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Influence of Female Hormones on the Anterior Cruciate Ligament

Heather Stone

University of North Dakota

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INFLUENCE OF FEMALE HORMONES ON THE ANTERIOR CRUCIATE LIGAMENT

by

Heather M. Stone
Bachelor of Science in Physical Therapy
University of North Dakota, 1999

An Independent Study
Submitted to the Graduate Faculty of the
Department of Physical Therapy
School of Medicine
University of North Dakota
in partial fulfillment of the requirements
for the degree of
Master of Physical Therapy

Grand Forks, North Dakota
May
2000
This Independent Study, submitted by Heather M. Stone in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

Beverly Johnson
Faculty Preceptor

Beverly Johnson
Graduate School Advisor

Chairperson, Physical Therapy
PERMISSION

Title  Influence of Female Hormones on the Anterior Cruciate Ligament

Department  Physical Therapy

Degree  Master of Physical Therapy

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Date  11/17/99
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“\text{I CAN DO ALL THINGS THROUGH GOD WHO GIVES ME STRENGTH}”

Philippians 4:13
ABSTRACT

Since 1972 the number of female athletes has increased more than 600% to a total of 1.9 million athletes. Unfortunately, "the quest for equal opportunity in sports has led many female athletes to equal opportunity for injuries, especially injuries to the anterior cruciate ligament (ACL)." For reasons that are still somewhat unclear the ACL injury rate is two to eight times higher for females compared their male counterparts. One intrinsic risk factor, which has devoured attention in recent years, is the influence female hormones have on the structure and integrity of ACL.

The purpose of this independent study was to review current studies and literature in order to determine whether or not hormones play a role in the increased incidence of female ACL injuries. Research in this area is limited, but of the studies reviewed there seems to be a strong correlation between the late proliferative and early luteal phases of the menstrual cycle and an increased incidence of female ACL injuries. The results of studies already published regarding female ACL injury and fluctuating female hormones, provide sound justification for further research.
CHAPTER I

INTRODUCTION

The United States women's soccer team made a dramatic statement about women's sports this year as they won the 1999 world cup championship, and drew a record crowd of 90,000 plus fans. One of the great things about this championship is the fact that this was not simply an economical statement. Although the women proved they could compete for the American sport dollar, they really proved much more. The U.S. women's team gave us a much clearer definition of women's sports. Instead of making themselves liable to comparisons with men's sports they presented themselves in contrast to men's sports. They flaunted their feminine side instead of hiding it, and they showed the world that "women can be attractive and feminine and yet be strong, powerful, and fiercely competitive." We owe these women a lot because they have opened a whole new arena for the way women's sports are supported and viewed.

In recent years the opportunity for female participation in athletics has dramatically increased. Since 1972 female athletic participation has increased more than 600% to a total of 1.9 million female athletes. Today because of Title IX women's participation in sports is the norm rather than the exception. Just 20 years ago only one of every 30 athletes was a female and today one out of every three is a female. Title IX which was passed in 1972 essentially states that, "any secondary or collegiate school that
receives federal assistance must offer equal athletic opportunities to men and women, requiring equity in areas of participation, scholarship dollars, and athletic benefits.\(^1\)

Unfortunately, "the quest for equal opportunity in sports has led many female athletes to equal opportunity for injuries, especially injuries to the ACL."\(^3\) Musculoskeletal injuries from sports are generally related to the sport rather than gender. However, for reasons that are still somewhat unclear the ACL injury rate is two to eight times higher for females compared to their male counterparts.\(^4-8\)

Women between the ages of 16-30 participating in sports that require pivoting, planting, cutting, straight-knee landing, and sudden deceleration such as soccer, basketball, volleyball, and cheerleading have the highest risk of experiencing an injury to their ACL.\(^9-12\) Reports from the NCAA Injury Surveillance System (ISS) between 1989-1993 showed that female soccer players were more than two times as likely to suffer an ACL tear than men, and in basketball they were four to five times more likely than their male counterparts.\(^8\) Using this same system to look at an additional five years (1994-1998), Adrent et al\(^7\) found a consistently high pattern of injury rate in women as compared to men. This particular system, which was developed in 1982, provides researchers with current reliable data regarding the number and type of injuries sustained by intercollegiate athletes. "Participation in the NCAA ISS system is voluntary and limited to the 931 member institutions. It collects a sampling that is representative of a national cross-section of NCAA institutions."\(^7\)

Numerous risk factors have been identified in attempt to come up with answers for why women injure their ACL more frequently, but linking one single factor to this injury rate has yet to be done. It is likely that a combination of risk factors, both intrinsic
and extrinsic play a role in the increased incidence of ACL injuries among the female athlete. This next section will outline both the intrinsic (uncontrollable) and extrinsic (controllable) factors, but the focus of this paper will be on the effect fluctuating female hormones have on the female ACL. Table 1 summarizes the risk factors breaking them down into three categories, the extrinsic factors, combination factors, and intrinsic factors.\textsuperscript{10,11,13-19}

Table 1. Risk factors related to ACL injuries.

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\textbf{Conditioning/Training/Experience}

Since the implementation of Title IX the number of female athletes has dramatically increased. In soccer alone there was a 50\% increase in female participation between the years of 1989-1995, compared to only a 9\% increase in the number of males.\textsuperscript{8} Early on many researchers blamed the increased incidence of female ACL injuries on this rapid increase of novice female athletes.\textsuperscript{7,14,18,20,21} They felt these novice players were introduced to a level of competition their bodies were not prepared for. Considering the fact that poor condition levels correlate directly with increased injury rate this statement does seem like a valid hypothesis. However, for it to be true then
today when female athletes have equal opportunity to begin training and conditioning at a very young age we should see a decreased incidence of injury.\textsuperscript{6,13} If we look at the 1994-1998 data from NCAA ISS we see that unfortunately this is not the case.\textsuperscript{7} Women are still injuring their ACL more often than men.

**Coaching/Funding**

Although highly speculative due to the number of different variables, coaching can be looked at as one of the extrinsic factors for female ACL injury. “According to a 1994 survey by the Chronicle of Higher Education, coaches of women's athletic teams are still paid only 59 cents on the dollar as compared to coaches of men's teams.”\textsuperscript{15} Needless to say compensation doesn't indefinitely mean a decrease in the quality, experience, or expertise, but one could definitely hypothesize that compensation plays a key role in the recruitment of top notch coaches.

Another factor worth looking at is the fact that funding for women's division I sports is still only 40% compared to that of men's sports.\textsuperscript{15} This can mean inferior equipment and athletic shoes, poor playing conditions such as bumpy fields and old courts, and less one on one time with a coach. This hypothesis does seem valid, but if it were true then one would expect to see a decrease in female ACL injury rates over the years as funding for women's sports has increased. Unfortunately this is not the case.

**Shoe-surface Interface**

When considering shoe-surface interface as an extrinsic risk factor we see that the higher the coefficient of friction is between the athlete's shoe and playing surface, the higher the rate of ACL injury.\textsuperscript{19} One might speculate that because funding for women's sports has not always been equal to that of men's, female athletes have been provided
with inferior shoes which put them at greater risk for injury. This seems logical, but with the passage of Title IX women's sports have received increased funding. Therefore shoe-surface interface should not be a variable when considering why females injure their ACL more often than males. Nonetheless it is an extrinsic factor for both genders.

**Muscle Strength and Endurance**

"The ACL is the primary static restraint to anterior tibial translation." However, it alone is unable to withstand the dynamic forces, which are placed on the knee joint daily. The most crucial role in maintaining proper functional knee stability is played by the quadriceps, hamstring, and gastrocnemius muscles. These muscles help protect the knee joint allowing it to withstand daily forces of up to two times our body weight, and forces that exceed five times our body weight during sporting activities.

It has been well documented that females have less quadriceps and hamstrings muscle strength than their male counterparts. In a neuromuscular study, Huston et al compared physiological differences between elite male and female athletes along with non-athletic sex-matched controls. They were compared in five different areas including: knee joint laxity, lower extremity strength, endurance, muscle recruitment order, and muscle reaction time. The results from the isokinetic strength comparisons portion of the study proved that there is significant difference (p<.05) in strength between men and women. At 60 degrees/sec with body weights normalized, both female athletes and controls demonstrated statistically weaker quadriceps and hamstring muscle strength compared to the male groups. Also of interest these Division I, NCAA athletes were only minimally stronger than their nonathletic female counterparts.
For muscle endurance isokinetic comparisons show that both female and male athletic groups have greater muscle endurance in both knee extension and flexion than their nonathletic counterparts, but the female groups still demonstrate significantly (p< .05) lower endurance than the male groups.\textsuperscript{13}

**Neuromuscular Efficiency**

Huston et al\textsuperscript{13} found with isokinetic testing that there is no significant difference in time to peak torque at 60 degrees/second for knee extension when comparing males and females, athletes and nonathletes. However, this study did show that with knee flexion the male athletes were significantly (p< .05) faster than the other groups. Time to peak torque at 240 degrees/second for the hamstrings mirrored the 60 degrees/second times. As mentioned earlier muscles play a very important role in stabilization of the knee joint and thus prevention of injury to the ACL. Because women require significantly more time to achieve maximal protective muscle contraction their ACL may be put at greater risk for rupture.

**Muscle Recruitment Order Preference**

Investigation of the order of muscle recruitment in response to anterior tibial translation has revealed a significantly different pattern among female athletes as compared to the other three groups in Huston et al's\textsuperscript{13} study. This difference can be seen when taking a closer look at each of the three phases, which include, the intermediate phase, the spinal phase, and the voluntary phase.

**Intermediate**

When considering the female athletes at the intermediate level we see a general tendency towards increased initial quadriceps muscle activity and decreased initial
hamstrings activity. This is opposite for the other three groups which preferred to initially use their hamstrings for knee stabilization. To summarize, the recruitment order for the female athletes was quadriceps-hamstrings-gastrocnemius, and the order for the remaining three groups was hamstrings-quadriceps-gastrocnemius. Since the quadriceps muscles are antagonists to the ACL this muscle recruitment pattern for the female athlete can be detrimental to the ACL.

Spinal

At the spinal level in response to anterior tibial translation, all four groups in Huston et al's study generally preferred a gastrocnemius-hamstring- quadricep muscle recruitment pattern.

Voluntary

The voluntary recruitment pattern, which was identical for all four groups, was hamstrings-quadriceps-gastrocnemius.

This finding of the quadriceps first muscle recruitment order among female athletes, reiterates the importance of a balanced muscle strengthening and endurance program for female athletes.

Muscle Reaction Time

At the spinal cord level Huston et al report no significant difference between the four groups in muscle reaction times for the quadricep and hamstring muscles. There is however, a significant difference in gastrocnemius muscle reaction times, with the athletic groups being faster than both of the nonathletic groups (female athletes, 41.2msec; female controls, 52.3msec; male athletes, 41.6msec; male controls 51.2msec).
When comparing responses at the cortical level both female groups reacted faster than the male groups, but the differences were not significant.

**Notch Dimensions/Ligament Size**

Studies have shown that athletes who sustain ACL injuries often have a narrower notch width than noninjured athletes. Intercondylar notch width is yet another intrinsic factor which must be considered when looking at risk factors for ACL injuries. The intercondylar notch, which is the site of origination for both the ACL and the PCL, is located on the distal femur. The intercondylar notch is often measured using the notch width index (NWI), which is equal to the width of the intercondylar notch divided by the width of the femur at the poplitial hiatus. A NWI of .21 or greater is considered normal, while a NWI of .20 or less is stenotic. It has been well documented that women have a narrower notch than men. This known fact leads some to believe that because the notch is narrower in women they are predisposed to injury. Shelbourne et al have successfully linked ACL injuries to a narrow notch width for both men and women. There are however, other studies, which show no association between notch size and risk of ACL injury; it is safe to say this is an issue that remains under debate.

Another related controversial issue is whether a small intercondylar notch indefinitely means a small ACL. LaPrade et al discussed the possibility of narrow notches containing smaller thinner ACL's. They thought smaller ACL's may lead to increased stress and impingement on the ligament thus predisposing it to rupture. Shelbourne et al believed that, "ACL tear rate may be primarily affected by the size of the ACL." Their study concluded that when knees were reconstructed with a standardized ACL there was no longer an increased incidence of ACL tears among
patients with narrow notches. Still other studies such as Muneta et al\textsuperscript{25} have found that both narrow and wide notches have the same size ACL. They believe, "this mismatch between the size of the ACL and the volume of notch may predispose the ACL to injury by rotational and translational movements of the tibia on the femur that could bind or impinge the ACL on the margins of the notch."\textsuperscript{25} Further research needs to be done before a definite conclusion can be drawn.

**Lower Extremity Alignment/Static Posture**

Noncontact ACL injuries, which are more prevalent in females than males, typically occur with either deceleration of the lower limb, forced hyperextension, or with forced tibial rotation.\textsuperscript{11,12,16} It is speculated that faulty static postures which place an individual in any of these positions may increase the stress on the ACL thus predisposing it to injury. "A static posture consisting of anterior pelvic tilt, anteverted hips, tight hamstrings, genu recurvatum, and subtalar joint pronation may place an individual in knee hyperextension and increased internal tibial rotation during dynamic movement, putting greater stress on the anterior cruciate ligament and exposing this ligament to forceful stretch."\textsuperscript{16} Loudon et al\textsuperscript{16} explored the relationship between selected static posture variables and prevalence of ACL injuries in the female athlete. The static posture variables included pelvic position, hip position, frontal knee position, sagital knee position, hamstring length, and subtalar joint pronation. The significant postural difference between the injured and the noninjured female athletes was a combination of knee hyperextension and excessive subtalar joint pronation, which was displayed by the ACL injured group. Although lower extremity alignment seems to be a risk factor, we have to remember that this is only one variable of the many intrinsic and extrinsic factors.
Additional research on faulty postures especially on dynamic faulty postures needs to be completed.

**Joint Laxity**

Most people agree that women in general are more flexible than men. Huston et al\textsuperscript{13} made a case for this when they found that there is greater laxity in the knees of nonathletes compared to athletes, and also greater laxity in females compared to males. A variety of sources have stated that connective tissue of women is more elastic than that of men.\textsuperscript{3,6,13,27} This increase in elasticity which leads to greater flexibility is thought to be a predisposing factor for female ACL injuries. Some have blamed the "completeness" of ACL tears on this increased elasticity, while others believe that the increased flexibility influences the degrees of knee flexion during landing, predisposing women to knee hyperextension.\textsuperscript{3,14}

Others such as Kibler et al\textsuperscript{28} also support the theory that increased knee joint laxity in females is a contributing factor to ACL injury. This topic does however, remain a controversial issue with researchers such as Grana et al\textsuperscript{29} finding no direct relationship between ACL tears and ligamentous laxity. The effect female hormones have on the laxity of the ACL is a topic which will be covered in more detail in chapter 3.

**Female Hormones**

The final intrinsic factor we will look at is one that has devoured much attention in recent years. With many of the extrinsic differences such as conditioning, training, and experience becoming equal between men and women one would expect to see a decrease in ACL injury rate among women. Unfortunately, this is not the case. Women are still injuring their ACL's more frequently than their male counterparts leaving
researchers searching for answers. Researchers have brought up the possibility of fluctuating female hormones predisposing women to ACL rupture. This fluctuation of female hormones throughout the normal menstrual cycle is the focus of this paper. In the remaining chapters the most recent articles and studies will be examined in hopes to answer the question of, do fluctuating female hormone levels throughout the menstrual cycle predispose women to ACL injury? If so what can physical therapists do to help combat this problem?
CHAPTER II

ANATOMY OF THE ACL

A ligament, which is responsible for the joining of bones, is composed of bands of dense regular connective tissue. $^{36-38}$ Although at first glance they may seem to be simple structures, ligaments are very structurally complex, and play a critical role in maintaining joint stability and motion. One of the most well known ligaments especially in the world of sports is the anterior cruciate ligament (ACL). In this chapter we will take an in depth look at the anatomy of the ACL.

Many consider that the primary function of the ACL is to prevent excessive anterior tibial translation on the femur. $^{36,38-40}$ Although this undoubtedly is one of its most important roles, the ACL also acts as a restraint during varus-valgus and axial tibial rotation of the knee. $^{36,39,40}$ The function of the ACL as a restraint of joint motion is directly related to its construction and design. The ACL acts as a bridge connecting the femur to the tibia. It is composed of fibroblasts surrounded by an extracellular matrix. $^{38}$ Proper function of this ligament is highly dependent upon the composition, organization, and interaction of the matrix components. These components include collagen, elastin, proteoglycans, glycoproteins, and water. Collagen makes up 75% of the dry weight of the ligament, of which 90% is type I collagen and the remaining 10% is type III. Elastin, which interacts with collagen to contribute tensile resistance and elastic recoverability, makes up five percent of the ACL. One percent of the dry weight can be attributed to
proteoglycans, which are macromolecules that organize the extracellular matrix and interact with tissue fluid. Yet another of its component whose role remains somewhat unclear at the present time is glycoproteins. It is believed that they may be noncollagenous protein molecules, which are responsible for facilitating interaction between cells and their surrounding matrix. The last component, water contributes 60% or more of the wet weight, providing lubrication for the gliding of collagen fibers as well as conferring viscoelastic properties to the ligament.

As a result of the ACL being enclosed in a mesentery like fold of synovium it is intraarticular yet also extrasynovial.\textsuperscript{38} Although it appears as a single cord the ACL is actually a collection of individual fascicles that fan out over a large area.\textsuperscript{36,38,39} These fascicles are divided into two separate groups: the anteriomedial band (AMB) and the posteriorlateral band (PLB). During knee extension the PLB is tight and the AMB is relatively lax, and in knee flexion the femoral attachment is brought into a more horizontal position thus causing the AMB to tighten and the PLB to loosen. “The functional significance of the ACL is that different groups of fascicles may function together throughout the range of motion.”\textsuperscript{38}

\textbf{Affects of Aging on the ACL}

As most tissues change with age, so too does the mechanical properties of the ACL tissue.\textsuperscript{37,41} Associated with aging, there is a decrease in strength and stiffness of the ACL. There is also a significant decrease in water content, and collagen concentration and synthesis. As the ACL ages the collagen fibril diameter gets smaller, as their concentration gets larger. “The increase in small collagen fibrils and the marked rise in their concentration may make the ligament more pliable.”\textsuperscript{41}
Also, it has been found that connective tissue playing a more passive mechanical role is of smaller diameter and a more uniform shape, while in contrary more active connective tissue is of larger diameter and a more nonuniform shape.\textsuperscript{37} This suggests that as a person ages and becomes less active collagen fibril diameter decreases, resulting in these age related changes.

**Bony Attachments**

The transition zone of fibrocartilage, which connects the rigid bone to the flexible anterior cruciate ligament, is a necessity to prevent stress concentration at the bony attachments.\textsuperscript{38} Mapping out the spatial orientation of the ACL we see that the ACL goes anteriorly, medially, and distally across the joint as it passes from the femur to the tibia. Along its course from origin to insertion the ACL twists on itself in a slight outward (lateral) spiral. This twist is not thought to be functionally relevant; rather it is believed that the twist is strictly a result of its bony attachments.

**Blood Supply**

The synovium, which forms a capsule around the ACL contains a rich supply of blood vessels.\textsuperscript{42} These blood vessels form a "web-like network of periligamentous vessels that ensheath the entire ligament."\textsuperscript{38,42} The ACL receives its main source of blood from the ligamentous branches of the middle genicular artery as well as some terminal branches of the medial and lateral inferior genicular arteries through soft-tissue origins (fat pad & synovium).\textsuperscript{38,42} The synovium and fat pad are important for the revascularization process following ACL injury.\textsuperscript{38,42,43} Therefore, utilization and preservation of these intra-articular soft tissues are important considerations in the repair and reconstruction of an injured ACL.
Nerve Supply

Although some are separate, many nerves are found accompanying vessels in the form of neurovascular bundles. Within the ACL four distinct sensory endings have been located. These include two types of ruffini end organs, pacinian corpuscles, and free nerve endings. We can conclude from the above information and from various other studies that, “in addition to its mechanical function the ACL also has a sensory afferent feedback mechanism known as proprioception.” It is through this mechanism that joint position sensibility, and muscular reflex stabilization is monitored. “Proprioception is a specialized variation of the sensory modality of touch and encompasses the neurosensibility of joint motion and position.” Proprioception serves as protection against excessive strain on the passive joint restraints during functional activity and provides prophylaxis to recurrent injury. Proprioception is intertwined with function, and “proprioceptive feedback is dependent upon the joint position and direction of movement.” Rupture of the ACL will significantly diminish the proprioceptive sensibility of the joint. It has been hypothesized that limb function relies more on proprioception input than on strength during activity. “The measures of proprioception are significantly correlated with function.”

Effect of Muscles

The ACL provides approximately 86% of the primary restraint to anterior tibial translation. Therefore; it is obvious as to why injury to this ligament is so detrimental to the stability of the knee joint. It has been documented in literature that females rely more heavily on ligamentous support in the knee, and males more on musculature support. Nonetheless, the muscles that cross the knee joint, the quadriceps, hamstrings, and
gastrocnemius have a significant effect on the ACL. Working against the ACL to promote anterior tibial translation are the quadriceps muscles, and working in its defense are the hamstring muscles.\textsuperscript{13,17,22,39} The quadriceps muscles exert the greatest amount of force at knee flexion angles between 30-40 degrees and full extension.\textsuperscript{12,13,39} Investigations of noncontact ACL injuries have revealed that a majority of these injuries occur at foot strike with the knee in an average flexion angle of 21 degrees.\textsuperscript{12} As foot strike occurs the quadriceps contract eccentrically producing maximal force within the muscle. Maneuvers such as landing and rapid deceleration produce eccentric contractions within the quadriceps. In addition unlike concentric contractions, eccentric contractions produce higher forces at higher velocities. Therefore, it is easy to see how a maximal eccentric contraction with the knee flexed approximately 21 degrees can produce enough force to tear the ACL. Furthermore, since females have been shown to be more quadriceps dominant and to have a decreased hamstring/quadriceps ratio they may be at greater risk for injury.\textsuperscript{3,13-15,17,39,44} This muscle imbalance among female athletes is just one of the many possible contributing factors to their increased incidence of ACL tears. Additional research on these imbalances needs to be completed before conclusions can be made.

**Hormonal Influence**

Female hormones have been thought to play a critical role in the structure and integrity of the human ACL. Studies have proven that female sex hormones have an effect on the composition and structure of a variety of tissues.\textsuperscript{13,33,35,45-47} For example, estrogen has an impact on the growth and development of bone, muscle, and connective tissue.\textsuperscript{35} It has also been shown to decrease the synthesis of collagen.\textsuperscript{33,46} Therefore it has
been proposed that during periods of fluctuation, female hormones also have an effect on the ACL. As a result the fluctuation of estrogen levels during the menstrual cycle may alter the metabolism, amount, type, and crosslinking of the collagen in the ACL. In order for this to be true the ACL must then have estrogen and progesterone receptors located on it to allow these hormones to manifest themselves.

Liu et al. described how immunohistochemical localization of both estrogen and progesterone receptors was performed on 17 human ACL specimens. Of these 17 specimens, which were obtained immediately at the time of surgery, 13 were from women and four were from men. The average age of the specimens was 57 years old, with a range from 18-78 years old. Eleven of the specimens were removed to allow completion of a TKA procedure; one was removed secondary to an above the knee amputation, and the remaining five were removed to allow for ACL reconstruction. The specimens were not considered to be positive for receptor sites unless there was clear evidence of intranuclear staining. The results of the study were nearly identical for both estrogen and progesterone receptor findings. Fourteen specimens stained positive for estrogen and fourteen also were positive for progesterone, while the remaining three showed equivocal staining. Of the 14 positive estrogen specimens 4/4 were from men, and 10/13 were from women. As compared to estrogen, 3/4 of the positive progesterone specimens were from men and 11/13 were from women. "Estrogen receptor-positive cells included fibroblasts, synoviocytes, and cells in the blood vessel walls of the ACL." The location of the progesterone receptors was found to be identical to that of the estrogen receptors.
The results of this study provide us with concrete evidence that estrogen and progesterone receptors do in fact exist on the ACL. As a result, there is a good possibility that these hormones either directly or indirectly, affect the structure of the ACL "by means of the identified target cells, such as synoviocytes, fibroblasts, and cells located in the blood vessel walls."\(^{35}\) The mechanism is still somewhat unclear as to how these fluctuating hormone levels may weaken the ACL, but administration of estrogen has been shown to acutely decrease both total collagen in rat tendon and fascia and collagen synthesis in rat periodontal tissue.\(^{47}\) Although this study didn't clearly explain how estrogen and progesterone concentrations affect the ACL, it did provide us with concrete evidence that these hormones do have receptor sites on the ACL. Knowing these hormone receptors exist is a necessity in order to determine how they affect the ACL because it is impossible for something to have an effect without first existing. Now that we have proof of their existence, chapter three will take a closer look at what effect fluctuating levels of these hormones may have on the structure and composition of the ACL.
CHAPTER III
HORMONAL INFLUENCE ON THE ACL

Most musculoskeletal injuries with the exception of ACL injuries are sport specific, rather than gender specific.\textsuperscript{8,17,18} As injury statistics are looked at one can clearly see that the number of women suffering ACL injuries is far greater than the number of men.\textsuperscript{7,8} Many studies have attempted to come up with answers for why this is the case.\textsuperscript{7,8,16,20,23,30,31,33} One factor, which has been under recent investigation, is the effect surging levels of female hormones have on the integrity of the ACL. At times during the menstrual cycle when estrogen and progesterone are at their highest levels the female athlete appears to be at greater risk for ACL injury.\textsuperscript{30,48} From the previous chapter we know that estrogen and progesterone receptors have been identified in the fibroblasts of the ACL, suggesting that female hormones have either a direct or indirect effect on its structure, via target cells. We will now take a closer look at the effect these hormones may have.

A clear understanding of the menstrual cycle is a necessity in order to comprehend how different phases of the cycle may predispose females to ACL injuries. The basis for this cycle is endocrine coordination between the hypothalamus, the pituitary gland and the ovaries. The way in which this coordination is achieved is through a complex interaction of several hormones. The menstrual cycle can be looked at as either
a 5-phase or 3-phase cycle. Some authors give a more detailed description of the normal menstrual cycle by separating it into five phases, while others describing the same cycle may simplify it into three phases. Whether it is broken down into 5-phases or 3-phases, the menstrual cycle is on average a 28-30 day cycle, varying from 24-35 days from woman to woman. For a better understanding of this cycle the following text takes an in depth look at each of the five phases.

**The Menstrual Phase**

The first phase, which occurs from days one to five, is the menstrual phase. It is during this phase that the female begins menstruating, and estrogen and progesterone are at low levels. As a result of these low hormone levels the hypothalamus and pituitary are stimulated causing a release of lutenizing hormone (LH) and follicular stimulating hormone (FSH). LH causes an increase in estrogen release by the ovaries; FSH stimulates the development of a follicle within the ovary.

**The Follicular Phase**

The follicular phase is the next to occur. This phase occurring from days six to twelve, is marked by the continual increase of estrogen and LH production. Through a negative feedback mechanism the rising estrogen levels cause the pituitary to significantly decrease its production of FSH, while at the same time prompting it to increase LH secretion.

**The Proliferative Phase**

Days 12-13 are considered the proliferative phase. It is during the beginning of this phase (day 12) that there is a surge in estrogen secretion causing a similar response in the production of LH. As estrogen begins to decline towards the end of this stage, there
is a resultant increase in the production of FSH and relaxin. Relaxin, which steadily increases until it reaches its peak near day 14, is thought to have systemic effects resulting in increased elasticity throughout the body’s connective tissue.⁶

The Ovulatory Phase

It is on day 14 of the normal menstrual cycle that ovulation occurs.⁴⁹ During this phase a mature egg is released from the follicle and ovulation takes place. It is also during this phase that the corpus luteum begins secreting progesterone, which prepares the uterus for pregnancy.

The Luteal Phase

The second half of this 28-day cycle is completed with the Luteal Phase. During this phase progesterone steadily increases and if fertilization does not take place it peaks around day 22.³¹,⁴⁹ As a result, the corpus luteum begins to shrink and there is a sharp decrease in progesterone secretion resulting in a breakdown and secretion of the endometrium. Also midway through this phase relaxin can again be detected, and peaks at day 20. On the 27th day of the cycle estrogen, progesterone, relaxin, FSH, and LH all reach their lowest levels, and on day 28 the cycle begins anew with the menstrual phase. Figure 1 summarizes the length and order of the five phases during a normal menstrual cycle.

Simplifying the cycle into three phases, we have the menstrual phase, the follicular phase, and the luteal phase. The only difference between the 5-phase and the 3-phase cycle is that with the five phases the follicular phase is divided into three separate parts, the follicular, the proliferative, and the ovulatory phase. Whether referred to in three phases or five phases the same changes are occurring.
Figure 1. Length and order of each of the five phases occurring during a normal menstrual cycle

From the above explanation we know that the female cycle involves a complex interaction of hormones, mainly estrogen, progesterone, and relaxin. Many studies have investigated the effect of these female sex hormones on a variety of tissues. All of these studies provide supporting evidence for the impact female hormones may have on the ACL. When looking at various studies done on rats we see that collagen and elastin metabolism in the rat’s uterus, joint capsule, periodontal tissue, skin, fascia, aorta, and tail tendon are all affected in the presence of female sex hormones.

The sex hormone that many studies tend to focus on is estrogen. Estrogen has been proven to have a significant impact on the growth and development of bone, muscle, and connective tissue. Estrogen has also been shown to decrease collagen synthesis in tendons, to increase collagen degradation in the aorta and fascia, and to decrease newly synthesized collagen in oral tissue. In addition relaxin receptors in the rat myometrium tend to increase in the presence of estrogen. Knowing that relaxin, a prominent hormone during pregnancy, increases the laxity of structures we can hypothesize that during surging levels of estrogen, relaxin may cause the ACL to become
more lax thus predisposing the female to injury. Also, when talking about the effect of female sex hormones one must not forget about progesterone. Progesterone has potential to act as a central nervous system anesthetic; it has also been shown to increase collagen content in the hip joint capsule.\textsuperscript{31,32,35}

It is reasonable to assume that the fluctuation and interaction of these hormones may have just as significant impact on the female ACL as they do on other tissues throughout the body. In fact, evidence for the impact of estrogen on the female ACL is described in a study done by Liu et al.\textsuperscript{33} This study specifically looked at the impact of estrodial on collagen synthesis in ACL fibroblasts. We can begin to see the importance of this if we first understand that collagen, which is produced by fibroblasts, plays a very crucial role in the load-bearing function of the ACL. Therefore, if fibroblast proliferation is decreased in the presence of estrogen then collagen synthesis will also be decreased. Liu et al\textsuperscript{33} expected to find just that, a decrease in both fibroblast proliferation and collagen synthesis of the ACL with rising levels of estrogen. The researchers investigated the influence of estrogen on the cellular metabolism of the ACL in rabbits. "The ACL fibroblasts were characterized by their proliferation and rate of collagen synthesis after exposure to various concentrations of estrogen. The techniques used were \textsuperscript{3}H\textsuperscript{[H]} thymidine incorporation, \textsuperscript{14}C\textsuperscript{[14]} hydroxyproline incorporation, and immunocytochemistry respectively."\textsuperscript{33} Estrogen levels comparable to those levels in the normal menstruating female were used (.025 to .3 ng/ml). For further information on the materials and methods of this experiment, please refer to the study itself. The results of this study clearly show the effects estrogen can have on fibroblast proliferation and collagen synthesis in the ACL.
Fibroblast Proliferation

“There was no significant difference calculated in fibroblast proliferation at concentrations between .025 and .25 ng/ml. However, a significant decrease in fibroblast proliferation was observed between log concentrations of .25 and 2.5 ng/ml, but not between log concentrations of 2.5 and 25 ng/ml.”\(^\text{33}\)

Collagen Synthesis

When comparing experimental and control groups it is evident that when the experimental ACL was treated with estrodial there was a decrease in collagen synthesis.\(^\text{33}\)

“At estrodial levels of between .025 and .25 ng/ml, collagen synthesis was reduced to 60% of the control. When the fibroblasts were tested with an estrodial level between 2.5 and 25 ng/ml, collagen synthesis was decreased to 50% of the control.”\(^\text{33}\)

We can conclude from this study that physiological levels of estrogen between .025 and .25 ng/ml as well as nonphysiological levels between 2.5 and 25 ng/ml have a negative effect on fibroblast proliferation and consequently collagen synthesis in the ACL.\(^\text{33}\) Therefore, as estrogen levels fluctuate throughout the female menstrual cycle, resulting changes are occurring in the metabolism of ACL fibroblasts. The structural and compositional changes that occur ultimately reduce the strength of the ACL, thus increasing the risk of injury to this ligament in the female athlete.

We can make further connections between the female menstrual cycle and ACL injuries as we look at a study done by Heitz et al.\(^\text{30}\) To date this was the latest study found regarding hormonal influence on the ACL. The purpose of their study was to “determine whether females experience significant differences in ACL laxity in conjunction with estrogen and progesterone surges during the normal 28-to 30-day menstrual cycle.”\(^\text{30}\)
The subjects in this study included seven females ranging in age from 21 to 32 years old with normal menstrual cycles (28-30 days). Subjects were not allowed to participate in this study if they had any of the following conditions: 1) bilateral knee pathology, 2) used hormone therapy, or 3) had a 90-degree tubercle-sulcus angle of more than 10 degrees. In this study they choose to break the menstrual cycle into three phases, naming phase I the menstrual phase (days 1-5), phase II the follicular phase (days 6-13), and phase III the luteal phase (days 14-28).

On days 1, 10, 11, 12, 13, 20, 21, 22, 23 estrogen and progesterone plasma levels were measured, along with ACL laxity using a KT-2000 knee arthrometer. “The follicular and luteal phases of the cycle were identified to establish peak values for these hormones. ACL laxity measurements were then compared with baseline and peak levels of estrogen and progesterone.” The results from this study, with permission from Ned A. Heitz, are included in Figure 2.

**Figure 2. Results from the study done by Heitz et al**

<table>
<thead>
<tr>
<th>Hormonal and ACL Laxity Changes Throughout The Menstrual Cycle (Mean ± SD)</th>
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<tbody>
<tr>
<td><strong>Phase of Menstrual Cycle</strong></td>
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<tr>
<td>Phase I (menstrual phase)</td>
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<tr>
<td>Phase II (follicular phase)</td>
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<tr>
<td>Phase III (luteal phase)</td>
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*Indicates significant changes compared with Phase I.

Figure 2. ACL laxity changes throughout phases I, II, III.

*Significantly greater than Phase I (P = .048). and III.

**Significantly greater than Phase I (P = .06).
Heitz et al\textsuperscript{30} found a significant increase in ACL laxity with surging levels of estrogen and progesterone during a normal menstrual cycle. Interestingly this study points out that just because there is an increase in the laxity of the ACL, it doesn’t mean the ligament is more susceptible to injury. “It is possible that increased ACL laxity may actually be the result of a protective mechanism designed to allow the ligament to elongate rather than rupture, in which case increased levels of circulating reproductive hormones may not be a contributing factor to increased female ACL ruptures.”\textsuperscript{30} This is the first known study to investigate this relationship. Further research in this area needs to be done. One limitation of this study lies in the fact that levels of the hormone relaxin were not measured and considered as a contributing factor. As Heitz et al\textsuperscript{30} point out future studies should not only consider relaxin as a factor, but should also attempt to identify relaxin receptors on the ACL.

As we continue our investigation of hormonal influence on the ACL we can look to yet another study, this one performed by Wojtys et al.\textsuperscript{31} These researchers performed a study with the intent of determining whether or not there is an increased incidence of ACL injuries at a specific point in the female monthly cycle. Twenty-eight women (average age 23± 11) with normal menstrual cycles and acute (less than 3 months) noncontact ACL injuries were studied. Each subject in the study was given a questionnaire in which they were asked to provide information concerning mechanism of injury, menstrual cycle, contraceptive use, and previous injury history. "A Chi square test was used to compute observed and expected frequencies of ACL injury based on three different phases of the menstrual cycle."\textsuperscript{31} Interestingly this study found that significantly more injuries than expected occurred during the follicular phase of the cycle.
specifically between days 10-14 when ovulation is taking place and estrogen is surging, and significantly less than expected occurred during the menstrual phase (days 1-9) of the cycle when hormone levels are at their lowest levels. "Because of estrogen's direct effect on collagen metabolism and behavior and because neuromuscular performance varies during the menstrual cycle it is logical to question the menstrual cycle's effect on knee injury rates."\textsuperscript{31}

Another interesting fact worth mentioning is that twenty out of twenty-eight (20/28) women reported having at least one premenstrual symptom (irritability, mood swings, food cravings, breast tenderness, or bloating), and stated that their athletic performance was hampered as a result of these premenstrual symptoms. Wojtys et al,\textsuperscript{31} point out that those women who do not suffer from PMS are less likely to sustain an injury to their ACL than symptomatic women. Various other authors have also reported that a woman's physical performance is decreased during the premenstrual phase leaving her more vulnerable to accidents and injuries during this phase of the monthly cycle.\textsuperscript{3,32,51,52} For example, analyzing data from a study completed by Moller-Nielson and Hammar\textsuperscript{52} of 1008 menstrual cycles in 86 female soccer players, we see that without regard to contraceptive status there was a significant (p<.05) increase in injury rate during the premenstrual and menstrual phases of the cycle. This increased susceptibility for traumatic injuries during the premenstrual and menstrual phases of the monthly cycle is especially true for women with premenstrual symptoms (PMS) such as irritability, swelling and discomfort in the breasts, and swelling and congestion in the abdomen. Also true of women who suffer from PMS is that they often demonstrate poorer performance of motor skills when compared to asymptomatic women. "Motor skill
deficits could make active neuromuscular mechanisms of the knee joint protection less effective.\textsuperscript{31} Moller-Nielson & Hammar,\textsuperscript{52} reported that neuromuscular changes that appear to be more prevalent in women suffering from PMS might be sufficient enough evidence as for why women have an increased likelihood of ACL injury during the premenstrual & menstrual phases of their cycle.

Why is this the case? No one knows for sure, but surging hormone levels could be an explanation. At this time in the monthly cycle when females perform tasks less efficiently, estrogen, relaxin, and progesterone levels are elevated. It is during the luteal phase that progesterone reaches its peak level before its steady decline. Progesterone may thus have important effects on certain abilities essential for performance, such as neuromuscular coordination, and reaction time. Progesterone has been linked as a causative factor to hyperventilation during pregnancy and during the luteal phase.\textsuperscript{32} This increase in ventilation has adverse effects on nonathletic females. A study showed that during this phase women were unable to reach as high a level of exercise as they were during the follicular phase. Yet another negative effect of progesterone is weight gain. This weight gain usually causes discomfort in the breasts, and a heavy dragging feeling in the abdomen; both of which affect performance of athletes and nonathletes alike.

Finding ways to treat and ultimately prevent PMS has been a difficult task. One way in which PMS has been halted is through the use of oral contraceptives (OC). Of the 28 subjects Wojyts et al,\textsuperscript{31} studied only five of the subjects were taking OC’s, but all five reported having minimal to no premenstrual symptoms, and felt that their athletic performance was not hindered during this phase of the cycle. This suggests that a stabilization of hormone levels throughout the cycle may be beneficial.
In taking a closer look at this relationship we must ask ourselves a couple of questions. First, do OC's have the potential to decrease the risk of injury by means of their effects on the hormonal cycle? And second, do OC's have an effect on joint laxity and neuromuscular coordination? Moller-Nielsen and Hammar\textsuperscript{32} concluded that, "there seems to be some support for a relationship between OC use and a decreased risk for sport injuries." They go on to say, "the relationship seems to be more obvious among women suffering from premenstrual symptoms and a preventive effect is also probable among women with ovulatory disturbances."\textsuperscript{32} To understand the relationships Moller-Nielsen and Hammar\textsuperscript{32} consider, one must not only thoroughly understand the menstrual cycle, but must also have a thorough grasp on the effect OC's have on the menstrual cycle.

Oral contraceptives contain synthetic steroids, which through negative feedback mechanisms inhibit FSH and LH production in the pituitary.\textsuperscript{32} This suppression of the pituitary thus prevents ovulation and development of the corpus luteum. Although ovulation and development of the corpus luteum are prevented, the exogenous steroids in the pill still allow endometrial growth, and during the fourth week of the cycle when placebo pills are taken this endometrial lining is then shed. As noted earlier the stabilization of hormone levels in a manner such as this, has the potential to decrease premenstrual symptoms. By decreasing premenstrual symptoms it has been proposed that a woman's chance of experiencing an ACL tear is also decreased.\textsuperscript{31,32} Another advantage of using OC is the fact that women loose less blood and thus have a decreased risk of experiencing anemia.\textsuperscript{32} Anemia can become a serious problem for American women as they loose one mg/day of iron through sweat, urine, and feces, and five mg/day
during menstruation while only replacing an average of two mg/day with their diet. The average female will therefore deplete her iron stores within 8-10 years. One consequence of anemia is that muscles will begin performing anaerobic work earlier, thus putting the muscles at higher risk for injury. The risk for bacterial infections is also increased in an anemic state because of reduced activity of white blood cells and defects in cellular immunity. Furthermore the estrogen component of OC's has been shown to make bone stronger and reduce the risk of stress fractures.\textsuperscript{32,33}

When looking at the advantages of OC's we must also look at the disadvantages. One disadvantage in particular is that OC's may actually increase joint laxity thus putting the female athlete at greater risk for injury.\textsuperscript{32} Additional disadvantages of OC's include side effects such as, headaches, dizziness, depression, and a possible increased risk of hypertension, breast cancer, and strokes.\textsuperscript{53} It is important to remember that OC's are not for everyone. OC's do affect some women more negatively than others, and there are possibilities of harmful side effects as listed above. Before taking OC's a proper gynecological examination should be done, and each individual woman should weigh her pro's and con's of taking the pill. At present there is at best a correlation between the decreased risk of ACL injury and OC use.\textsuperscript{32} Hopefully future research will reveal more concrete evidence of the effects OC's have on sports related injuries.

Overall it is important that athletes be educated at a young age, along with their coaches and various health professionals, about the increased risk of injury at specific times in the menstrual cycle, and most importantly about preventative measures which can be taken to decrease the incidence of ACL rupture among women.
CHAPTER IV

DISCUSSION/CONCLUSION

The ACL of the knee is like the goalkeeper of a soccer team. Both are very intricate parts of their respective bodies, providing stability and power to their team. Like a goalkeeper that defends the net from incoming soccer balls, the ACL defends the stability of the knee joint by acting as a primary restraint to anterior tibial translation. Just as a soccer team would be in distress and utter chaos without their goalie so, too would the knee joint be compromised without a healthy ACL. Furthermore just as the goalkeeper's goals against average is affected by the rest of the team's performance, so too is the stability of the knee joint affected by its surrounding muscles and ligaments.

Acting alone the ACL is unable to tolerate forces of one to two times the body weight associated with normal daily activities, let alone forces of up to five times the body weight associated with sports activities. Dynamic muscle stabilization protects knee joints, allowing knees to withstand such stress and strain. Knee joint surface geometry, the menisci, and secondary ligament stabilizers also play a role in functional stability, but those roles are minor compared with the stabilization provided by the quadriceps, hamstring, and gastrocnemius muscles at the knee. The hamstring muscles act as an agonist to the ACL, while the quadriceps act as antagonists. Since the quadriceps muscle is on average 50-100% stronger than the hamstring muscle, it is necessary that there be a "balance of power" between these muscle groups in order to
prevent an ACL rupture. Furthermore, females tend to be quadriceps dominant, so it becomes even more important for them to maintain adequate hamstring strength.

This balance of muscle power however, is not the sole explanation for why female athletes participating in sports such as soccer and basketball continue to experience noncontact ACL tears more frequently than their male counterparts. This brings us to the purpose of this paper, which, was to determine whether or not fluctuating female hormones predispose females to ACL injury. This question was addressed through a review of current literature regarding ACL injuries among females.

"The incidence, severity, costliness, and potential for long-term disability resulting from ACL tears make their prevention a high priority in the medical and research communities."54 In the majority of sporting activities the noncontact mechanism of injury, which often includes either rapid deceleration, pivoting with internal or external rotation, or landing with varus or valgus collapse of the knee is the most common mode of ACL rupture. In soccer this is especially true for the female athlete. When considering that the movements occurring most frequently in soccer are also the movements associated most closely with the noncontact mechanism of injury, it is obvious as to why. However, since soccer is a sport played by both genders one would expect to see equality of injury rates between males and females if this mechanism is the sole explanation. This, then brings up the question of, what about the female knee, specifically the ACL is different in this compromised state compared to the male knee?

Identifying the factors which, put females at risk is the first step in coming up with ways in which to prevent these disabling injuries. An array of extrinsic and intrinsic risk factors has been identified; many of which were covered in the introduction of this
paper. To review, a few of the extrinsic factors include, shoe-surface interface, conditioning, training, muscle strength, experience, coaching, and funding. A few of the combination factors include, neuromuscular efficiency, order of muscle recruitment, and endurance. Finally, a few of the intrinsic factors include, joint laxity, limb alignment, notch dimensions and ligament size, quadriceps dominance, and fluctuating female hormones. Investigation of these factors has provided little conclusive evidence. In the continued search for an answer to why females experience a greater number of ACL tears, fluctuating female hormones seems to be a valid hypothesis. The study of how female hormones affect the ACL has gained increasing popularity in recent years.

Before something can have an effect it must first exist. For this reason when studying the effect female hormones have on the ACL it is crucial to know that Liu et al\textsuperscript{35} have proved the existence of estrogen and progesterone receptors on the ACL. These receptors have been located in fibroblasts, synoviocytes, and cells in the blood vessel walls of the ACL. Because of the existence of these receptors researchers have found it logical to question the effect these hormones may have on the integrity of the ACL. In a study of rabbit ACL's, researchers found a significant decrease in collagen synthesis by ACL fibroblasts in the presence of increasing levels of estrodial.\textsuperscript{34} This suggests that surging levels of estrogen such, as during the late proliferative/early luteal phase of the menstrual cycle may in fact disrupt the structure and composition of the ACL causing women to be more susceptible to injury sometime after day 14 of the menstrual cycle.

Studies have confirmed this speculation, but research in this area is limited. From the studies accomplished to date, there is at best an association between the luteal phase
of the menstrual cycle and increased risk of ACL injury. In agreement, Wojtys et al.\textsuperscript{31} found an increased incidence of female ACL injuries during days 10-14 of the menstrual cycle when estrogen levels are surging, and the ACL is apparently more lax. Although this study was considered reliable it could not be validated. The reason being that researchers relied on the recall ability of their 40 subjects through a interviewer-administered questionnaire rather than taking blood or urine samples at the time of injury to more accurately document what phase of the cycle the participants were in. Nonetheless a strong association between noncontact ACL injuries and days 10-14 of the menstrual cycle was found indicating a need for further research to confirm these associations.

To date the only study found which looked at human ACL laxity in response to fluctuating hormone levels was executed by Heitz et al.\textsuperscript{30} They found a definite relationship between increasing ACL laxity and surging levels of estrogen and progesterone. Several authors have speculated that this increased joint laxity is to blame for the increased incidence of female ACL injuries.\textsuperscript{1,13,17,28} In opposition, I find it interesting to note that Heitz et al.\textsuperscript{30} bring up the possibility of this increased ACL laxity at various points in the menstrual cycle as being beneficial to the female athlete. They speculate the increase in laxity may actually be a protective mechanism allowing the ligament to elongate rather than rupture.

Besides their effect on the laxity of the ACL, hormones have also been blamed for the increased incidence of ACL injuries because of their effect on the neuromuscular system. Several studies have reported that women perform tasks less efficiently during the premenstrual and menstrual phases of their monthly cycle.\textsuperscript{31,52} It was also found that
PMS negatively affects a woman's ability to perform motor skills. "Motor skill deficits could make active neuromuscular mechanisms of knee joint protection less effective." Moller-Nielson and Hammar believe that the neuromuscular changes that appear to effect symptomatic women more often than asymptomatic, may be the reason for the increased incidence of female ACL injuries. Also of interest they note that women taking OC's had a lower injury rate suggesting a beneficial effect of hormone stabilization. Do OC's actually decrease a woman's chance of injury? Limited research regarding this question has left many wondering.

Although the study of the effect female hormones have on the ACL is new and forthcoming, there is enough evidence which, shows a strong correlation between the luteal phase of the menstrual cycle and occurrence of ACL injury. If we want to decrease the incidence of female ACL injuries then everyone involved must be aware of the possible causative factors. This includes all medical professionals, coaches, and female athletes and nonathletes alike. As physical therapists, we can impact this disabling injury through continued research efforts, and through furthering patient and community education and awareness. Because the benefits of exercise and sports which, decrease the risk of heart disease and stroke, lower blood pressure and cholesterol levels, and prevent obesity, out weigh the risk of ACL injury it is important that exercise continue to be a part of every women's life, even during this phase of the monthly cycle. If female athletes and coaches of women's teams are aware of the increased risk of injury at this time in the monthly cycle, they can implement preventative measures in hopes to decrease the incidence of injury.
Other than oral contraceptives, females have no control over their monthly menstrual cycle. Attempts have been made to link OC's to a decreased injury rate suggesting that a stabilization of hormones is beneficial to the female athlete, but without definitive research it is purely speculative. Even if OC's decrease injury rate they are not an option for every female. For this reason it is important to find a preventative method suitable for every woman. Caraffa et al\textsuperscript{55} provide convincing evidence for how this may be accomplished in their prospective controlled study of 600 soccer players from 40 semiprofessional or amateur teams. In this study they looked at the possible preventive effect of gradually increasing proprioceptive training on four different types of wobble-boards during three consecutive soccer seasons. Half of the group, or 300 players trained 20 minutes per day with five different phases of increasing difficulty, while the control group trained as they normally would without any balance training. By the end of this study researchers found an incidence of 1.15 ACL injuries per year per team among the control group, and .15 injuries per year per team for the proprioceptively trained group (p< .001).\textsuperscript{55} These results show that proprioceptive training does significantly reduce the incidence of ACL injuries. Unfortunately this study did not specify whether the 600 soccer players were male or female, but the study was based in Italy and women's soccer is still in it's genesis stage there, so I'm assuming that the majority if not all of the players were men. Although it is unfortunate for the scope of this paper that the subjects were likely not female players, I think it is reasonable to assume female players would have the same benefits from this type of training.

Proprioceptive training is definitely within the realms of physical therapy. Physical therapists have the knowledge and skills to devise a proprioceptive program,
which they can then begin encouraging female athletes and coaches to implement as part of their regular training regime. These programs should begin at early ages, and would be beneficial for both genders.

Also within the realms of physical therapy prevention is muscle strengthening, and technique modification. Since studies have shown that elite female athletes have quadriceps dominance as opposed to a hamstring dominance, which is seen in males, it is necessary that the female leg be strengthened in a balanced manner. As Mary Lloyd Ireland, MD, president of Kentucky Sports Medicine Clinic states, "hamstrings, lower back, and hips, all need to be trained diligently to achieve strength parity. Try to balance strength among the muscles in and around the knee."22

When considering that the majority of female ACL injuries occur as a result of the noncontact mechanism of injury, one can see the importance of teaching correct technique modification. The body mechanics associated with the noncontact mechanism of injury can be referred to as the position of injury.11 Table 2 compares the body mechanics of the position of injury to the position of safety.

Training sessions should be set up to teach coaches, trainers, athletes, and health professionals landing and cutting maneuvers, which incorporate these safety mechanics in order to put less strain on the knee. Upon implementing a prevention program such as this, two Division I Kansas' basketball teams "reduced the rate of ACL tears by 89% in two years."11 As the saying goes, "you play how you practice", so coaches should teach and enforce these safe body mechanics at all times during an athletes career, and physical therapists and other health professionals should educate the community on this important issue.
Table 2. Body mechanics of the position of injury, and of the position of safety.

<table>
<thead>
<tr>
<th>Position of Injury</th>
<th>Position of Safety</th>
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<tbody>
<tr>
<td>Back</td>
<td>Normal Lordosis</td>
</tr>
<tr>
<td>Flexed and Rotated to the Opposite Side</td>
<td>Flexed, Neutral Adduction/Abduction, and Neutral Rotation</td>
</tr>
<tr>
<td>Hips</td>
<td>Flexed</td>
</tr>
<tr>
<td>Adducted and Internally Rotated</td>
<td>Flexed</td>
</tr>
<tr>
<td>Knees</td>
<td>Flexed</td>
</tr>
<tr>
<td>Extended With a Valgus Moment</td>
<td>Flexed</td>
</tr>
<tr>
<td>Tibia</td>
<td>Neutral</td>
</tr>
<tr>
<td>Externally Rotated</td>
<td>Neutral</td>
</tr>
<tr>
<td>Landing Pattern</td>
<td>Controlled Two-Footed Land</td>
</tr>
<tr>
<td>Uncontrolled One Footed Land</td>
<td>Controlled Two-Footed Land</td>
</tr>
<tr>
<td>Weight</td>
<td>Midline with Weight Balanced at Mid-Foot</td>
</tr>
<tr>
<td>Forward With Weight on Balls of Feet</td>
<td>Midline with Weight Balanced at Mid-Foot</td>
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</table>

A few other key prevention ideas include, pre-sport conditioning, training in techniques specific to the sport, and competing against others of similar skill level. These prevention ideas obviously won't eliminate ACL ruptures, but they may prove to substantially decrease the increased incidence of injury seen in females.

In pulling this information together and tying the final knots, we see that unfortunately there are still a lot of loose threads to be woven. Although it is likely that more than one factor claims this troubling phenomena, substantial evidence has pointed us in the direction of a hormonal based cause. The results of studies already published regarding female ACL injury and fluctuating female hormones, provide sound justification for further research. At the present time there is at best an association between the menstrual cycle and risk of ACL injury. For this reason additional prospective studies with larger sample sizes should be executed to determine exactly
when during the menstrual cycle most injuries occur. Other areas of research, which may prove to be beneficial, include studies, which look at the hormonal effect on the integrity of the ACL, and also studies, which attempt to identify relaxin receptor sites on the ACL. These are just a few examples of the many areas that would benefit from further research. Further research regarding preventative measures would also be extremely beneficial especially for today's competitive female athlete.
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