). The risk of sudden death with ARVC is about 5.4 times higher during competitive sports than during sedentary activity. It is theorized that engaging in physical activity acutely increases right ventricular afterload, causing ventricular cavity enlargement and stretching of diseased myocardium, which may precipitate ventricular arrhythmias and favor reentrant circuits (18). ARVC has a typical EKG appearance with T-wave inversions in the right precordial leads beyond V1. The diagnosis may be confirmed with noninvasive imaging studies such as echocardiography or cardiac MRI. Endomyocardial biopsy may be pursued if imaging studies are equivocal. Due to the high risk of SCD during competition, the diagnosis of ARVC in an athlete leads to disqualification from sports participation.

The prevalence of ARVC is higher in males than females. Bauce et al. evaluated 171 consecutive patients fulfilling the ARVC diagnostic criteria. In this study 71% of the patients were males and, in addition, the men had larger right ventricular (RV) volumes, lower RV ejection fraction, and more severe LV involvement (54). Despite the gender-associated differences in disease prevalence, there was no significant difference between genders in the incidence of life-threatening ventricular arrhythmias. The reason for these gender-related differences remains unclear.

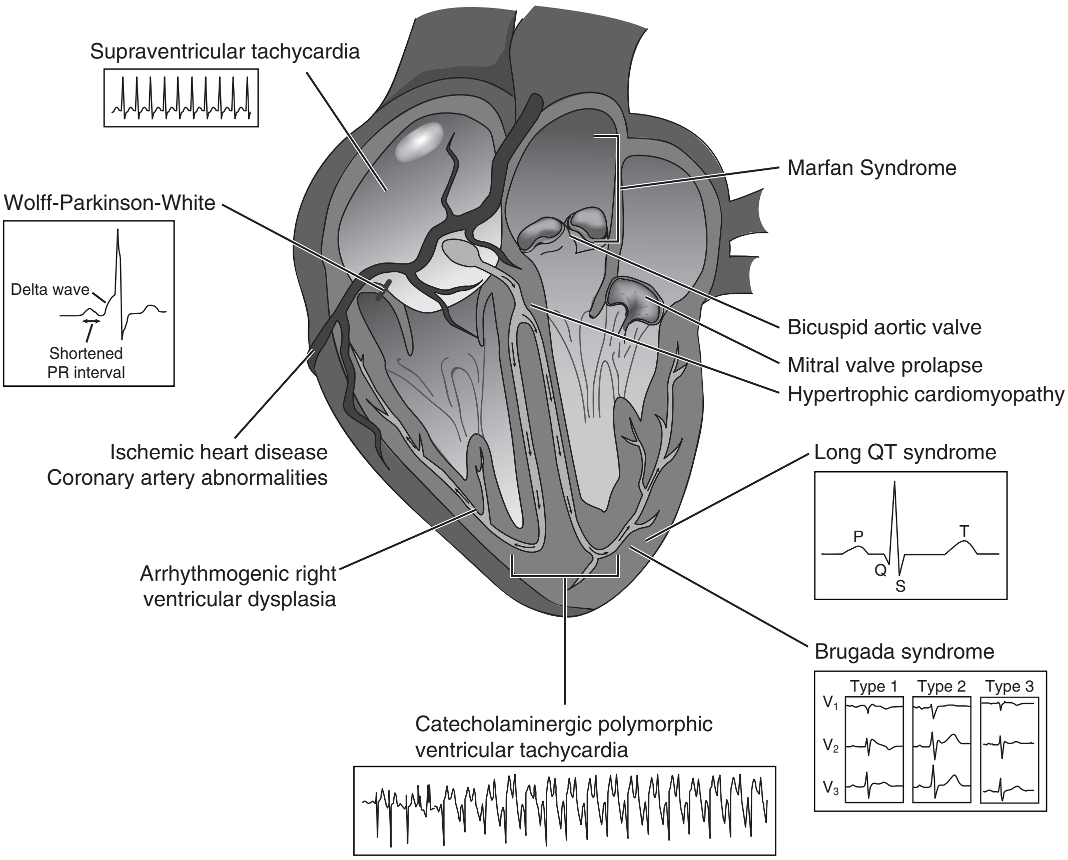

FIGURE 18.2: Cardiovascular diseases in athletes.

Long QT Syndrome. The long QT syndrome (LQTS) is an inherited ion channel disorder characterized by prolongation of the QT interval on EKG and a predilection for *torsades de pointes* polymorphic ventricular tachycardia. LQTS is characterized by variable penetrance: while some patients remain completely asymptomatic, others experience syncope, seizures, or SCD (6). Several genetic mutations have been implicated in LQTS, though the most frequently encountered—LQT1, LQT2, and LQT3—contribute to about 99% of all genotyped cases (55). The EKG is almost always abnormal in LQTS, demonstrating a prolonged QT interval. The heart is structurally normal in most patients, and these syndromes are often clinically silent prior to a catecholamine surge and SCD in times of extreme stress (49).

LQTS has a distinct sex-specific prevalence, with females representing approximately 70% of all congenital cases. Furthermore, female sex itself is an independent risk factor in the development of arrhythmias in LQTS (56). Interestingly, the risk of aborted cardiac arrest or SCD with LQTS is age-dependent. Boys are at three- to fourfold higher risk for cardiac events compared to females. After puberty, a sex risk reversal occurs. Adult women aged 18 to 40 have a higher risk and higher cumulative probability of cardiac events as compared to men. The age-dependent incidence of cardiac events between genders is likely related to shortening of the QT interval after puberty in boys attributed to elevation in testosterone levels (57).

Brugada Syndrome. Brugada syndrome is an inherited arrhythmia disorder characterized by coved-type ST elevations in the right precordial leads. This disease typically presents as non-prodromal syncope, aborted cardiac arrest, or SCD. Though the prevalence of Brugada syndrome is relatively low, it accounts for at least 20% of SCD cases in patients with structurally normal hearts (58). There is a stark contrast in prevalence of Brugada syndrome between genders, with the disease affecting eight- to tenfold more males than females (59). The exact pathophysiology of this gender discrepancy is not completely understood, but it is thought to be a result of sex hormones, namely testosterone, affecting ventricular repolarization (59).

Catecholaminergic Polymorphic Ventricular Tachycardia. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a heritable channelopathy that classically manifests as syncope or SCD during exercise, emotion, or stress (60). CPVT is typically associated with a normal resting EKG and a structurally normal heart and only becomes suspected with exercise- or catecholamine-induced ventricular ectopy. Mutations in the *RyR2*-encoded cardiac ryanodine receptor 2/calcium release channel represent the most common genetic subtype of CPVT and account for 50% to 60% of cases. These mutations are thought to result in the excessive release of calcium during sympathetic stimulation. This results in calcium overload, delayed depolarization, and ventricular arrhythmias (60). The majority of cardiac events occur during childhood, with more than 60% of individuals experiencing syncope or cardiac arrest by the age of 20 (61). Gender is an important risk factor in the etiology and pathogenesis of CPVT. Priori et al. (60) performed genetic mutation screening in a series of patients with the clinical phenotype of CPVT as well as their family members. Genotype-phenotype analysis showed that male sex was a strong risk factor for syncope in patients with *RyR2* mutation. Patients with an identified *RyR2* mutation were also noted to have earlier onset of symptoms. Furthermore, there was a strong predominance of symptomatic females among patients with nongenotyped CPVT. Tester et al. (62) demonstrated that most *RyR2*-positive patients were males, while most *RyR2*-negative patients were females. The exact pathomechanism behind this gender discrepancy remains unclear.

Wolff-Parkinson-White and Atrioventricular Reentrant Tachycardia. In Wolff-Parkinson-White (WPW) syndrome, an accessory pathway exists that connects the atria and ventricles, allowing for electrical activity to bypass the atrioventricular node. This accessory pathway allows for the action potential propagated to the ventricles to "reenter" the atria in an arrhythmia called atrioventricular reentrant tachycardia (AVRT). Clinically, this rhythm disturbance can manifest as palpitations, lightheadedness, or syncope. Although SCD is rare in WPW, atrial fibrillation is a particularly dangerous rhythm for patients with an accessory pathway since the accessory pathway allows for direct conduction of atrial fibrillation waves to the ventricles, bypassing the atrioventricular node, which normally slows the signal. This direct one-to-one conduction can drive ventricular tachycardia, which can in turn degenerate into ventricular fibrillation. The classic EKG finding of WPW is shortened with PR interval with a slurred upstroke in the QRS complex, known as a delta wave. A relatively long atrioventricular (AV) conduction time favors the manifestation of pre-excitation in WPW and may play a key role in the clinical significance of an accessory pathway (63). There is also a gender difference in the native conduction system of the heart. Men have longer PR, atrial-His, and His-ventricular intervals as well as longer AV block cycle lengths than women (56). Because of these longer conduction intervals, arrhythmia via accessory pathway, as is seen in WPW and AVRT, is more common in men compared to women. Patients with recurrent or severe symptoms related to WPW can be successfully treated with radiofrequency ablation (RFA) of the accessory pathway.

Supraventricular Arrhythmias. Supraventricular arrhythmias are rhythm disturbances that arise from the atria or the atrioventricular node. These rhythm disturbances are not generally life-threatening, but can cause pre-syncope, syncope, dyspnea, palpitations, and impaired exertional tolerance in the athlete. The most common cause of sustained supraventricular tachycardia (SVT) in the athlete is AV nodal reentrant tachycardia (AVNRT) (64). In AVNRT, a reentrant circuit exists within the AV node, allowing for rapid electrical conduction and causing elevated heart rate. AVNRT is twice as common in women as men. This is thought to be related to shorter conduction times and shorter AV block length cycles in females, as previously described. Due to excellent success rates, many electrophysiologists recommend RFA, wherein part of the atrioventricular node is ablated to remove the accessory pathway, for initial treatment of AVNRT (65). RFA is equally effective in both women and men, and more than 95% of cases can be successfully treated with RFA (66). The incidence of SVT is also influenced by sex hormones. In premenopausal women, the number of SVT episodes and symptoms are more pronounced during the luteal phase of the menstrual cycle when progesterone levels are elevated (67).

Atrial fibrillation is another common type of SVT that can impair athletic performance. Atrial fibrillation is characterized by disorganized electrical impulses most often originating from the left atrium near the pulmonary veins. If rapidly conducted, this abnormal electrical activity can cause elevation in heart rate with palpitations, shortness of breath, lightheadedness, and heart failure. Men have a 1.5-fold higher risk of developing atrial fibrillation than women, though the absolute number of women with atrial fibrillation is higher due to increased longevity compared to men. Furthermore, women with atrial fibrillation tend to have a lower quality of life and more symptoms than men (56).

Structural Heart Disease

Hypertrophic Cardiomyopathy. Responsible for approximately 26% of all SCD events in U.S. athletes, hypertrophic cardiomyopathy (HCM) is the most common cardiac abnormality leading to SCD (68). HCM is an autosomal dominant disease characterized by gross myocardial hypertrophy, contractile dysfunction, abnormal systolic anterior motion of the mitral valve with left ventricular outflow tract obstruction, and electrophysiological disturbances. The characteristic appearance on pathology is myocyte disarray defined by a marked variation in myocardial cell shape and arrangement. The structural and functional abnormalities of myocyte disarray are thought to lead to aberrant electrical conduction that provides the substrate for abnormal electrical pathways that may degenerate into lethal arrhythmias (69). The clinical manifestations of HCM are variable. The majority of patients live without significant morbidity (70), though progression of the disease is unpredictable. Patients may present with exercise-induced syncope or pre-syncope, progressive dyspnea, angina, or signs and symptoms of heart failure. The first manifestation of HCM may be SCD. The characteristic HCM murmur is a systolic murmur that increases with maneuvers that decrease preload, such as going from squatting to standing or performing the Valsalva maneuver. A high clinical suspicion for HCM with prompt evaluation and diagnosis in the athletic population is critical for surveillance and appropriate management. Since aerobic activity has been linked with SCD in patients with HCM, it is recommended to exclude athletes with HCM from all competitive sports.

As HCM is an autosomal dominant condition, one would expect a fairly equal male-to-female distribution. However, a multicenter study evaluating 969 consecutive patients from Italy and the United States found a 3:2 male-to-female distribution. Furthermore, female patients were older and more symptomatic than male patients upon initial evaluation. Female sex was independently associated with the risk of symptom progression or death from heart failure or stroke when compared with male gender (71). These findings were further corroborated by Terauchi et al. (72), who investigated sex differences in the clinical features of HCM caused by cardiac myosin-binding protein C mutations (MYBPC3). Females with MYBPC3 mutations showed later onset of the disease, but were more symptomatic at diagnosis and had more frequent heart failure events. Another recent genotyped cohort study by Page et al. reported higher disease penetrance in males than females (73). These sex-related differences in disease penetrance and presentation are believed to be due to differences in sex hormones, particularly in estrogen, which is thought to have cardioprotective and myocardial modulating properties.

Congenital Heart Disease. Congenital heart disease encompasses a variety of cardiovascular lesions with variable presentations. Some congenital defects may be clinically overt at birth, necessitating prompt surgical correction, while others may first come to medical attention during sports participation. Congenital heart disease can be categorized by the type of defect present. Shunt lesions include atrial septal defect, patent foramen ovale, ventricular septal defect, and patent ductus arteriosus. Valvular lesions include bicuspid aortic valve, mitral valve prolapse, congenital pulmonic stenosis, and coarctation of the aorta. Cyanotic heart disease includes tetralogy of Fallot, transposition of the great vessels, total anomalous venous return, truncus arteriosus, and tricuspid atresia. Though significant gender-related differences are not observed in many of the congenital heart diseases, there may be some key differences in cardiac outcomes. A study from the CONgenital CORvitia (CONCOR) Dutch national registry evaluated over 7,000 adults with congenital heart disease. Though the male-to-female distribution was similar, the study identified sex differences in select cardiac outcomes. Women had a 33% higher risk of pulmonary hypertension and a 33% lower risk of aortic outcomes (aneurysm, dissection, or aortic surgery), a 47% lower risk of endocarditis, and a 55% lower risk of implantable cardioverter defibrillator use. The risk of arrhythmia also appeared to be lower in females. No sex difference in mortality was found (74). Whether these sex-specific differences in cardiac outcomes have a biologic or genetic basis is yet to be determined.

Aside from cardiac outcomes related to congenital heart disease, there are a few select disease processes with sex-specific differences. Bicuspid aortic valve and mitral valve prolapse have been identified as disease processes with important differences in clinical manifestations and prevalence between males and females.

Bicuspid Aortic Valve. The bicuspid aortic valve is one of the most common congenital heart defects, affecting approximately 1% of the population (75). An athlete with a bicuspid aortic valve is at risk for many potential cardiovascular complications, including aortic stenosis, aortic regurgitation, endocarditis, thoracic aortic aneurysm, and aortic dissection. Some athletes with bicuspid aortic valve may remain asymptomatic, while others may experience symptoms related to these valvular abnormalities, such as exertional dyspnea, dizziness, syncope, palpitations, or atypical chest pain. The physical examination of an athlete with a bicuspid aortic valve may reveal a click best heard at the left lower sternal border followed by a systolic ejection murmur. Transthoracic echocardiography is the most common modality used in the diagnosis of bicuspid aortic valve. The bicuspid aortic valve is more prevalent in males than females, with an estimated 3:1 ratio between the two sexes (75). Most cases of bicuspid aortic valve are thought to be familial—as such, this gender-related difference is thought to be due to a genetic cause.

Mitral Valve Prolapse. Mitral valve prolapse (MVP) is another common congenital valvular abnormality, with an estimated prevalence of 2.4% in the general population (76). Mitral regurgitation is the most common complication associated with MVP, and its severity is the main predictor of left ventricular and left atrial abnormalities (77). MVP is also associated with embolism, arrhythmia, and SCD. The athlete with MVP-associated mitral regurgitation may experience various nonspecific symptoms, such as chest pain, dyspnea on exertion, palpitations, and dizziness. Physical examination may reveal a nonejection click followed by the holosystolic murmur characteristic of mitral regurgitation. Transthoracic echocardiography is typically used to diagnosis MVP and its valvular complications. MVP is more common in women than men. A study at the Mayo Clinic evaluated the clinical characteristics, echocardiographic parameters, and clinical outcomes of 4,461 women and 3,678 men diagnosed with MVP. It found that women had less posterior prolapse, less leaflet flail, and less frequent severe regurgitation than men. Left ventricular and atrial dimensions were smaller in women than in men, but larger when indexed to BSA. In patients with severe regurgitation, women were less likely to undergo cardiac valve surgery. At 15 years, women with no or mild mitral regurgitation had better survival than men, but those with severe mitral regurgitation had worse survival (78). These findings suggest a sex-difference in disease mechanisms associated with MVP. Further investigation is needed to better define the biology behind these differences, as well as implications for athletes.

Marfan Syndrome. Marfan syndrome is an autosomal dominant connective tissue disorder with a wide range of characteristic musculoskeletal, ocular, and cardiovascular manifestations. Athletes with Marfan syndrome are characteristically tall and thin, with disproportionately long limbs and long, thin facies. Joint hyperextension is common among patients with Marfan syndrome. It is important for the sports physician to be familiar with this phenotype so that the risk of SCD in this patient population may be reduced. Marfan syndrome accounts for approximately 2% of SCD in U.S. athletes (79), most commonly because of aortic rupture from progressive aortic root dilatation. MVP or mitral valve degeneration may also occur (80). Athletes with Marfan syndrome are typically asymptomatic—thus, the clinical recognition of this disease is critical in monitoring for silent progression of aortic dilatation. Due to the risk of aortic injury, it is typically recommended that patients with Marfan syndrome avoid isometric exercises, high-intensity activities, or collision sports. No significant sex-related differences have been observed in the incidence or clinical manifestations of Marfan syndrome.

Coronary Artery Abnormalities. Coronary artery abnormalities are the second leading cause of nontraumatic SCD in young athletes (81). This heterogeneous group of diseases includes anomalous origin of the left anterior descending artery, tunneled coronaries, myocardial bridging, coronary fistulae, and single coronary arteries. These abnormalities may lead to transient myocardial ischemia during intense activity, which can cause lethal arrhythmia in the form of VT or VF. About one third of athletes will experience syncope, angina, or exertional dyspnea prior to an SCD event (82). Physical examination is oftentimes normal, and definitive diagnosis is typically made by CT of the coronary arteries, coronary angiography, or cardiac MRI. Aydar et al. (83) retrospectively evaluated coronary angiography in patients referred for left heart catheterization. Females were found to have a significantly higher incidence of coronary artery abnormalities, primarily due to anomalous origin of the left anterior descending artery or circumflex artery. Men were found to have a higher incidence of myocardial bridging, but the incidence of coronary fistula was similar between the two groups. The sex-associated difference in pathophysiology is unclear.

Peripartum Cardiomyopathy. Peripartum cardiomyopathy (PPCM) is a cardiovascular disease unique to females. PPCM is defined as the development of heart failure within the last month of pregnancy or within 5 months postpartum in the absence of any determinable etiology of heart failure and without heart disease prior to the last month of pregnancy (84). The signs and symptoms of heart failure in the peripartum athlete may be similar to normal pregnancy. Dyspnea and tachycardia are the most common clinical features upon presentation (85). A careful physical examination may reveal elevated jugular venous pressure, rales, the presence of an S3 gallop, and characteristic murmurs of tricuspid or mitral regurgitation. Transthoracic echocardiogram is typically used to confirm the diagnosis of PPCM. The prompt initiation of standard heart failure therapy is of critical importance in PPCM, with careful avoidance of potentially teratogenic therapies (angiotensin-converting enzyme inhibitors, for example) if the patient is still pregnant. The prognosis of females with PPCM is variable, with an estimated 1-year mortality of 6% to 10% in the United States (86). Left ventricular function typically recovers within 6 months of diagnosis.

Coronary Heart Disease

Most of the cardiovascular diseases previously discussed present in the younger athlete. SCD in "master's athletes"—athletes older than 35 years old—is most often related to underlying atherosclerotic coronary heart disease (CHD) with resultant myocardial ischemia and myocardial infarction during activity. It is estimated that 80% of SCD in athletes older than 35 is due to CHD (52). Important sex-related differences are present in the epidemiology, clinical presentation, and outcomes of CHD.

Coronary Heart Disease Risk Factors. Risk factors for the development of CHD include diabetes mellitus, dyslipidemia, hypertension, tobacco use, obesity, and physical inactivity. There are some key gender-related differences in the risk associated with CHD in men and women, however. There is a significantly lower age-associated risk of CHD in women than in men—specifically, the risk of death due to CHD in women is similar to that of men 10 years younger (87). CHD is unusual in the premenopausal woman, particularly in the absence of other strong CHD risk factors. The Women's Ischemia Syndrome Evaluation (WISE) study demonstrated that young women with endogenous estrogen deficiency had a more than sevenfold increase in CHD risk (88). Estrogens are believed to have several cardioprotective effects, including regulating metabolic factors, inflammation, and coagulation, as well as causing vasodilatation through activity at alpha- and beta-receptors (89). The vasodilatory properties of estrogen are further illustrated by the effect of smoking on CHD risk. Smoking increases the risk of first acute myocardial infarction (MI) in females younger than 50 more than in males (90). Smoking is believed to cause downregulation of estrogen-dependent receptors of the endothelial wall (91). Accordingly, the transition to menopause represents a key CHD risk factor in women. A dramatic rise in the incidence of CHD and the severity of presenting symptoms in females was seen after menopause in the Framingham study (92). The risk associated with menopause cannot be completely attributed to change in sex hormones, however. The Women's Health Initiative (WHI) study evaluated the use of hormone replacement therapy (HRT) for primary prevention of CHD and found no difference in primary/secondary cardiovascular outcomes or in all-cause mortality (93). The Heart and Estrogen/progestin Replacement Study (HERS) evaluated the use of HRT for secondary prevention in females with known CHD and found no change in rate of CHD events (94).

Other CHD risk factors also exhibit sex differences. Women who have diabetes are more likely to suffer cardiovascular complications than men. A meta-analysis demonstrated that the risk of fatal CHD is 50% higher in females with diabetes compared to males with diabetes (95). The risk of hypercholesterolemia is less in younger females compared to males, though this risk increases significantly after menopause (96).

Coronary Heart Disease Clinical Presentation. The clinical presentation of CHD may differ in women compared to men. In fact, CHD can represent a diagnostic challenge due to the variable clinical presentations associated with it, such as dyspnea on exertion, angina pectoris, and heart failure, or less obvious symptoms like nausea, vomiting, abdominal pain, and fatigue. In the Myocardial Infarction Triage and Intervention (MITI) project, women with MI were significantly more likely to present with atypical symptoms like upper abdominal pain, dyspnea, nausea, and fatigue (97). Furthermore, in a study of over 1 million people in the National Registry of Myocardial Infarction, 42% of women with MI presented without chest pain, compared to 31% of men (98). Additionally, females presenting with classic anginal pain are more likely not to have CHD. Kaski et al. studied a series of patients with syndrome X, defined as angina pectoris, a positive stress test, and a normal coronary angiography. The patients with syndrome X were primarily postmenopausal females (99). Despite this, another study evaluating patients presenting with symptoms of obstructive coronary artery disease found substantial overlap of symptoms in men and women (100).

Coronary Heart Disease Outcomes. Sex differences are appreciated in the outcomes associated with CHD as well. Women with CHD have less of a risk of SCD compared to men. A 38-year follow-up from the Framingham Heart Study evaluated the incidence of SCD in women compared to men. This study found that the risk of SCD was approximately one half that of men in patients with CHD (101). It also demonstrated that about two thirds of SCD in women occurred in the absence of prior overt CHD, compared to a rate of about one half in men. Women with CHD are also more likely to develop congestive heart failure. In a retrospective examination of clinical characteristics, left ventricular ejection fraction, and end-diastolic pressure and volume in a series of patients undergoing diagnostic cardiac catheterization, female sex was an independent predictor of congestive heart failure, despite having a higher ejection fraction. Diastolic dysfunction was thought to be the primary mechanism behind this gender discrepancy (102).

A prospective cohort study across 388 U.S. hospitals found that women presenting with stable angina had higher in-hospital mortality than men, though there was no significant difference in mortality between sexes presenting with acute coronary syndrome (ACS) (103). Furthermore, a retrospective examination of percutaneous coronary intervention (PCI) cases across 22 hospitals found that compared with men, women had higher unadjusted procedural mortality, higher vascular complication rates, and more strokes. When adjusted for clinical risk factors and BSA, women had similar PCI mortality risk when compared to men. Interestingly, women remained at higher risk for stroke, vascular complications, and repeat in-hospital revascularization than men, even after risk adjustment (104). This was believed to be due to smaller body size of women on average.

Thus overall, there are important sex differences between men and women in both coronary heart disease presentation and outcomes. While some of these differences may relate to underlying biological differences between sexes, differences in outcome may also be related to disparate care. These findings highlight the need for physicians involved in medical evaluation of athletes to recognize that fitness in athletes of either gender does not preclude the possibility of coronary heart disease.

CONCLUSION

In this chapter, we have highlighted some important gender differences in exercise physiology and cardiovascular disease in athletes. While quality data exist with regard to the incidence of various cardiac conditions by sex, more research is needed regarding the mechanisms of these sex differences, as well as insight into the extent to which disparities in index of suspicion or care contribute to observed differences. As athletic participation in the general population increases, it will only become more important to diagnose and manage cardiovascular disease in the athlete with an attention to sex-specific differences.

Summary of Sex Differences in Cardiovascular Disease

Cardiovascular Disease	Sex With Higher Prevalence
Sudden cardiac death (SCD)	Males (15,16)
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Males (17,18)
Long QT syndrome (LQTS)	Females (18,19)
Brugada syndrome	Males (19)
Catecholaminergic polymorphic ventricular tachycardia (CPVT)	Males (*RyR2* mutation subgroup) (19,20)
Wolff-Parkinson-White syndrome/ atrioventricular reentrant tachycardia (WPW/AVRT)	Males (20,21)
AV nodal reentrant tachycardia (AVNRT)	Females (21)
Atrial fibrillation	Males are at higher risk, though females have higher prevalence (21,22)
Hypertrophic cardiomyopathy (HCM)	Current data suggest males, though more studies are needed to further validate (22,23)

(*continued*)

Summary of Sex Differences in Cardiovascular Disease (*continued*)

Cardiovascular Disease	Sex With Higher Prevalence
Congenital heart disease	Similar between sexes (23,24)
Bicuspid aortic valve	Males (24,25)
Mitral valve prolapse (MVP)	Females (25,26)
Marfan syndrome	Similar between sexes (26)
Coronary artery anomalies	Females, though data are limited (26,27)
Peripartum cardiomyopathy	Females (27,28)
Coronary heart disease (CHD)	Males (28–31)

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19

SPORTS PULMONOLOGY

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PULMONARY SYMPTOMS DURING AND/OR AFTER EXERCISE

Optimal exercise and athletic performance is contingent upon a healthy respiratory system. The respiratory system enables gas exchange and allows oxygen delivery to the exercising body. A number of medical conditions may affect respiratory function with symptoms manifesting during and immediately after exercise. These symptoms and medical conditions occur in both sexes. However, the nature of the symptoms, reporting of symptoms, prevalence, and management vary between men and women. Thus, it is important to consider gender when evaluating an individual with respiratory symptoms during exercise.

Symptoms

The most common respiratory symptoms during or after exercise include dyspnea (shortness of breath), wheezing, cough, chest pain, and chest tightness.

Dyspnea

Dyspnea is a normal result of exercise. It can be difficult to determine whether the dyspnea is pathologic or due to deconditioning. A careful history and physical examination are important to differentiate if further evaluation of the shortness of breath is warranted. Common causes of dyspnea in athletes include asthma and exercise-induced bronchoconstriction (EIB), which is discussed in detail later in the chapter. Pulmonary function testing may be required to evaluate for asthma or chronic obstructive pulmonary disease (COPD) as well as other lung etiologies. If pulmonary function testing is normal and/or there is suspicion for a cardiac cause, cardiac testing may be indicated. Dyspnea with exercise can also be secondary to gastroesophageal reflux, aspiration of foreign body, infections, anemia, obesity, and metabolic disorders. Rare acute causes include spontaneous pneumothorax and pulmonary embolism.

Wheeze

The pathophysiologic basis of wheezing is turbulent airflow due to airway narrowing. Wheezing is a common symptom associated with asthma and EIB and, as such, should be evaluated for with pulmonary function testing. However, certain conditions such as foreign body aspiration, vocal cord dysfunction, exercise-induced glottis dysfunction, and laryngeal or subglottic stenosis/obstruction can also masquerade as asthma and present with wheezing and stridor. These conditions may occur only in the setting of exercise or be worsened by exercise. Evaluation by laryngoscopy or challenge testing should be performed if these conditions are suspected.

Cough

Cough is a common symptom reported by individuals presenting for evaluation of respiratory symptoms during exercise (1). The clinical history is vital in determining the nature of the cough, including the duration of cough (acute or chronic), associated sputum production, or symptoms of other disorders. Conditions such as allergic rhinitis, sinusitis, postnasal drip, and gastroesophageal reflux can commonly present as a cough, which may worsen with physical activity. Infection or a postinfectious cough must also be ruled out. In addition, medications such as angiotensin converting enzyme (ACE) inhibitors are also associated with a chronic cough. Lastly, asthma may present with a variant that may only manifest with a cough.

Chest Pain or Chest Tightness

Chest pain or chest tightness is commonly associated with cardiac conditions. These symptoms may not be considered when evaluating for asthma or exercise-induced bronchoconstriction. However, they can be common presenting symptoms of asthma. Immediate investigation and evaluation of cardiac etiologies is vital to exclude a life-threatening etiology of symptoms.

ASTHMA

Asthma is a chronic disorder characterized by inflammation of the airways. This inflammation can result in mucus hypersecretion and bronchial smooth muscle constriction with subsequent airflow obstruction, which is variable and often reversible. This obstruction results in many of the previously described symptoms, such as dyspnea, wheezing, cough, and/or chest tightness. Asthma is a heterogeneous disorder that varies on the basis of age of onset, severity of disease, triggers or stimuli, and response to treatment.

Epidemiology

Asthma is increasing in prevalence both in the United States and worldwide, particularly in industrialized countries. According to the Centers for Disease Control and Prevention (CDC), in 2010 there were 17.2 million (8.7%) adults with asthma and 4.6 million (8.5%) children with asthma in the United States and Puerto Rico. Current asthma prevalence is highest among adults aged 18 to 24, adult females, and multirace and black adults. Asthma prevalence is higher among females (10.7%) compared with males (6.5%) (2). There is significant morbidity and mortality associated with asthma, with approximately 500,000 hospitalizations annually due to asthma and nearly 5,000 deaths per year with asthma reported to be the underlying etiology of death (3). Females have a higher asthma death rate (11.6 per million) compared with males (8.8 per million) (4). Thus, the burden of disease in asthma remains high, especially for women.

Risk Factors

Genetic Predisposition

There is a strong relationship between family history and development of atopic disease, such as asthma, allergic rhinitis, and/or atopic dermatitis. Studies of gene linkage, twin cohorts, and familial aggregation have confirmed this association. While asthma exhibits a complex inheritance pattern, in the United States, if one parent has allergic asthma the child has approximately a 20% chance of developing asthma. If both parents have allergic asthma this increases to an approximately 40% chance (5). There have been multiple genetic linkages associated with asthma, and this is an ongoing area of research.

Environment

Environmental factors affect the development of asthma as well as trigger asthma exacerbations in individuals with preexisting disease. A causal relationship has been established between exposures to house dust mites, cockroaches, tobacco smoke (prenatal exposure and environmental exposure after birth), and respiratory syncytial virus and the subsequent development of asthma in susceptible children (6). Multiple environmental factors exacerbate asthma and should be identified in an individual with asthma and mitigated. The formation of immunoglobulin E (IgE) antibody (sensitization) to environmental allergens typically starts occurring around ages 2 to 3. Indoor allergens, especially cockroach, cat, and dust mite, commonly exacerbate asthma in sensitized individuals.

Other Common Contributors to Asthma

Chronic asthma can also be exacerbated by multiple nonallergic triggers. These include irritants, pollutants, medications, and worsening of comorbid conditions such as chronic rhinosinusitis, tobacco use, obstructive sleep apnea, and gastroesophageal reflux. These must be evaluated for in all patients with asthma. Common triggers of asthma are further discussed in the next section.

Pathophysiology

Airway inflammation is a hallmark feature of asthma and leads to airway obstruction, reactivity, and remodeling. The specific pattern of inflammation varies depending on the chronicity and severity of the disease, which can affect responsiveness to therapy. Many inflammatory cells contribute to infiltration of the airways including eosinophils, mast cells, macrophages, T lymphocytes, and neutrophils. Inflammation can also affect airway epithelial cells and adhesion proteins. The airway inflammation results in bronchial hyperresponsiveness and respiratory symptoms, especially with exposure to stimuli. These triggers can include cigarette smoke, upper respiratory infections, chronic rhinosinusitis, allergens, irritants or pollutants, exercise, medications, and/or underlying medical conditions such as allergic rhinitis, obstructive sleep apnea, or gastroesophageal reflux. For example, in a sensitized individual, antigen (allergen) exposure will activate mast cells and recruitment of additional inflammatory cells into the airways. The antigen binding with the specific IgE antibody to the allergen leads to mast cell degranulation and release of histamine, prostaglandins, leukotrienes, and cytokines into the airways. These mediators result in bronchoconstriction, mucus secretion, and mucosal edema. Over time, there is hypertrophy of the smooth muscle of the airways and thickening of the lamina reticularis below the basement membrane.

Clinical Presentation and Differential Diagnosis

Asthma, being a heterogeneous disorder, presents in a variety of ways. In children, it may present as a chronic cough. In some patients, it may appear to be isolated, occurring during exercise, allergen exposure, or upper respiratory tract infection. However, typically the characteristic symptoms of asthma are repeated episodes of wheezing, cough, dyspnea, or chest tightness. The onset of asthma typically occurs in childhood and is strongly associated with atopic dermatitis and allergic rhinitis. However, asthma inception can also occur in adulthood and may or may not be associated with allergic disease. The differential diagnosis of asthma is broad (Table 19.1); however, these entities must be considered in all patients, especially those who do not respond to standard treatment for asthma.

Diagnosis and Testing

Pulmonary function testing is used to detect airway flow obstruction on expiration and bronchial hyperresponsiveness. Spirometry measures the maximal volume of air exhaled from the point of maximal inhalation (forced vital capacity, FVC) and the volume of air exhaled during the first second (forced expiratory volume, FEV_1). Obstruction is indicated by decreased FEV_1 and decreased FEV_1/FVC ratio when compared to matched controls. This airway obstruction leads to a classic scooped or concave appearance of the expiratory flow volume loop (Figure 19.1). This concave pattern is due to the dynamic collapse of the airways.

TABLE 19.1: Differential Diagnosis of Asthma

Adults	Children
Vocal cord dysfunction	Foreign body
Laryngeal or subglottic stenosis	Tracheomalacia
Laryngotracheomalacia	Tracheoesophageal fistula/web
Foreign body	Vascular rings
Tumors	Vocal cord dysfunction
Chronic obstructive pulmonary disease	Bronchiolitis
Immunodeficiency	Cystic fibrosis
Cystic fibrosis	Bronchiectasis
Bronchiectasis	Bronchopulmonary dysplasia
Cardiac disorders	

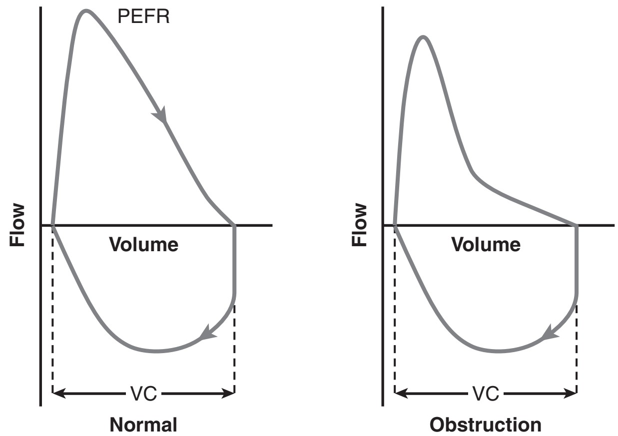

FIGURE 19.1: Flow volume loops.
VC, vital capacity.

Once obstruction is noted on spirometry, reversibility with bronchodilators such as the beta-adrenergic agonist albuterol is assessed. An improvement in FEV_1 of at least 12%, with also at least a 200 mL increase in volume after administration of a bronchodilator, suggests bronchial hyperreactivity. If this correlates with a suggestive clinical history, the diagnosis of asthma can be made.

Methacholine bronchoprovocation testing can also be performed to measure the degree of airway hyperresponsiveness. This is typically only performed if the patient has normal baseline spirometry and the diagnosis of asthma remains in question. Methacholine is a cholinergic agonist that acts on airway smooth muscle muscarinic receptors to produce bronchoconstriction. There are different protocols for these challenges, but positive results are often presented as the concentration of methacholine that results in a 20% decrease in FEV_1.

Classification of Asthma

While asthma is a disease of various phenotypes, classically it has been divided into two subtypes: allergic asthma and nonallergic asthma, with aspirin-induced asthma (aspirin exacerbated respiratory disease or AERD) representing a smaller subset of asthma patients. The National Asthma Education and Prevention Program *Expert Panel Report 3* guidelines classify patients with asthma on the basis of their symptoms and spirometry before treatment has been initiated. Asthma severity is defined by current impairment and future risk. The classification of asthma severity may change with time. The current classification of asthma in individuals 12 years of age or older is detailed in Table 19.2 (7).

Management

Asthma treatment is complex, however; the overall goal is symptom control. Patient education remains a vital component of management. Education should focus on recognizing symptoms and triggers of asthma, emphasizing the rationale for use of medications and the importance of adherence to therapy. The health care provider should review inhaler technique, environmental modifications of potential triggers, and knowledge of appropriate response to asthma symptoms and when to call a physician or seek further care (8).

Medications for asthma are typically divided into two categories: quick-relief medications (also known as rescue medications), which are used on an as-needed basis, and maintenance medications (also known as controller medications) that are used daily. A stepwise approach for management of asthma in patients 12 years or older is detailed in Figure 19.2) (7).

SPECIAL CONSIDERATIONS IN WOMEN WITH ASTHMA

Epidemiology

Asthma is an especially relevant and important disease for women. There are sex-related differences in asthma epidemiology. According to the CDC, current asthma prevalence is higher among females (10.7%) compared with males (6.5%) (2). There appears to be an early childhood sex bias in asthma in which prepubertal males are more frequently affected than females (3). However, women experience a peak occurrence of allergic disease, including asthma, in the second decade of life resulting in a higher overall prevalence of asthma in adult females than males (2).

TABLE 19.2: Classification of Asthma Severity

Components of Severity		Classification of Severity (Youths Aged ≥ 12 Yr and Adults)			
		Intermittent	Persistent Mild	Persistent Moderate	Persistent Severe
Impairment	Symptoms	≤2 days/wk	>2 days/wk, but not daily	Daily	Throughout the day
Normal FEV_1/FVC: 8–19 yr: 85% 20–39 yr: 80% 40–59 yr: 75% 60–80 yr: 70%	Nighttime awakenings	≤2x/mo	3–4x/mo	>1x/wk, but not nightly	Often 7x/wk
	Short-acting $beta_2$-agonist for symptom control (not prevention of EIB)	≤2 days/wk	>2 days/wk, but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation
	Lung function	• Normal FEV_1 between exacerbations • FEV >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1 yr	≥2/yr		
		Consider severity and interval since last exacerbation; frequency and severity may fluctuate over time in any severity category			
		Relative annual risk of exacerbations may be related to FEV_1			

EIB, exercise-induced bronchoconstriction; FEV_1, forced expiratory volume; FVC, forced vital capacity.

Source: Adapted from Ref. (7). National Asthma Education and Prevention Program. *Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma*. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health; 2007.

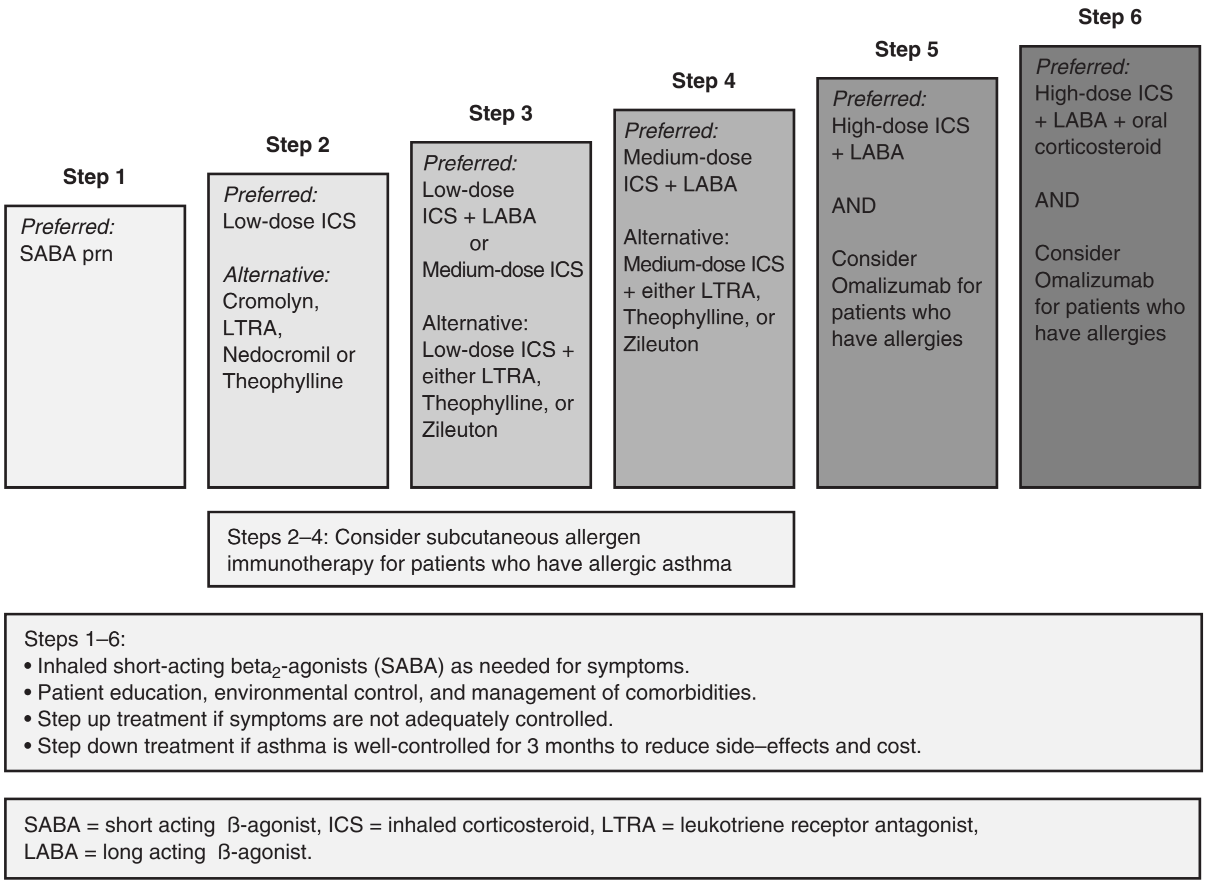

FIGURE 19.2: Stepwise approach for managing asthma in patients 12 years or older.

ICS, inhaled corticosteroid; LABA, long acting β-agonist; LTRA, leukotriene receptor antagonist; SABA, short acting β-aganist.

Source: Adapted from Ref. (7). National Asthma Education and Prevention Program. *Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma*. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health; 2007.

In general, the lifetime likelihood of developing asthma is about 10.5% greater in women than men (3).

Hormonal Effects

Worsening of asthma symptoms has been associated with fluctuations in the menstrual cycle and hormone levels, and 20% to 40% of women with asthma report perimenstrual exacerbation of asthma. This perimenstrual worsening is seen most commonly in women who experience a longer menstruation and more premenstrual symptoms (4,9,10). Women with a perimenstrual component to their symptoms tend to have a greater asthma severity and greater health care utilization when compared to other asthmatics. In addition, perimenstrual worsening of asthma seems to be associated with an increase in peripheral eosinophilia, increase in mast cell tryptase in the endometrium, and lower progesterone levels in the luteal phase when compared to women without asthma (4). On pulmonary function testing, there are changes in airflow and diffusion capacity in women with asthma throughout their menstrual cycle (11). Thus, there may be an increased inflammatory response in asthma that correlates with changes in sex hormones.

In the postmenopause phase, there appears to be a generalized decrease in asthma symptoms and IgE level (12). After menopause, the difference in asthma prevalence between men and women lessens. However, patients who have been on hormone replacement therapy for more than 10 years have been shown to have almost twice the incidence of asthma than women who have not been on this therapy (13,14). These hormonal variations illustrate the importance of discussing changes in reproductive health in women with asthma as it may impact their disease progression.

Pregnancy

The prevalence of asthma in pregnancy is approximately 7% (5), making it one of the most common illnesses to complicate pregnancy (15). During pregnancy, approximately one third of patients with asthma experience an improvement in symptoms, one third experience a worsening of symptoms, and one third of patients symptomatically remain the same (16). Worsening of symptoms in pregnancy tends to occur during weeks 17 and 36 of gestation. The exact mechanism behind asthma in pregnancy is unknown; however, physiologic changes during pregnancy, immunologic response to the fetus, atopic changes, and underuse of medication are all possibilities (17).

Morbidity, Mortality, and Reporting of Symptoms

There are various other sex-related differences in asthma disease expression. Females have a higher asthma death rate (11.6 per million) compared with males (8.8 per million) (3). Hospitalized asthma patients (age 15 and above) are up to three times more likely to be female. These differences do not appear to be related to differences in adherence to controller medications or differences in health care evaluation and treatment (18–20). In addition, it appears African American women require more intensive care unit admissions than men or white women for asthma (19). This suggests an inherent difference between women and men with asthma.

Multiple studies have noted that women are more likely to report asthma symptoms and activity limitation when compared to men, as well as more likely to describe their symptoms as severe (21). Women with asthma report more frequent use of oral corticosteroids, rescue inhalers, and unscheduled physician visits than men (12,21–23). There is ongoing research examining the nature by which women may perceive airflow obstruction differently than men. This can be influenced by reduced inspiratory muscle strength, improper metered-dose inhaler technique, or anxiety surrounding symptoms of dyspnea and perception of airflow obstruction (4).

Bronchial Hyperreactivity

There is a greater prevalence of bronchial hyperreactivity, which can be used to assess asthma (i.e., methacholine challenge testing) in women (24). This may be due to the smaller caliber of the large and small airways in women when compared to men or to an intrinsic difference in sensitivity to stimuli. Women appear to have increased bronchial hyperresponsiveness to tobacco smoke. During childhood, girls with tobacco exposure have a greater decrease in FEV_1 growth when compared to boys. As adults, women who use tobacco have a greater reduction in their FEV_1 when compared to men with similar tobacco use (25,26).

Treatment

The medical management of asthma between men and women is similar. However, in analysis of the difference between men and women in adherence to asthma guidelines, women are more likely to have a written asthma action plan, use their peak flow meters, and have regularly scheduled outpatient visits for asthma. In a study examining the possible effects of sex-specific asthma education, this type of education appears to improve asthma care as well as quality of life (20,23,27).

Obesity

Obesity and its relation to asthma is a topic that is especially salient for females. Cross-sectional epidemiologic studies have shown that obesity is a risk factor for asthma among women but not men (28). There appears to be an increased incidence of asthma-like symptoms in obese or overweight school-aged girls (29). There are over 250,000 new adult cases of asthma each year in the United States in which obesity appears to play a role (28,30). The most consistent reported effect of obesity on lung function is a decrease in functional residual capacity and expiratory reserve volume. These mechanical effects of obesity on the lung may also alter airway smooth muscle contractility and increase airway responsiveness.

While an overall understanding of mechanisms of disease in asthma are vital, knowledge of gender differences in asthma epidemiology and disease manifestation is also important to the management of both men and women with asthma. As can be gathered from our findings, there is a need for ongoing research in this area.

EXERCISE-INDUCED BRONCHOCONSTRICTION

EIB refers to the transient narrowing of the airways during or after exercise (31,32). This occurs in individuals both with and without asthma. Airway hyperresponsiveness is seen more commonly in endurance athletes, especially swimmers and winter sports athletes, than in the general population (33).

Epidemiology

EIB occurs in approximately 80% to 90% of individuals with asthma. The prevalence of EIB has been increasing in elite athletes, most recently estimated to be at least 30% (34). In elite athletes, EIB occurs more frequently in the absence of asthma. These individuals typically have normal pulmonary function testing at baseline and a variable response to inhaled corticosteroids.

Pathophysiology

The exact mechanism of the bronchoconstriction in EIB is not completely understood. During exercise, the large airways provide humidity to condition the inspired air. The increase in minute ventilation results in loss of respiratory water and heat. Thus, the airway dehydration and airway cooling during exercise and subsequent rewarming after exercise are proposed mechanisms (35). Furthermore, the change in osmolarity of the airways triggers an increase in inflammatory mediators including histamine, eicosanoids such as cysteinyl leukotrienes (cystLT), and prostaglandin D2 (PGD2) from inflammatory cells, leading to airway smooth muscle contraction and edema (35,36). In elite athletes, high-intensity training and an increase in minute ventilation can lead to a type of "overuse syndrome" that results in injury to the airway. This is especially seen in swimmers training in chlorinated pools and winter sports athletes who are exposed to cold and dry air. The airway damage, inflammation, and remodeling can mirror that seen in individuals with asthma (37,38).

Clinical Presentation and Differential Diagnosis

The primary symptoms of EIB include cough, wheezing, dyspnea, chest pain, and/or chest tightness during or immediately following exercise. The symptoms typically clear within an hour of exercise completion. There is a refractory period of up to 3 hours after the initial exercise in which, if exercise is resumed, there is little or no bronchoconstriction (5). However, respiratory symptoms alone do not correlate well with airway obstruction during exercise and have a poor predictive value for diagnosing EIB (1,39).

The differential diagnosis of EIB is similar to that of asthma. In addition, evaluation for exercise-specific conditions such as exercise-induced glottic dysfunction, supraglottic laryngeal obstruction, and vocal cord dysfunction may be indicated. Shortness of breath and/or stridor that spontaneously resolves after completion of exercise should prompt evaluation for exercise-induced laryngeal obstruction (33). Conditions such as allergic rhinitis, chronic rhinitis, gastroesophageal reflux, and hyperventilation syndrome are also common in athletes and should be considered (40).

Diagnosis

Since history alone does not carry a high positive predictive value for EIB, confirmation of airway obstruction during exercise is imperative. It is important to remember that in elite athletes expiratory flows can far exceed those of the predicted values and should be accounted for in determining the degree of obstruction (33).

Tests to evaluate for EIB include direct and indirect challenge tests. Direct challenge tests involve pharmacologic agents, usually methacholine or histamine, which act directly on the airway smooth muscle receptors and trigger bronchoconstriction at varying concentrations. These tests have a high sensitivity to detect bronchial hyperreactivity but a low specificity. Indirect challenge tests include eucapnic voluntary hyperpnea (EVH) (which is recommended for athletes), hyperosmolar tests with saline or mannitol, and laboratory or field exercise challenge tests (39,41).

The exercise challenge is specific but not very sensitive, especially in subjects without asthma. Subjects exercise on a treadmill or ergometric cycle for a period from 4 to 8 minutes with an intensity to raise ventilation to 50% of the predicted maximum voluntary ventilation. A fall in FEV_1 of at least 10% is criterion for a positive test. In elite athletes the maximum ventilation is often unable to be reached (31,42,43). In addition, false negatives can occur when the conditions where the testing occurs do not mimic the conditions in which the subject normally exercises. Conditions such as temperature, humidity, air pollution, and environmental allergens can affect these results. In these situations a field exercise test may be required.

EVH is the preferred method for evaluation of EIB in athletes. This requires the voluntary hyperventilation of dry air containing approximately 5% of carbon dioxide. There are established protocols used to elicit bronchoconstriction at differing ventilation rates and times. A fall in FEV_1 of at least 10% at two or more time points is criterion for a positive test.

The hyperosmolar (hypertonic) saline challenge involves administration of increasing doses of inhaled 4.5% saline to increase the osmolarity of the airways. Inhalation of hyperosmolar saline leads to an increase in inflammatory mediators and airway narrowing in susceptible individuals. A fall in FEV_1 of 15% or more after challenge is criterion for a positive test. The mannitol challenge is similar to this. Mannitol is a hyperosmolar agent in a dry powder formulation. It induces smooth muscle contraction by releasing mediators from airway cells. Graduated doses are administrated in doubling doses until a fall in FEV_1 of 15% is noted or a maximum dose of 635 mg of inhaled mannitol is reached.

Management

Management of EIB involves both pharmacologic and nonpharmacologic measures. In patients with coexisting asthma, optimal control of the underlying asthma is essential. Treatment for other exacerbating or comorbid conditions such as gastroesophageal reflux, rhinitis, and exercise-induced laryngeal obstruction should be initiated. Use of facial masks may be beneficial in reducing cold air, pollutants, or allergen exposure, but they are not always tolerated (44). A pre-exercise warm-up can be helpful in reducing subsequent bronchoconstriction (45,46). This is likely due to the refractory period that occurs after exercise in which, after the initial release of inflammatory mediators, airways are less likely to constrict (5).

Pharmacologic therapies to treat EIB depend on the presence or absence of underlying chronic obstructive asthma. In patients with EIB and asthma, the recommendations for therapy follow the guidelines previously discussed in the section on asthma. In individuals with EIB and especially in athletes, a short-acting $beta_2$-agonist should be prescribed for on-demand use. Inhaled short-acting $beta_2$-agonists can be used 15 to 30 minutes prior to exercise for prevention of symptoms and after exercise if symptoms occur. $Beta_2$-agonists work to induce bronchodilation and attenuate the release of inflammatory mediators. However, daily use of a $beta_2$-agonist (or even use greater than two to three times a week) can lead to tolerance and ineffectiveness of the medication (34). In these instances, a controller medication may need to be added. Inhaled corticosteroids are a preferred method of asthma therapy in athletes (and in nonathletes) and are accepted by sports officials (47,48). Inhaled corticosteroids reduce airway inflammation and bronchial hyperreactivity. These medications cannot be used for prophylaxis and should be taken as maintenance therapy. If this does not achieve control, a combination of inhaled corticosteroid and long-acting inhaled $beta_2$-agonist may be initiated (34). Leukotriene modifiers given orally prior to exercise are beneficial in combating the inflammatory effects of leukotrienes during exercise, which lead to mucus production and airway edema (39). Theophylline is not recommended for prophylactic use in EIB and is reserved for individuals with severe chronic asthma not controlled by first-line therapies.

SEX DIFFERENCES IN RESPIRATORY MECHANICS DURING EXERCISE

There are intrinsic differences between men and women that affect respiratory mechanics during exercise. These variations in pulmonary function and other elements of respiratory mechanics are important to consider, especially in the evaluation of the female athlete.

Pulmonary Function

Optimal respiratory function during exercise requires adequate expiratory and inspiratory airflow. During exercise there is an expiratory flow limitation that leads to increased end expiratory lung volumes and increased expiratory flow rates. As a result there is increased elastic work of breathing (WOB) due to decreased lung compliance as the lung volumes increase. This can lead to fatigability and increased respiratory symptoms with exercise. In a study by Guenette et al., the degree of expiratory flow limitation was measured in endurance-trained men and women during cycle exercise. At maximal exercise, endurance-trained female subjects experienced expiratory flow limitation more frequently than endurance-trained male subjects. End expiratory lung volume (EELV), which is the volume of air remaining in the lung at the end of spontaneous expiration, was also assessed. With the onset of exercise, EELV decreased in both men and women when compared to resting measurements. In men, this measure tended to remain decreased, while in women EELV increased at 89% and 100% of maximal exercise. This translates into a significantly higher mechanical WOB in women than men during progressive exercise (49).

This increase in WOB in endurance-trained females does seem to impact perceived respiratory symptoms during exercise. WOB can be divided into resistive WOB and elastic WOB. Elastic WOB is further divided into the WOB required for muscles to overcome the elasticity of the lung during inspiration and the WOB required for expiratory muscles to overcome the elastic outward recoil of the chest wall during expiration. Resistive WOB can be further divided into the airflow resistance during inspiration and airflow resistance during expiration. A follow-up study by

Guenette et al. examined these four individual components in order to determine which is responsible for the higher total WOB in women during exercise. They determined that the total WOB is higher in women due to a substantially higher resistive WOB, which is inversely proportional to the size of the lungs and airways. No difference in the elastic WOB was found between women and men during exercise (50).

In addition to this increase in WOB, female long-distance runners display a higher oxygen uptake and higher lactate levels, implying a higher physiological strain for females as compared to males (51).

Another notable measure in exercise is maximal breath hold time, which affects many recreational and athletic activities (e.g., swimming and diving). Females on average weigh less, have lower FVC and FEV_1, and have lower hemoglobin and hematocrit levels compared to their male counterparts, which would lead one to assume a physiologic difference in maximal breath hold times between men and women. Despite these anthropometric and physiologic differences, female and male subjects appear to have similar maximal breath hold times (52).

Fatigability of Inspiratory Muscles

As described already, females tend to have more frequent expiratory flow limitation, higher end expiratory lung volumes, and higher total and resistive WOB compared to their male counterparts. The function of the diaphragmatic and respiratory muscles during exercise is also a vital component to optimal respiratory function. However, studies have shown men in fact experience diaphragmatic fatigue more frequently than women. Fatigue was not only more frequent, but also more severe among men (53). In addition, females demonstrate a slower rate of inspiratory muscle fatigue than males. There is no significant difference in the time to recovery between females and males (54).

CONCLUSION

Knowledge of sex-related differences in sports pulmonology (summarized in the following table) is critical to the evaluation and management of both males and females with respiratory symptoms during exercise. There are differences in the prevalence and expression of chronic respiratory conditions, such as asthma, between sexes. In addition, there are intrinsic differences between males and females in respiratory mechanics and pulmonary function that can affect performance during exercise, especially in endurance sports. Evaluation and management of individuals with respiratory symptoms during exercise should follow current guidelines, when available. However, awareness of the specific aspects of these respiratory symptoms that are unique to each sex is crucial in formulating a complete treatment plan.

Summary of Sex Differences in Sports Pulmonology

Sport Pulmonology Topics	Sex Differences
Asthma	• Prepubertal males more frequently affected than females (3) • Higher overall presence of asthma in adult females (2) • Lifetime likelihood of developing asthma 10.5% greater in women than men (3) • Females have a higher asthma death rate compared with males (4) • Hospitalized asthma patients age 15 and older are more likely to be female (18–20) • Women with asthma report more frequent use of oral corticosteroids, rescue inhalers, and unscheduled physician visits than men (12,21–23) • Obesity is a risk factor for asthma among women, but not men (28)
Hormonal effects on asthma	• 20% to 40% of women report perimenstrual exacerbation of asthma (4,9,10) • Difference in asthma prevalence between sexes lessens after menopause (12)
Asthma in pregnancy	• Most common illness to complicate pregnancy with approximately 7% prevalence (5,15)
Bronchial hyperreactivity	• Greater prevalence in women (24)

(*continued*)

Summary of Sex Differences in Sports Pulmonology (*continued*)

Sport Pulmonology Topics	Sex Differences
Tobacco exposure	• Women have increased bronchial hyperresponsiveness to tobacco smoke (25,26) • Tobacco use in adult women results in greater reduction in FEV_1 than in matched men (25,26)
Respiratory mechanics during exercise	• More frequent expiratory flow limitation in endurance-trained females when compared to men (49) • Exercising females have higher end expiratory lung volumes resulting in higher mechanical work of breathing than men (49) • Females also have higher resistive work of breathing due to smaller lungs and airways (50)
Breath hold times	• Similar maximal breath hold times between men and women, despite women on average having a lower weight, lower FVC and FEV_1, and lower hemoglobin levels (52)
Fatigability of inspiratory muscles	• Men experience more frequent and more severe diaphragmatic fatigue than females (53)
Time to recovery from inspiratory muscle fatigue	• No difference between men and women (54)

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SPORTS NUTRITION

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INTRODUCTION

Dietary behaviors are a crucial component of athletic training and competition. Consuming an optimal balance of energy, macronutrients, micronutrients, fluid, and electrolytes helps maximize athletic performance. However, among athletes, dietary requirements depend on factors such as the frequency, intensity, time, and type of physical activity. In addition to maximizing athletic performance, meeting dietary requirements is essential to minimize the risk of injury and promote repair—before, during, and after exercise. Substantial differences exist between female and male athletes and should be considered when encouraging athletes to meet dietary recommendations. Nutrition requirements for female and male athletes are not the same. Biological, social, and environmental factors influence sex differences in food intake, metabolism, and nutrient bioavailability. Therefore, the purpose of this chapter is to provide evidence-based nutrition recommendations for female and male athletes through a comprehensive overview of the role and recommendations for total energy requirements, carbohydrate, protein, fat, vitamins, minerals, and water.

- Females report greater nutrition-related awareness and knowledge when compared to males (1).
- Females report consuming more fruits, vegetables, whole grains, and dairy products than males (1).
- Female athletes are more likely to restrict energy intake, especially when competing in sports that accentuate body shape and size (2).
- Resting metabolic rate (RMR) is lower in females than males (3).
- There are sex differences in substrate utilization during exercise such that females oxidize more lipids and fewer carbohydrates (4–9).
- Skeletal muscle glycogen utilization and hepatic glucose production is lower in females than males during moderate and intense endurance exercise (10).
- Reported food intake for women is lowest during the periovulatory period of the menstrual cycle when plasma estradiol levels are high (11).
- Phillips et al. demonstrated females exhibit lower oxidation of leucine, a branched chain amino acid correlated to protein synthesis, during exercise compared to males (12,13).
- Overall protein requirements are lower for female than male athletes, 1.3 to 1.4 grams per kilogram of body mass per day (abbreviated as g/kg/d) and 1.7 g/kg/d, respectively (14).

SEX DIFFERENCES IN EATING BEHAVIOR

Males and females differ in their eating attitudes, dietary habits, and food choices as a result of biological and sociocultural factors. The most commonly reported difference between males and females is total energy intake. On average, males consume more energy than females due to their higher mean body mass, energy expenditure, and energy needs (11). In athletes, females are less likely to meet daily caloric requirements (15). Research suggests that males eat faster and take bigger bites of food and sips of beverages when compared to females. Furthermore, when food volume consumption is the same, males ingest more calories than females, suggesting that males consume more energy-dense food items (15). Similarly, male athletes eat more meals per day than females. Among endurance athletes, males report consuming as many as nine meals per day; however, because of the heightened energy needs from physical activity, male athletes can fall short of their total daily energy needs (16).

Females are at a greater risk of inadequate energy consumption. Several studies have reported suboptimal energy intakes for female athletes across a variety of sports (2,17–19). Even when comparing female and male athletes in the same sport, females report dietary intakes characterized by insufficient energy and macronutrient (20). Hoogenboom et al. evaluated the nutrient intakes of female collegiate swimmers and reported only 9.4% of female swimmers consumed 100% of their calculated energy needs (21). Inadequate calorie intake in female athletes is often coupled with inadequate calcium intakes. Low calcium consumption presents the risk of compromised bone health, low bone density, and osteoporosis later in life (18,22).

Regarding food choices, women report consuming more fruits and vegetables, cereals, and whole grains; males report consuming greater amounts of meat products (including nonlean meats such as pork, beef, and sausage), eggs, alcohol, high-sucrose foods, and high-starch foods. Consequently, females eat more fiber and nutrient-dense foods, and males eat more saturated fat and cholesterol (1,23). Both female and male athletes report insufficient carbohydrate consumption, excessive fat consumption, and sufficient or excess protein intakes. This often varies by type of activity or sport. For example, football and baseball players have reported higher fat intakes when compared to triathletes and marathon runners, whose total energy is primarily comprised of carbohydrates but is still too low to accommodate their high carbohydrate utilization (24).

Eating behaviors among female athletes can be largely explained by sociocultural influences. While female athletes report healthier food choices, eating disorders and disordered eating are also more commonly reported and have no clear biological basis (19,21). In fact, the sports recording the highest rates of eating disorders are lean (cross-country, swimming) and aesthetic (diving, gymnastics) sports (18,19). In a study comparing body image and performance goals between the sexes, males' valued speed, power, and size while females esteemed low body fat above all else. The female athletes viewed leanness as a competitive advantage that could enhance performance and were more inclined to practice restrained eating, even if it meant falling well below their energy and macronutrient recommended dietary allowance (RDA) ranges (2). A similar study surveying males reported an average goal body weight that was 104% of their current weight. The researchers also reported that weight gain, as long as it was in the form of more muscle mass, was revered among 87% of the male athletes (25). Dieting, restricted eating, consuming fewer meals per day, and suffering from eating disorders may manifest from female athletes' exposure to body image ideals, pressures to be thin, and media promotion of weight-restricting behaviors (21).

ENERGY

For athletes, adequate energy intake is the balance of energy expended and energy consumed to optimize athletic performance. Total daily energy expenditure is represented by four subcomponents: basal metabolic rate, thermic effect of food, nonenergy activity thermogenesis, and exercise energy thermogenesis. The terms kilocalorie (kcal) and calorie are often used interchangeably when describing energy derived from foods sources. The kilocalorie represents the amount of heat needed to raise 1 kilogram of water 1° Celsius. Calories consumed from foods and fluids provide the energy to maintain weight, replenish glycogen stores, and repair damaged tissue. Daily caloric needs depend on the frequency, intensity, time, and type of physical activity. Energy needs fluctuate in response to the duration and intensity of the physical activity, as well as the environmental conditions during training. Determining individualized energy requirements is a crucial component of the diet prescription. Inadequate energy intake can be detrimental to performance; it is associated with loss of muscle mass or inadequate promotion of muscle mass, is detrimental to bone density, and increases the risk of early fatigue, which can translate to increased risk for injury. In addition, inadequate energy intake among female athletes increases their risk for menstrual and endocrine dysfunction.

Energy Expenditure

For nonathletes, RMR is the largest component of total daily expenditure, representing nearly 75% of individuals energy needs over a 24-hour period. RMR accounts for the energy required to maintain the body's cellular processes for life, such as heartbeat and respiration, while in an awake and postabsorbtive state. Basal Metabolic Rate (BMR) is often used interchangeably with RMR. Age, sex, body weight, hormones, and body composition influence an individual's RMR. The RMR for adult females is approximately 10% to 15% lower than males due to a higher proportion of fat to muscle mass. Another difference between healthy weight females and males is the average decline in RMR per decade between the ages of 20 and 96 years, by 2% and 2.9%, respectively (3). The decrease in metabolic rate accelerates around the age of 40 years in males and 50 years in females (26,27). The loss of fat-free mass associated with menopause may explain the later and more accelerated decline in metabolic rate for females (26,27). Using 2,400 calories as the recommended energy requirement for the average healthy female or male, a 2% to 2.9% decline in energy requirements per decade would translate to a 48 to 72 daily calorie restriction. Though 48 to 72 calories seems trivial, the clinical significance is the compounding effects of the metabolic decline. A daily 50-calorie surplus in energy intake per day may result in a 5-pound weight gain each year. However, maintaining metabolically active muscle mass can hinder the decline in metabolism and is more frequently the case in athletes of both sexes. The thermic effect of food represents approximately 25% of total daily energy expenditure and is used to express the energy expended for digestion.

Physical activity, categorized as nonexercise activity thermogenesis and exercise energy expenditure, poses the greatest fluctuation when determining total daily energy expenditure. Energy requirements used for nonexercise-related activities of daily living vary depending on an individual's lifestyle. Active individuals would expend more energy a day simply by sitting less and walking more than someone who is sedentary, thereby increasing their nonexercise activity thermogenesis. For athletes, exercise energy expenditure may result in an energy requirement greater than RMR, based on frequency, intensity, duration, and type. Exercise energy expenditure on any given day may range from zero calories for a nonexerciser up to several thousand calories for an athlete during training or competition.

Determining Energy Requirements

Several methods are used to determine energy needs. These methods include using stable isotopes (i.e., doubly labeled) or indirect calorimetry (i.e., whole room calorimeter or metabolic cart). The measurement of energy expenditure is costly, requiring expensive equipment and skilled staff. Therefore, several prediction equations have been developed to estimate RMR. Most of the predictive equations used to estimate energy needs incorporate height, sex, weight, and age as variables. Fat-free mass is included in the Cunningham equation, thus providing a more accurate estimation for athletes' needs, though adding a barrier to its use in common practice since measuring body fat is required (28,29). The Harris-Benedict and Cunningham equations are the most commonly used in sports nutrition to estimate the RMR of athletes. Of the two, the Harris-Benedict equation is typically used to estimate BMR, then multiplied by an activity or injury factor to determine total daily energy expenditure (29).

Harris-Benedict Equation

Adult Male: $BMR = 66.473 + (13.7516 \times \text{weight in kg}) + (5.0033 \times \text{height in cm}) - (6.7550 \times \text{age in years})$ (29)

Adult Female: $BMR = 655.0955 + (9.5634 \times \text{weight in kg}) + (1.8496 \times \text{height in cm}) - (4.6756 \times \text{age in years})$ (29)

Activity Factors

1.2	Little to no exercise
1.37	Light exercise
1.55	Moderate exercise
1.725	Heavy exercise
1.9	Very heavy exercise

CARBOHYDRATES

Carbohydrates are one of the three macronutrients and a primary source of energy for the body and brain. In humans, carbohydrates are stored in the muscle and liver as glycogen, as well as a small amount of circulating blood glucose. Consumption of carbohydrates helps to maintain these stores, providing quick and accessible energy for everyday tasks. Carbohydrates are ultimately catabolized into glucose, the preferred source of energy for the brain, muscles, and central nervous system. Compared to nonathletes, athletes require more carbohydrates due to increased energy needs and utilization. Adequate carbohydrate consumption ensures optimal energy metabolism, immediate fuel during training and competition, and rapid post-workout muscle recovery. However, both male and female athletes consistently fall short of the recommended guidelines for carbohydrate intake (19,21,30). Between 45% and 65% of total calories should come from carbohydrates to prevent fatigue, increase muscle glycogen storage capacity, and optimize athletic performance.

Carbohydrates are comprised of multiple subcategories: monosaccharides, oligosaccharides, and polysaccharides. Monosaccharides and disaccharides are commonly referred to as simple carbohydrates. Monosaccharides (glucose, fructose, and galactose) are distinctively sweet compared to other carbohydrates. Disaccharides include lactose, maltose, and sucrose and consist of two monosaccharides. Oligosaccharides and polysaccharides are larger, complex carbohydrates that consist of three or more monosaccharides. Oligosaccharides and polysaccharides are commonly referred to as complex carbohydrates and include starch (amylose and amylopectin), glycogen (glucose storage in humans), and fiber. The difference between starch and fiber resides in their glucose linkages. In starch, monosaccharides are joined by alpha-linkages that are easily cleaved during the digestive process. However, monosaccharides in fiber are joined by strong beta glucose linkages and require specific enzymes or bacteria for digestion, which humans lack. Nondigestible fiber, such as cellulose, is associated with a number of health benefits, including the maintenance of bowel regularity, and should hold a secure portion of a healthy balanced diet (31–35).

Carbohydrate Metabolism During Exercise

The primary function of carbohydrates is to produce energy in the form of adenosine triphosphate (ATP) (36). ATP fuels endergonic cellular reactions that affect mechanical energy for muscle movement. It is also an important coenzyme required for body temperature regulation during exercise. All carbohydrates follow the glycolytic pathway, whereby energy is attained through aerobic and/or anaerobic respiration. The reactions from the oxidation of glucose in the glycolysis pathway and subsequent oxidation of pyruvate result in a total production of 36 ATP molecules (36).

During energy production, glucose is derived from either circulating blood glucose or glucose stored as glycogen. The average adult stores between 300 and 400 grams of glycogen in muscle (37). Males typically possess higher muscle-to-body weight ratios than females that results in a greater glycogen storage capacity, closer to 400 grams (6,9,38). Higher levels of muscle glycogen extend the time and amount of work that an athlete can perform before the body begins converting other substrates (36). Oxidation of alternative substrates can lead to muscle breakdown and adverse by-products such as lactic acid, therefore maintaining optimal glycogen capacity recommended for athletes.

Carbohydrate Loading

Athletes can augment glycogen stores through carbohydrate loading. Trained muscle is able to store more glycogen than untrained muscle (39). Consuming a carbohydrate-rich diet (50% to 75% of total calories) 3 to 4 days consecutively leading up to competition has been shown to increase both muscle glycogen stores per kilogram body weight and improve muscle stamina (9). This phenomenon is of particular interest to endurance athletes. For example, distance runners, who practice carbohydrate loading, may not run faster initially, but are able to sustain a faster pace throughout the duration of their race, resulting in a better overall performance (40–42) (Figure 20.1).

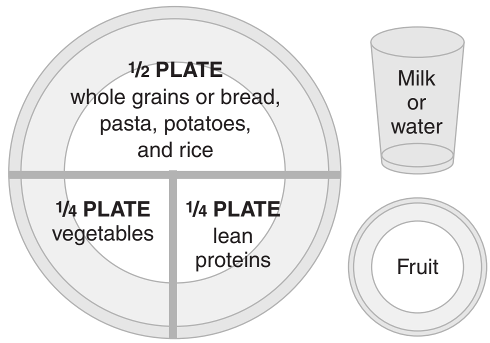

FIGURE 20.1: How to build a training plate. Carbohydrate needs increase when preparing for competition. Use this plate model to add more carbohydrate fuel to maximize glycogen storage.

Sex Differences in Carbohydrate Metabolism and Requirements

Recent research suggests that carbohydrate loading may not be as advantageous for females as compared to males. Among male athletes, carbohydrate loading is associated with better performance outcomes such as increased stamina and maximal oxygen (O_2) consumption (4–6,43–45). Researchers hypothesize that the sex hormones estrogen and progesterone promote glycogen sparing during intense exercise such that fat is more commonly utilized as energy compared to carbohydrates. Similarly, females oxidize fewer carbohydrates during low- and moderate-intensity endurance exercise when compared to males. Estradiol, the most biologically active form of estrogen, is a female steroid hormone produced by the ovaries. Estradiol is involved in menstrual cycle regulation and ovulation and has been linked to energy metabolism. Animal studies have been conducted to investigate the effects of estradiol on glycogen metabolism. In animal studies, administration of estradiol to male rats was associated with increases in lipid availability and utilization during exercise, decreases in glycogen utilization, and increases in work output and exercise duration (46–49).

Female and male athletes use fuel sources differently during exercise that last longer than 90 minutes. Males oxidized more carbohydrates than females, and females metabolized more fat than males. Even when matched in terms of training, females use fewer carbohydrates than males. The higher content of intramuscular fat in women may account for the differences in metabolism. As with glycogen loading, hormonal differences in estradiol levels may also play a role (4,43,46,49–51).

Despite the reported differences in glycogen utilization and loading between females and males, the carbohydrate recommendations for both are determined by calculating total energy needs requirements (9). The minimum carbohydrate requirement for the average adult is 130 grams per day. More specifically, carbohydrates should contribute 50% to 55% of total caloric requirements. Sugar should comprise no more than 25% of those carbohydrates. Due to increased energy demand and output, athletes have slightly higher recommendations. Approximately 45% to 65% of total energy intake should consist of carbohydrates. In terms of dietary fiber, no differences have been established between active and nonactive individuals. Based on total energy needs, males are recommended to consume 38 grams of fiber per day, and females are recommended to consume 25 grams per day (52,53).

Carbohydrate needs can also be estimated using body weight in kilograms and activity level. Regardless of sex, athletes require between 5 and 10 grams of carbohydrates per kilogram of body mass per day (g/kg/d). Endurance athletes usually require between 7 and 10 g/kg/d while individuals engaged in low-intensity training may require no more than 5 g/kg/d (52,54).

FATS

Fat is our most highly concentrated energy source that fuels our bodies through low- and high-intensity work. Unlike carbohydrates and protein, which provide only 4 calories per gram, fat provides 9 calories per gram. Once glycogen stores are depleted, energy production is sustained through the metabolism of fat circulating in plasma and stored in muscle and adipose tissue. Fats are essential for the regulation of numerous bodily functions, including molecular signaling, cellular membrane structure, digestion, insulation, joint lubrication, and vitamin transport. In addition, fat adds flavor and texture to foods and provides sustained satiety after eating. Contrary to the common misconception that dietary fat intake and body fat are inversely associated with athletic performance, athletes need fat. However, some types of fat are more beneficial than others.

Types of Fat

Fats are distinguished as a group of compounds that are soluble in organic solvents of no or low polarity, but are not soluble in water. The nonpolar nature of fat is due to mostly carbon and hydrogen atoms comprising a large portion of the molecule. Typically this nonpolar region is a fatty acid. Lipids are commonly found in foods and the human body as triglycerides, phospholipids, and sterols. Triglycerides are the most common form of fat found in the diet (95%). Animal fat, butter, oil, and margarine are examples of triglycerides that we consume. Fats, such as those derived from animals, are soluble at room temperature whereas most oils, such as vegetable oil, are in the liquid state. Triglycerides are classified by their chain length, level of saturation, and molecular shape. Triglycerides, according to their chain length, are classified as short-chain fatty acids (usually fewer than 6 carbon atoms in length), medium-chain fatty acids (6 to 12 carbon atoms in length), or long-chain fatty acids (14 or more carbon atoms in length). Fatty acid chain length determines the method of digestion and absorption. Short- and medium-chain fatty acids are metabolized more quickly than longer fatty acid chains. The number of carbon-carbon double bonds determines the level of saturation. All carbons are bound to hydrogen such that the chains are saturated with hydrogen. Saturation results in a more stable structure with limited molecular mobility. Unsaturated fats (vegetable oils) have a double bond between carbon atoms, and polyunsaturated fats have several double bonds. Double bonds introduce kinks in the fatty acid chains, which prevent the chains from matching up and solidifying at room temperature. With the assistance of a catalyst, double bonds in unsaturated fats can be hydrogenated to solidify at room temperature. Naturally occurring cis-isomer arrangements are converted to trans-arrangements, resulting in trans saturated fats that behave more like saturated fats. Saturated and trans saturated fats are both associated with higher levels of low density lipoprotein (LDL) or "bad" cholesterol and lower levels of high density lipoprotein (HDL) or "good" cholesterol and should be consumed in moderation (55).

Omega-3 fatty acids have been researched for their potential gains in athletic performance. Several studies looking at omega-3 fatty acid have reported enhanced oxygen transport to the muscles and tissues, improved aerobic metabolism, decreased constriction of bronchial tubes (airways) during exercise, increased production of recovery-related hormones, and reduced inflammation of joints, muscles, and surrounding tissue (56–60). Linoleic acid, also known as omega-6 fatty acid, has a double bond at the sixth carbon on its fatty acid chain. Linolenic acid, or omega-3 fatty acid, has a double bond at the third carbon on its fatty acid chain. The recommended ratio of linoleic to linolenic acid for optimum health is between 1:1 and 5:1 (61).

Fat Metabolism

Contrary to carbohydrates, which can be metabolized both aerobically and anaerobically, fat can only be metabolized under aerobic conditions. During low-intensity exercise, plasma triglycerides are the preferred fuel source. As intensity increases, metabolic preference shifts to carbohydrates. As intensity and duration continue to rise, glycogen stores diminish and intramuscular fat oxidation becomes the primary source of fuel (6,43,62,63).

Protein-bound blood triglycerides and intramuscular triglycerides are metabolized for energy by the same beta-oxidation pathway in the mitochondria. Lipases hydrolyze lipids into component fatty acids and glycerol. Fatty acids are split per carbon pairs and metabolized to acetyl-Coenzyme A (acetyl-CoA) in the cycle. At each two-carbon interval, the abridged chain reenters the beta-oxidation cycle until it has been completely reduced to acetyl-CoA. Carbohydrates play a vital role in this metabolic pathway and are required for the complete oxidation of fats. At the termination of the beta-oxidation cycles, each fatty acid yields 14 molecules of ATP. The additional phosphorylation of glycerol delivers another 2.5 to 4.5 molecules of ATP. It is important to note that glycerol may also be used for other energy needs. For example, glycerol, which is metabolized like a carbohydrate, may be converted to sugar in the liver and used to regulate blood glucose when liver glycogen stores have been exhausted.

At approximately 60% to 65% of the body's maximum oxygen consumption (VO_2 max), fat oxidation is at its highest and most efficient. At a VO_2 max higher than 65%, substantial fat oxidation is still taking place. Endurance training can lead to an increase in the body's capacity to burn fat by increasing the size and quantity of mitochondria (location of beta-oxidation) and the number of metabolic enzymes involved in the pathway (63).

Dietary Fat Recommendations

Similar to dietary carbohydrate recommendations, female and male dietary fat recommendations are based on total energy intake, body weight, and activity level. Differences in fat oxidation are not incorporated into dietary fat recommendations. Research findings are mixed regarding the ideal fat consumption for athletes. Some evidence suggests that appropriate ranges are activity or sport specific. Studies of cyclists and triathletes report total fat intakes between 27% and 32% of total food energy (17,64). Research on female swimmers reports intakes as low as 22% energy from fat (65,66), while other studies report above 40% for female and male swimmers (22,67–69). Proximity to race day may also influence fat intake. Some studies report decreased fat intake leading up to competition, while others showed no change (24,70). Variability also exists among countries. One study reported that Croatian gymnasts consumed an average of 30% total energy from fat (18). Other studies have reported that Kenyan runners consumed only 13% total energy from fat (53,71). On average, fat in the diet should account for 20% to 35% of total calories; athletes may benefit from no more than 25% of total calories from fat (52,53).

Other recommendations based on body weight rather than caloric load suggest 1 gram of fat per kilogram of body weight per day for active individuals and low-intensity sports, and up to 2 grams per kilogram of body weight per day for endurance athletes (52,53). Athletes who have difficulty maintaining weight and/or consuming sufficient calories to meet energy output may require higher intakes of dietary fat. For health benefits, unsaturated fats from fruits, vegetables, nuts, oils, and cold-water fish are preferred to saturated and trans saturated fats from animal products or processed and fried foods. Increased fat utilization is believed to spare glycogen, which can result in stamina gains and increased performance. The "fat loading" theory suggests that the body adapts to the available fuel by burning fat more efficiently. However, when tested in a research setting, fat loading did not result in significant performance improvement and was shown less beneficial than conventional carbohydrate and fat intakes (72,73). Consumption of medium-chain triglycerides is another approach to augmenting performance. Medium-chain triglycerides are catabolized and absorbed more quickly when compared to long-chain fatty acids and are believed to deliver energy as fast as carbohydrates; however, results of research investigating the effects of medium-chain triglyceride consumption on performance are conflicting (74–76).

Glycerol, a three-carbon compound found in triglycerides and phospholipids, has been consistently shown to aid athletes competing in endurance activity performed in high temperatures (76–79). This is because glycerol is a humectant, meaning it can hold water. Consuming glycerol prior to competitions where excessive water loss is a risk allows the body to retain more water. This gives rise to a "hyperhydrated" state. Advantages were observed in studies assessing Olympic triathletes, mountain bikers, and tennis players subjected to hot environments who were hyperhydrated prior to competing (77–79). However, the World Anti-Doping Agency has banned the use of excess glycerol as an athletic aid.

Sex Differences in Fat Metabolism

Females naturally have a higher percentage of total body fat than men. The normal percent body fat range for a nonathlete female in her mid-20s is 25% to 31%, while that of an age-matched, nonathlete male is 18% to 25%. As an individual's fitness increases, percent body fat decreases. The normal body fat range for active females and female athletes is 21% to 24% and 14% to 20%, respectively. The normal body fat range for active males and male athletes is 14% to 17% and 6% to 13%, respectively. Essential body fat, defined as body fat necessary for life and reproduction, is also higher for females to ensure appropriate body composition for childbearing and adequate hormone regulation. For all persons, athletes and nonactive individuals, essential body fat ranges from 10% to 12% in females and 2% to 4% in males (80,81).

Females exhibit unique metabolic responses to ingested and stored fat. Comparisons between equally conditioned males and females during the same endurance activity show proportionately higher fat oxidation rates in females. This may result from higher essential fat requirements and greater levels of intramuscular fat, which would suggest greater availability and accessibility to fat for energy conversion (4–6,43,44). Hormones are also believed to potentially influence this metabolic process. Estrogen's active form, estradiol, is the hormone suspected of influencing fuel utilization. Estradiol has been linked to energy metabolism and greater fat-to-carbohydrate conversion in animal studies (46–49). There are no differences in the recommendations for dietary fat exist between males and females, despite these findings (53).

PROTEIN

Proteins play a fundamental role in athletic performance. They vary in structure and function. Connective tissues, tendons, certain organs, and muscle fibers are made of fibrous proteins. Fibrous proteins are insoluble in water and primarily serve a structural purpose in the body. Globular proteins are also found in animals and transport substances throughout the body. Unlike fibrous proteins, globular proteins are soluble in water. Hemoglobin is an example of a globular protein that serves as a transporter, carrying oxygen from the heart to the tissues. Enzymes are also globular proteins that facilitate metabolic reactions. Enzymes are often referred to as catalysts as they speed up biochemical reactions (82).

The functions of proteins are not limited to structure, transport, and catalysis. Proteins are also involved in movement (muscles), hormone synthesis (insulin), nutrient storage (ferritin), pH balance (amphoteric buffers), fluid and osmolarity homeostasis, immunity (antibodies), and regulation of various cellular responses (rhodopsin). While protein performs a variety of functions in the body, it does not make a significant contribution in energy production; protein contributes only 2% to 4% of total ATP (16,83,84).

Amino Acids

Amino acids are the building blocks of proteins whose order and properties largely determine a protein's chemical behavior. Humans require both essential and nonessential amino acids. Essential amino acids must be consumed through the foods that we eat. Nonessential amino acids can be synthesized in the body.

Higher quality proteins have higher biological value, meaning the body absorbs a greater proportion of the ingested protein. A protein's biological value is determined by the amino acids that it is comprised of; an appropriate combination of amino acids, including all of the essential amino acids, will be better absorbed and incorporated into the body. In deamination and transamination, discussed later in the chapter, proteins lose their nitrogen atoms for storage or through new protein formation. These processes will only occur if the protein cannot be synthesized by the body (nonessential) and is not in high demand. Comparison of a protein food to albumin from egg protein is a way to assess protein quality. Albumin is recognized for its complete distribution of essential amino acids. Egg-matched quality for whey protein is highest at 104/100, 100/100 for a whole egg, and 91/100 for cow's milk. Beef and soy are slightly lower at 80/100 and 74/100 (8,85,86).

Protein Metabolism

Proteins are digested in descending order of structure: first polypeptides, then smaller peptides, and finally the original amino acid building blocks. Amino acids enter a pool for reconstruction into proteins as needed by the body. Hair, skin, nails, muscle, enzymes, and hormones all source from this pool. The liver is the main regulatory station for protein synthesis, maintaining bodily protein requirements through transamination and deamination. Transamination takes place when the nitrogen from one amino acid is cleaved and reused for the synthesis of another amino acid. In situations of protein excess, deamination occurs. Through deamination, amino groups are removed from proteins, leaving behind long skeleton chains of carbon, hydrogen, and oxygen. These carbon-rich structures can be converted to glucose for energy or may be stored as fat to later be metabolized for energy. The residual ammonia enters the urea cycle and is excreted. Excessively high protein intake yields a greater need for urea excretion, which can increase overall water loss. Consequently, athletes on high protein diets who sweat during exercise are at an increased risk for dehydration (8,12).

Muscle Building

Many athletes believe that protein is the sole dietary factor necessary for muscle growth. Strength-building and power-lifting athletes are especially notorious for overconsuming protein (87,88). Furthermore, common sources for their protein surplus includes powders and supplements. The standard amino acid supplement not only costs more than high-protein food alternatives, but also contains less than 15% the amount of high-quality amino acids in a 1-ounce serving of meat (89).

Protein intake only needs to be altered slightly for muscle-building purposes and is no more important than obtaining sufficient levels of other macronutrients for lean muscle mass gains. The daily recommendation per kilogram of lean muscle desired is an increase of only 1.2 to 1.7 grams of protein. Carbohydrate intake must also increase by 5 to 12 grams per kilogram. From a net energy perspective, carbohydrates make up a larger fraction of total energy volume than protein. It is necessary to accompany the increase in calories with an increase in resistance and strength-building exercises so that the added energy is not stored as fat (89,90).

Protein Timing

Consuming protein prior to physical activity and following physical activity in conjunction with carbohydrates have both been associated with enhanced absorption and improved muscle growth and repair. Intermittent extremes in protein intake have been linked to blunted muscle gains as compared with moderate consistent ingestion across the day (91–93). Optimal muscle synthesis peaks at a maximal dose of 20 grams at a time. This 20-gram maximal dose value has been established for both females and males, regardless of size and sport (94,95). Hence, it is recommended that athletes evenly distribute their protein consumption throughout the day for optimal utilization (6,7,92,93).

Sex Differences in Protein Metabolism and Requirements

Protein recommendations for sedentary individuals are between 12% and 15% total calories, or 0.8 gram per kilogram body weight per day; whereas protein recommendations for athletes are between 1.2 and 1.7 grams per kilogram body weight. Athletes need higher quantities of protein due to increased muscle breakdown and tissue repair, higher lean body mass and lower body fat, protein metabolism during endurance or high-intensity exercise, and a potential increase in urinary protein loss (89,90). Males need more protein than females, closer to 1.7 grams per kilogram of body weight, because of generally higher lean body mass ratios and greater amino acids oxidation during exercise, especially long-duration, high-intensity work. Research of top tier athletes suggests even higher protein requirements, as these athletes will oxidize higher amounts of amino acids due to increased bodily demands for energy (4,6,7,12,85).

Percentage intakes based on total energy assume that total energy intake is adequate. Athletes must be careful to consume enough calories to accommodate their activity levels. Most athletes do well in consuming sufficient amounts of protein (85). However, vegetarian athletes, young athletes who are growing and developing, and athletes with other types of restricted diets may be at risk for inadequate protein intakes (85).

FLUID AND ELECTROLYTES

Water

Just as a car cannot function without gas, humans cannot function without water. It is the single most important nutrient in our diets. Water makes up approximately 60% of our bodies, 70% of our brains, and 90% of our lungs (82). Its main functions include thermoregulation, digestion, nutrient and oxygen transport, waste elimination, and joint and tissue lubrication (82). Water also serves as a medium for a number of chemical reactions underlying these processes. Temperature regulation, oxygen and energy transfer, and the structural role of water in muscle tissue make this nutrient especially critical to athletic performance (96–98). One of the easiest and most beneficial practices athletes can enlist to optimize their performance is sustaining their hydration levels throughout exercise. Well-hydrated athletes benefit from a normal rise in heart rate, regulated core body temperature, improved cardiovascular endurance, and prolonged muscle glycogen usage (82).

Fluid Balance

Body fluid is tightly maintained within 0.2% of total body weight through systems that increase water retention and increase water loss (82). Osmoreceptors in the hypothalamus and baroreceptors that regulate blood vessel pressure stimulate the release of hormones and enzymes that control water volume. Sixty-five percent of our body water is intracellular, while 35% is outside of the cell (96). Sodium is the primary component in the plasma that dictates the balance between intracellular and extracellular fluid, and in turn influences the receptors and hormones responsible for fluid balance (89). During exercise lasting more than an hour or higher in intensity, more water is lost than sodium. Under conditions of dehydration, the electrolyte-water balance in the blood, or blood osmolality, rises. The hypothalamus detects this change and signals the pituitary gland to release an antidiuretic hormone. In response to the antidiuretic hormone, the kidneys retain water (99).

Humans lose fluid through their sweat, skin, urine, feces, apocrine glands (armpits and groin), and respiration. Individual variations in metabolism lead to different fluid loss rates for all of the aforementioned (82). Males have larger and more active apocrine glands than females, as well as more androgenic steroids, which work in conjunction to increase axillary fluid secretions in the armpit (100). Individual differences may also be amplified by sport-type and environmental conditions. Warm environment, prolonged exercise, and high-intensity training can increase fluid loss through sweat and urine (101–104). Multiple studies have reported that the majority of athletes training in warm environments fail to consume adequate fluid and electrolytes to offset their losses (105–107). Cold, dry, or high-altitude environments raise fluid loss through respiration. When dry air is inhaled, the lungs humidify it and small amounts of water vapor are lost during each exhalation. The combination of dry air and lower temperatures increases our respiratory rate, leading to increased fluid losses. Athletes exercising in cold or high-altitude environments, such as cross-country skiers, may need to take extra precautions to ensure sufficient fluid intake (108).

Thirst

Sensations of thirst change in response to plasma sodium concentrations. When dehydrated, plasma osmolality concentrations increase, stimulating the urge to drink. Conversely, a decrease in plasma osmolality, which could generate from overhydration, suppresses thirst. Despite this physiological response, accumulating evidence suggests that thirst may actually be an inaccurate gauge of fluid needs (101,108). Research by Volpe et al. found that among college athletes involved in various sports, as many as 60% initiated practice in a dehydrated state (109). Other studies report that underhydrated athletes fail to consume enough fluid during and after competition to offset their losses (105–107). Performing under a dehydrated state has been shown to cause an increased heart rate and suboptimal performance (110). However, consuming fluid within an hour of training or competition is associated with lower heart rates and attenuated core body temperatures (82). Therefore, it is essential for athletes and coaches to implement and maintain a rigid fluid-replacement plan to avoid the negative effects of dehydration and ensure optimal performance.

Thermoregulation

During physical exertion, muscles can generate up to 20 times the amount of heat when compared to muscles at rest (111). One of the unique properties of water is its exceptionally high capacity for heat absorption and therefore its ability to perform as a homeostatic regulator of temperature. Thermoregulation is maintained through two mechanisms of action. The first is vasodilation and constriction, which adjusts the amount of blood that reaches the surface of the skin. The second is through sweat. As the sweat evaporates it also helps to cool the skin, which then cools the blood and ultimately lowers core body temperature (89).

Electrolytes

Electrolytes are positively or negatively charged minerals that control the on-and-off state of nearly all brain and muscle cells. They go hand-in-hand with water due to their ability to carry an electrical current through water, since water alone is a poor conductor of electricity. Electrolytes most closely associated to athletic performance include sodium, chloride, potassium, calcium, and magnesium. Heavy sweating and increased urinary output can lead to appreciable electrolyte losses during and after exercise. Sodium and chloride are lost in the greatest concentrations through sweat; however, prolonged and intense exercise can lead to substantial potassium losses as well. Individual variation prevents the determination of the exact concentrations of electrolytes lost through sweat. While magnesium and calcium losses are very small in comparison to other electrolytes, dietary needs are still higher for both minerals to account for losses through sweat.

Potassium deficiency is often blamed as the underlying cause of muscle cramping during activity, however sodium is to blame (101,112). Potassium lost through sweat only represents a small fraction of total body potassium loss, whereas sodium lost through sweat can account for as much as 20% of total body sodium loss. A moderate to vigorous 2-hour workout can deplete as much as one fifth of total body sodium (101,112). Athletes who train several hours per day in hot environments or who sweat heavily have an increased risk for excessive sweat sodium loss (103,104,113). Drinking plain water replenishes fluid loss, but does not compensate for electrolyte losses. In fact, plain water can increase the risk of electrolyte imbalance by diluting the blood, increasing urinary fluid excretion, and decreasing the urge to drink. Electrolyte imbalance and low sodium pose more threat than just cramping (112,114). Hyponatremia, a condition marked by dangerously low blood sodium, can lead to nausea, vomiting, cardiac and neurological abnormalities, and even death. A higher incidence of hyponatremia has been reported in female when compared to male athletes, most likely due to lower total body water volume (115–117) (Figure 20.2).

The ingestion of salt and salty foods is biologically driven through cravings following a workout and excessive sweat loss, minimizing the risk for developing hyponatremia (118). However, much like thirst, salt cravings may not manifest into significantly higher consumption of those minerals. Another biological mechanism to protect an athlete from hyponatremia is increased hunger resulting in greater total energy consumption. A high-calorie, well-balanced diet naturally includes higher levels of vitamins and minerals. Consequently, many athletes eating to meet their energy needs instinctively meet their increased mineral requirements. Other ways in which mineral needs can be easily met is by the consumption of sports drinks during and after workouts. Unlike water, sports drinks include the electrolytes lost in greatest concentrations through sweat. Though often avoided for their higher sugar content, sports drinks contain carbohydrates for the restoration and sparing of muscle glycogen, improved absorption, and increased palatability to provoke drinking (119–123). Consequently, sports drinks are a good alternative to plain water to foster fluid and electrolyte replenishment during and after practice and competition (106).

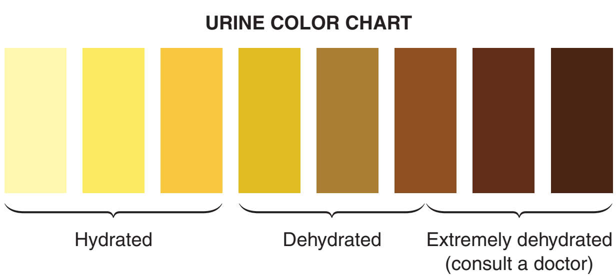

FIGURE 20.2: Urine color chart. The urine color chart uses urine color as an indicator and ongoing monitor of hydration status.

Assessing Fluid and Electrolyte Needs

Because so many variables contribute to individual fluid and electrolyte needs, a personalized approach is necessary to determine the appropriate dietary requirements for each individual athlete (101). Examples of individual discrepancies include heavy and salty perspirers who exhibit extraordinarily higher fluid and electrolyte losses relative to their teammates when engaged in the same activity (112–114). Beyond mere sweat observation, there are several ways that athletes, coaches, and practitioners can gauge fluid and electrolyte losses and needs. Assessing urine output and concentration is one of the easiest, cheapest, and simplest ways to determine hydration status. Maintaining a light yellow urine color indicates adequate hydration. Low urinary output and dark brownish-colored urine denotes dehydration (112–114). Nearly clear urine and heavy output suggests fluid intake in excess of need/loss. Another affordable means of assessing hydration status observes skin turgor. When skin on the back of the hand is pulled up and released and does not return to its original state, this may signal dehydration. Keep in mind that skin turgor is not a conclusive test of hydration, but rather one physical parameter that should be used in conjunction with other assessment methods. A more involved and reliable way to determine fluid needs is by weighing oneself before and after training or competition. The difference in body mass represents the total water lost, taking into account fluid consumed during training (124,125). Specific gravity of urine and plasma and/or urinary osmolality are two other methods to establish hydration status. These methods are less common in sports settings and often limited to labs due to higher costs and the need of equipment.

Fluid and Electrolyte Requirements

When fluid loss information is available from pre- and post-workout weigh-ins or other methods, athlete-specific formulas can be employed. Formerly, experts advised consuming 100% of water weight lost in pounds after a workout. However, subsequent research pointed out that a 1:1 ratio does not account for increases in drinking-related urinary output. For complete rehydration, it is now encourage to consume 150% of total water lost after exercise (124,125). The American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine published a comprehensive position statement on fluid and electrolyte replacement before, during, and after exercise.

Their recommendations include 5 to 7 mL of water or sports drink per kilogram of body weight at least 4 hours before activity. During exercises, these organizations suggest adherence to an individual hydration program that prevents total body water loss above 2% of total body weight. Following exercise, at least 16 to 24 ounces of fluid should be consumed for every pound of body weight lost. Note that the minimum requirement equates 16 ounces consumed to 1 pound of fluid lost. And finally, in terms of electrolytes balance, the benefits of sports drinks and salty foods are accredited (85,126).

Fluid and Electrolyte Timing

One of the important pillars of the American Dietetic Association, Dietitians of Canada, and American College of Sports Medicine's publication is the emphases on fluid and electrolyte timing. The timing of intake can have an impressive impact on performance. The experts advised consuming 5 to 7 mL of fluid per kilogram of body weight, which translates to about 1 ounce of fluid per 10 pounds of body weight, approximately 4 hours prior to competition (85,126). Why 4 hours? The rationale behind this time frame is that 4 hours allows for adequate time to consume more fluid if necessary or to excrete excess prior to work (127). Within an hour preceding training, athletes may still gain advantages from drinking, including lower heart rates and decreased core body temperatures. Replacing fluid and electrolytes during exercise has also shown positive effects on temperature and heart rate. Post-workout fluid and electrolyte replenishment is arguably the most critical to hasten the body's recovery (82).

Sex Differences in Fluid and Electrolyte Balance

Our bodies range between 45% and 75% water, with 60% as the mean marker for both males and females. Because muscle contains roughly 75% more water than adipose tissue, fat is inversely correlated with total body water. Males average approximately 10% higher in body water percentage due to a generally higher proportion of lean muscle mass and lower total body fat relative to females. Females typically exhibit around 50% body water and males fall around 60%. Obese individuals may have as little as 40% body water due to high fat mass, and sometimes even less depending on the severity of their condition. Athletes, who have a higher proportion of lean muscle, may have as much as 70% total body water (89,101).

General rules of thumb for fluid requirements have been tailored throughout the years. Initially consuming half of one's body weight in ounces was the general recommendation and is still the common acceptable practice used today. Because males typically weigh more than females, their fluid needs are higher. A sort of innate compensation, similar to that described with dietary mineral intake, accounts for males' increased fluid needs. Males tend to consume more energy in their diets, and at least 20% of our fluid comes from the food we eat, so men naturally consume more fluid than females (101).

MICRONUTRIENTS AND SPORT

Micronutrients are vitamins and minerals that humans require in minute quantities and that play key roles in energy metabolism and muscle function. Humans need to consume a wide range of vitamins and minerals from our diets in order to satisfy the needs of our bodies and prevent the adverse effects that result from deficiencies. Vitamins are carbon-containing molecules that may be water- or fat-soluble. The primary purpose of vitamins in physical activity is the conversion of the three macronutrients into usable fuel for the body. In addition to energy metabolism, vitamins also help in red blood cell synthesis, immune health, skeletal integrity, and protection against oxidative damage (128).

Minerals are inorganic nutrients in simple elemental form. They are often consumed and found in trace amounts in the body. While miniscule in concentration, minerals serve a generous set of services in the body. Calcium is the most abundant mineral in the body that, along with phosphorus and magnesium, contribute to bone structure and integrity. Iron is the central atom in hemoglobin. Sodium and chloride are crucial to nerve and muscle stimulation. Magnesium is involved in over 300 metabolic reactions. Copper is the main element involved in the respiratory electron transport chain. Zinc, like magnesium, is a cofactor in many enzymatic reactions and aids in tissue repair (128).

Exercise impacts the turnover of micronutrients, increasing demands on the metabolic pathways in which these nutrients are required. Higher energy and oxygen consumption also raises oxidative stress, which may increase antioxidant-vitamin needs (129). While in theory athletes should need more micronutrients due to the increased utilization and demand of exercise, there are no athlete-specific recommendations in place that differ from the dietary guideline ranges for the general population. It can be safely assumed that due to increased metabolic processes and macronutrient needs, athletes require slightly higher levels of micronutrients. Nonetheless, there may be an inherent recompense at play: Athletes consume micronutrients in excess of standardized ranges due to higher total energy intake. Increased food consumption, given a balanced diet, results in inevitably higher vitamin and mineral intake. This does not insulate all athletes from the risk of deficiencies. Athletes with restricted eating habits and endurance competitors are susceptible to vitamin and mineral shortages, which have been associated with poor performance and compromised physical health and well-being (130). The literature recognizes vitamins A, C, E, D, and the major B vitamins, electrolyte minerals, and iron, copper, and zinc, for their supporting role in athletic performance. In this section, we review each of these vitamins and minerals with respect to athletic performance as well as their specific sex needs.

Vitamins

It is not unusual for athletes to mistake vitamins as sources of energy. In fact, one study found that 65% of athletes believed that vitamin and mineral supplementation increased their total available energy (84). While these nutrients are devoid of energy units, the athletes were not entirely wrong to associate energy with micronutrients.

B Vitamins

Many vitamins are involved in mitochondrial energy metabolism. Those best known for their energy-aiding effects are the B vitamins. Each of the B vitamins has a unique mission in energy metabolism. Thiamin's main metabolic role is in carbohydrate metabolism, riboflavin partakes in the electron transport chain, niacin contributes to several metabolic pathways as nicotinamide adenenine dinucleotide (NAD) or nicotanimide adenine dinucleotide phosphate (NADP), B_6 contributes to muscle growth and repair via amino acid manufacturing, and folic acid and B_{12} are vital to red blood cell synthesis. Deficiencies in B vitamins often result in fatigue, decreased endurance, and even anemia (130). Nowadays, B-vitamin deficiency is rare thanks to an increase in fortified foods. The RDA values for adolescents is between 0.9 and 2.0 mcg per day, and 2.4 mcg per day for 14- to 18-year-olds and adults. Pregnant and lactating women have slightly higher needs, at 2.6 mcg/day and 2.8 mcg/day, respectively (131). Animal proteins and fortified foods such as cereal, nuts, lentils, and some dairy products are good sources of B vitamins.

Vitamin D

Vitamin D is one of the most common vitamin deficiencies in the United States. We derive vitamin D from ultraviolet exposure, fatty fish, dairy, and fortified soymilk and orange juice. Evidenced by that list, dietary access to vitamin D is limited, while the functions of vitamin D are not. Calcium absorption and bone development, mineralization, and integrity rely on adequate levels of vitamin D. Insufficient vitamin D levels have been connected to increased incidence of fractures in athletes and depressed mood states (132–134). Even with above-average energy intakes, adequate vitamin D levels may still be a concern. Athletes at a higher risk for deficiency include those who compete in indoor sports (e.g., gymnastics, wrestling) or live in northern regions where outdoor exposure may be limited (135). The RDA for both male and female athletes is approximately 600 IU per day (131). Athletes lacking sufficient serum vitamin D levels may want to supplement with 200 IU to boost plasma concentrations (Table 20.1).

Antioxidants

The antioxidant nutrients beta-carotene, vitamin C, and vitamin E act as protective effects against free radical damage. Antioxidant activity is of particular importance in active individuals who have increased oxygen consumption. The elevated oxygen consumption exposes the muscles to a higher degree of oxidative stress. Elevated levels of reactive oxygen species in athletes have been associated with muscular and skeletal dysfunction leading to fatigue (129). Antioxidants are also affiliated with the maintenance of adequate immune function, which may be compromised by the added stress of exercise. In addition to its role against oxidative damage, vitamin C is implicated in collagen synthesis related to joint and muscle fitness and tissue repair. The RDAs for vitamin C are slightly different between males and females, at 75 mg per day (mg/d) for women and 90 mg/d for males. Different RDA values are also established for vitamin A. Females should consume 700 mcg of vitamin A per day, and males require around 900 mcg per day. The intake variations between sexes for these two vitamins are attributable to generalized differences in body mass and metabolic utilization. Vitamin E has an RDA value of 70 mg/d for both males and females (131). Deficiencies in these nutrients are rare and slow to develop. Symptoms may include joint pain and abnormal bone development with insufficient vitamin C. Poor ocular health arises without adequate vitamin A. Cell membrane degeneration in erythrocyte, neuronal, and muscle cells occurs if vitamin E is missing (128,130).

TABLE 20.1: Food Sources of Vitamin D

Food	IU per serving	Percent DV
Cod liver oil, 1 tablespoon	1,360	340
Swordfish, cooked, 3 ounces	566	142
Salmon (sockeye), cooked, 3 ounces	447	112
Tuna fish, canned in water, drained, 3 ounces	154	39
Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)	137	34
Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup	115–124	29–31
Yogurt, fortified with 20% of the DV for vitamin D, 6 ounces (more heavily fortified yogurts provide more of the DV)	80	20
Margarine, fortified, 1 tablespoon	60	15
Sardines, canned in oil, drained, 2 sardines	46	12
Liver, beef, cooked, 3 ounces	42	11
Egg, 1 large (vitamin D is found in yolk)	41	10
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75–1 cup (more heavily fortified cereals might provide more of the DV)	40	10
Cheese, Swiss, 1 ounce	6	2

IU, international unit; DV, daily value, currently set at 400 IU.

Source: USDA nutrition database.

Minerals

Iron

Iron is a critical nutrient for athletes as it plays a key role in energy production as a carrier of oxygen, both in the form of hemoglobin in the blood and myoglobin in the muscles (136). Depletion is not very common in athletes, but may be prevalent in athletes with restricted diets and females due to menstruation (66,134,137,138). There is speculation that among endurance athletes, iron requirements may increase by as much as 70% (139,140). More research is needed to determine increased requirements for endurance sports. Iron deficiency in athletes has been correlated with poor muscle function and decreased stamina and strength (130,138). Iron deficiency impairs performance even when anemia is not present (130,138). For children under the age of 13, 10 mg of iron is recommended for daily intake. Between the ages of 14 and 18, the RDA is 11 mg/d for males and 15 mg/d for females. After age 18, the RDA is 8 mg/d for males and 18 mg/d for females. The requirements change for females during and after conception, at 27 mg if pregnant and 9 mg if lactating. After age 51, the RDA is 8 mg/d for both sexes (131). The difference in iron requirements between sexes is due to the onset of menses and menopause in females (134). Because iron plays a vital role in physical activity, athletic performance may increase the requirements due to losses in sweat, feces, and urine, intravascular hemolysis, and impaired absorption (130,137–139). Iron-rich foods overlap with many B-vitamin dense foods, such as lean animal proteins, beans, and fortified foods.

Calcium

As stated earlier, calcium is the most abundant mineral in the body. Calcium enables exercise through its many roles in intracellular messaging, nerve transmission, muscle contraction, and bone health. Calcium is lost in small concentrations in sweat. Excessive sweating, high sodium and phosphorus intake, and exorbitant caffeine consumption all marginally reduce total body calcium (128). Active females and endurance athletes may be at higher risk for bone density problems related to this mineral. A number of research studies into the dietary habits of female athletes report inadequate consumption of this mineral (18,22,67). Women also experience greater bone loss as they age due to hormonal fluctuations and weakened absorption postmenopause (141). Deficiencies are linked to poor muscle function and bone degradation. The RDA value is 1,000 to 1,300 mg/d for both males and females of all ages (131). Dairy products, baked beans, and some cruciferous vegetables provide substantial amounts of calcium per serving.

Magnesium

Magnesium is involved in more than 300 enzymatic reactions in the body, participating in the metabolism of glucose, lipids, proteins, and nucleic acids. It is estimated that as much as 60% of adults in the United States do not consume sufficient magnesium. Small amounts of magnesium are also lost through sweat. It has been suggested that low magnesium status is indirectly related to strength improvement as well as the incidence of muscle cramps. However, of the various symptoms related to magnesium deficiency, muscle cramps are not one. Chronic inflammation and stress response are the two largest concerns with magnesium deficiency, but these side effects are mostly prevalent in obese and overweight individuals. In athletes, restriction of magnesium has been associated with increased oxygen requirements and decreased endurance (142). RDAs differ between males and females, and across age groups. Initial recommendations are the same for both sexes. Between ages 4 and 8, children need 130 mcg per day, followed by 240 mcg from ages 9 to 13. After age 14, sex differences appear. At the higher end, males require between 400 and 420 mcg per day, while females require 360 mcg per day during development and between 310 and 320 mcg per day after age 18. Pregnancy increases the RDA to 350 to 360 mcg per day (131). Magnesium is found in an array of healthy foods: halibut, nuts, soy, oatmeal, and potatoes, to name a few.

Zinc

Zinc is another trace mineral with various roles and benefits to sports performance. Zinc plays a part in a number of enzymatic reactions, DNA and RNA transcription and translation, amino acid fusion, and the promotion of tissue repair through collagen and skin protein synthesis. Insufficient zinc levels in athletes have been connected to weight loss, fatigue, decreased stamina, and heightened risk for osteoporosis (130). Slight differences in zinc requirements exist as a result of spermous zinc loss in males (143). For children under age 8, the RDA is 3 to 5 mg/d. From age 9 on, the RDA for females is 8 mg/d, and 11 mg/d for males. Zinc loss during pregnancy and lactation increase female needs to 11 to 12 mg/d (131). Oysters are an excellent source of zinc, topping the scales with 74 mg per 3-ounce serving. Crab and lobster, beef, pork chops, baked beans, and yogurt also have appreciable quantities of zinc. Because zinc is most highly available in animal-sourced foods, vegetarians and vegans should monitor their zinc consumption. Several good non-meat sources of zinc include chickpeas, fortified cereals and oatmeal, milk, and almonds.

Sex Differences in Micronutrients

The micronutrient requirements are not sex-gender specific for any except iron. However, differences in gross energy intake and food choices should be taken into consideration to account for varying male-female needs (15,23). Because females are more susceptible to dieting and restricted eating, female athletes may be at a higher risk of deficient micronutrient consumption (2,17–19). Calcium is of particular concern for female athletes, a population characterized by inadequate calcium consumption, sweat calcium loss, and menopausal bone density loss (18,22,68). Similarly, vitamin D, the most common vitamin deficiency in Western countries, should be closely managed for all athletes, but especially females who may need vitamin D to help enhance calcium absorption. Female athletes should also be conscious of their iron and more specifically heme-iron intake. Female athletes typically consume less meat than males and experience iron loss through menses (1,23). B vitamins and zinc intakes also need close monitoring for females who do not consume a lot of meat or shellfish. Because males tend to consume fewer fruits, vegetables, and whole grains than females, male athletes may be at a greater risk than females for low intakes of antioxidant vitamins and magnesium (1,23).

CONCLUSION

Two Key Macronutrient and Micronutrient Function and Food Sources for Athletic Performance

Nutrient	Function	Recommendation	Food Sources
Carbohydrates	Fuel for performance Glycogen repletion	5 to 7 g/kg moderate intensity 7 to 10 g/kg high intensity	Fruit, dried fruit Whole grain breads, rice, pasta, oatmeal
Protein	Structural support and transport Maintains body tissue, muscles, ligaments, tendons, organs, bones, hair, nails, skin Enzyme and hormones Fluid balance Acid-base balance Antibodies	1.2 to 1.6 g/kg Maximum level 2.0 g/kg	Lean meats (chicken breast, pork, turkey) Fish Seafood Low-fat milk, yogurt, cheese Eggs Beans, nuts, lentils, tofu, hummus
Vitamin D	Calcium absorption Bone mineralization	600 IU/day	Fatty fish Dairy Fortified milk and juice Ultraviolet light exposure
Calcium	Supports bone structure Muscle function	1,000—1,300 mg	Low-fat milk, cheese, yogurt Fortified orange juice Dark leafy greens (spinach, kale, collard greens) Almonds
Iron	Energy production Oxygen carrier	Females (19–50 years) 18 mg (> 51 years) 8 mg Pregnancy (all ages) 27 mg Males (19–51 years) 8 mg (> 51 years) 8 mg	Lean meats Beans Fortified foods Consume with vitamin C-rich foods to increase absorption
Magnesium	Enzymatic reactions Metabolism of glucose, lipids, proteins	Females (19–30 years) 310 mg (31–50 years) 320 mg (> 50 years) 320 mg Pregnancy (19–30 years) 350 mg (31–50 years) 360 mg Lactation (19–30 years) 310 mg (31–50 years) 320 mg Males (19–30 years) 400 mg (31–50 years) 420 mg (> 50 years) 420 mg	Wheat bran Almonds Soybeans Nuts, beans Low-fat chocolate milk Banana Avocado

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