The Effect of Serum Estradiol (E₂) and Progesterone (P₄) Levels on Knee and Ankle Joint Laxity

INTRODUCTION:
Epidemiological studies have revealed a two to eightfold increase in the incidence of anterior cruciate ligament (ACL) injuries among women athletes compared to male athletes (1,2). Biomechanical, anatomic, neuromuscular and hormonal factors have been implicated as predisposing an individual to knee ligament trauma, and yet there is very little evidence that identifies one or a combination of these factors as putative risk factors for knee ligament injury. Myklebust (3) et al documented a higher incidence of injuries among female athletes in the days prior to and just after ovulation. Likewise, Wojtys demonstrated that women athletes involved in non-contact sports were at increase risk of ACL injury during the ovulation phase of the menstrual cycle. These findings introduce the hypothesis that the biomechanical behavior of the ACL changes during the menstrual cycle, and predisposes the athlete for injury.

The aim of this investigation was to measure serum levels of estradiol (E₂) and progesterone (P₄), knee and ankle joint laxity (indirect measures of the biomechanical behavior of ligaments) during the menstrual cycle. The hypothesis was that knee and ankle joint laxity increases throughout the menstrual cycle as serum concentrations of estrogen and progesterone are elevated.

METHODS:
Both female and male (control) collegiate athletes were approached and informed consent was obtained. There were two groups: 10 women with normal menstrual cycles (mean age 20.7, range 18-26) and 5 males (mean age 24.8, range 19-28). In the month prior to testing the OvuQuick (Quidel Corporation, San Diego CA) urine test was used for the women to confirm the exact time of ovulation.

Knee and ankle laxity and blood concentrations of estradiol and progesterone were measured for females at four consecutive visits throughout the menstrual cycle and for males at equivalent time intervals. For the females, the visits corresponded as follows: visit 1 (early follicular phase; days 1-3), visit 2 (late follicular phase; days 11-13), visit 3 (mid-luteal phase; days 20-22) and visit 4 (late luteal phase; days 27-28). Baseline concentrations of estrogen and progesterone were obtained among the women during the early follicular phase of the following cycle (visit 5) to validate that a normal cycle was completed. Serum concentrations of estrogen and progesterone were determined using radioimmunoassay.

Knee and the ankle joint laxity were measured at each visit. Knee laxity was measured with the KT-1000 Knee Arthrometer (MedMetrics Corp, San Diego CA). Anterior-posterior (A-P) laxity was defined as the total A-P translation between the shear loads of ~90 N (posterior) and 130 N (anterior). At each visit, subjects underwent three sequential measurements of each knee.

Ankle laxity was measured by standard stress radiography, which included measurements of the anterior drawer and talar tilt. The Telos device (Telos Corp., Greisheim, Germany) was used to apply 150 N forces to the ankle joint. All x-rays were obtained and marked by the same technician and numbered to blind the measurement procedure. The x-ray films where analyzed using a digitizing table DigiPad type 5A (GTCCO Corp, Columbia MD). At each visit, anterior drawer (neutral and anterior load) and talar tilt views (neutral, inversion load, and eversion load) were obtained. Only the right ankle was used to measure ankle laxity to minimize exposure of the subjects to radiation.

The anterior drawer measurement used a reference point at the posterior border of the tibial articular surface. Translation was measured as the shortest distance between this reference point and the talar articular surface, and laxity was determined as the difference between loaded and neutral films.

The talar tilt measurement used a line fit to the dome of the talus and a line fit to the roof of the ankle mortise. Total talar tilt was measured as the total angular change between the inversion and eversion positions.

A paired t-test for means was used to compare joint laxity values between visit 1; the early follicular phase when E₂ is low and visit 2; late follicular phase when E₂ is high. A paired t-test for means was used to compare laxity values between visit 1; early follicular phase when P₄ is low and visit 3; mid luteal phase when P₄ is high. The p-value was adjusted for multiple comparisons.

ESSENTIAL RESULTS:
Anterior-posterior knee laxity did not change for the females between visits 1 and 2 (p=0.45) and did not change between visits 1 and 3 (p=0.27) (figure 1). Likewise, there were no changes for the males.

Ankle laxity, as measured by the anterior drawer, did not change for the females between visits 1 and 2 (p=0.48) and did not change between visits 1 and 3 (p=0.41) (figure 2). Similarly, the anterior drawer did not change for males.

Ankle laxity, as measured by total talar tilt, for females did not change between visits 1 and 2 (p=0.35) and did not change between visits 1 and 3 (p=0.31) As well, there were no changes in talar tilt for males.

**DISCUSSION:**
Our investigation does not support previous research that has documented a positive correlation between knee laxity and serum levels of estradiol. The concentrations of serum estradiol may not be high enough in our sample to produce the fluctuations in knee laxity seen in other reports. The mean concentrations of estradiol during follicular phase in our group of athletes was 171.4 pg/ml compared to 778 pg/ml in work by Heitz. These differences in estradiol concentrations may explain why our findings are different.

Although knee and ankle laxity appeared to be greater among females than males we found that laxity does not fluctuate during a normal menstrual cycle. Our results are in agreement with an unpublished report that revealed no significant changes in anterior translation of the tibia throughout different faces of the menstrual cycle (Svein Barene).

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**REFERENCES:**
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