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Menstrual Cycle Variations of Corneal Topography and Thickness

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ABSTRACT

Two studies were performed to investigate dimensional stability of the cornea throughout the female menstrual cycle. In the first study, changes of corneal curvature, topography, and thickness were measured for six women for one complete menstrual cycle. Steepening of horizontal and vertical curvatures occurred at the beginning of the cycle, and flattening occurred after ovulation. Corneal thickening occurred on the second day of the cycle and around the time of ovulation, then thinning and another slight thickening on day 21. In the second study, more detailed information was sought on the timing of corneal thickness changes throughout any cycle. Corneal thickness was studied for two subjects throughout three consecutive cycles. Both subjects showed a slight decrease in thickness toward the end of the menses; thickening occurred at ovulation followed by thinning. Thickening also occurred 4 days after ovulation. Consideration of changes in urine levels of estrogen and pregnanediol suggests that rises in estrogen are accompanied by increases in corneal thickness.

Key Words: corneal thickness, corneal topography, menstrual cycle, hormone levels, estrogen, pregnanediol

During the female menstrual cycle a number of physiological changes occur. These changes may be accompanied by variations in corneal shape and thickness possibly affecting contact lens wear and comfort.

A number of studies[1-6] have attempted to correlate changes in corneal parameters with other changes occurring in the menstrual cycle. Leach et al.[2] found that the time course of corneal thickness changes compared well with that of plasma concentrations of estrogen and progesterone reported in the literature. They observed no significant changes in corneal curvature. Feldman et al.[5] and Soni[6] found that corneal thickness was lowest just before ovulation. These observations have not been supported by Manchester,[1] El Hage and Beaulne[3] or Hirji and Larke,[4] all of whom report no significant changes in corneal thickness with time in the cycle. Ideally, the study of corneal variations during the menstrual cycle would require control over other influences on corneal dimensional stability, such as time of day,[7] as well as knowledge of exact times within any menstrual cycle. The present study is aimed at such analysis.

METHODS

The corneal parameters considered in this study are horizontal and vertical central corneal curvature measured with a Bausch & Lomb keratometer, a complete topographical assessment achieved with the autocollimating photokeratoscope of Clark,[8] and central and peripheral corneal thickness using a modified Haag-Streit pachometer attached to a Nikon slitlamp.[7] Corneal topography is specified by three variables: (1) photokeratoscope sphere radius, which is the radius of the sphere best fitting the central three millimeters of the cornea in the initial photokeratoscopic analysis; (2) radius (R); and (3) asphericity (Q) values from a rotationally symmetric mathematical model fitted to the human cornea.[9] The R value provides a measure of the instantaneous curvature at the corneal apex, and the Q value specifies the type of conicoid best representing the cornea.[7] Corneal thickness was measured centrally and at 20° and 40° nasally and 20° and 40° temporally.

Two studies were carried out to investigate

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the stability of corneal parameters throughout the menstrual cycle.

First Study

Six women, all aged 19, participated in the first section of the study. Corneal dimensions were measured for each subject on weekdays for at least one full menstrual cycle, at the same time of day for any subject. Cycle lengths varied from 20 to 44 days, with a mean of 33 days. To overcome the considerable variability of cycle lengths between subjects, the following considerations were used in analyzing the data. Inasmuch as the time from ovulation until the end of the cycle is reasonably constant (about 14 days),[10] the last 14 days of all cycles are comparable provided all subjects had ovulatory cycles. Also, the last 5 days before ovulation when the level of estrogen is increasing (see Fig. 1) and the times just before the menses and during the menses should also be comparable. Any variation in cycle length is due to variations in the time between the beginning of menstruation and the time of ovulation.[10]

For each of the six subjects, the mean value of each corneal dimension was calculated. The variation from this mean was then calculated for 3 days before and 6 days during the menses (in this group of subjects the duration of the menses was 5 or 6 days). Variation from this mean was also calculated for each of the 20 days counted back from the end of the cycle. Thus, the sections compared for the six subjects are: (1) time before menstruation during which urine levels of estrogen and pregnanediol are low[11, 12] (urine concentrations of hormones are used instead of serum levels because urine levels give a representative picture of hormone levels throughout the day whereas serum levels can vary at different times within the one day according to a personal communication from M. A. Smith); (2) time of the menses (days 1 to 5 or 6); (3) time before ovulation (equivalent to days 9 to 13 in a 28-day cycle, during which the urine level of estrogen is increasing[11, 12]); (4) ovulation (approximately day 14 or 15 in a 28-day cycle; here urine levels of estrogen are at a maximum[11, 12]); and (5) time from ovulation until the beginning of the next cycle (pregnanediol peaks during this time, and estrogen shows a second peak, lower than that at ovulation[11, 12]).

Second Study

In the first study, it was impossible to determine whether or not the women experienced anovulatory cycles. To provide more detailed information, a second study was performed on corneal thickness of two subjects for three consecutive cycles. One of these subjects (aged 20) kept a record of her cycles only. The other, who was aged 26, was able to measure her basal body temperature and assess cervical mucus to determine the time of ovulation.[10, 11] Billings and Westmore[10] state that at the time of ovulation, or shortly after, there is a small but definite elevation in body temperature due to increase in the concentration of the hormone progesterone. A significant shift is at least 0.2°C (approximately 0.4°F).

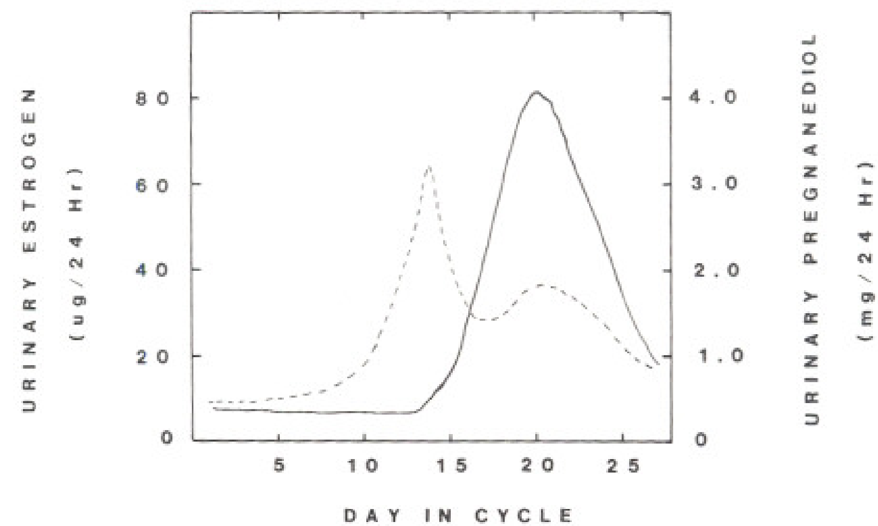

FIG. 1. Variation of urinary estrogen and pregnanediol levels during the female menstrual cycle (data of G. Smith, personal communication). Solid line, pregnanediol.

RESULTS

First Study

The changes in horizontal and vertical central corneal curvature with time in the menstrual cycle for the mean of the six subjects are shown in Figs. 2 and 3. Steepening of both horizontal and vertical curvatures as indicated by the keratometer occurs at the beginning of the cycle, and flattening occurs after ovulation. Vertical radii show less stability than horizontal radii.

Variations of photokeratoscope sphere radius and R and Q values for the mean of the six subjects are shown in Figs. 4 to 6. Neither photokeratoscope sphere radius nor R value variations show similarity to radius variations as determined by the keratometer. Both exhibit much larger fluctuations than do the keratometry values. There is a decrease in Q value at the beginning of menstruation followed by an increase; there is an increase a few days after ovulation. The variation in corneal thickness for the mean of six subjects at the five corneal locations during the cycle is shown in Fig. 7.

Second Study

The corneal thickness results for the two subjects are shown in Figs. 8 and 9. The mean results for subject 2 for her three cycles are shown in Fig. 10. (This was done for subject 2 because she was able to keep records of basal body temperature and cervical mucus, and these indicate that ovulation had occurred in each of these cycles.) Because subject 1 was not able to keep a record of her basal body temperature or cervical mucus, it is difficult to determine exactly her times of ovulation. However, as the time of ovulation usually occurs 10 to 16 days

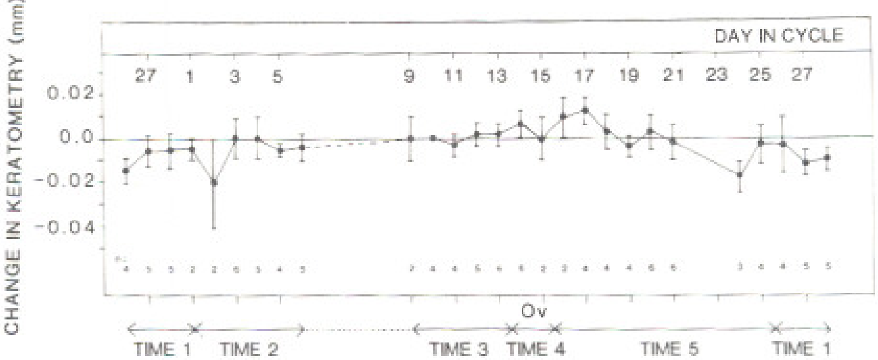

FIG. 2. Variations of horizontal corneal radius of curvature (from keratometry) during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day; positive values indicate corneal flattening.

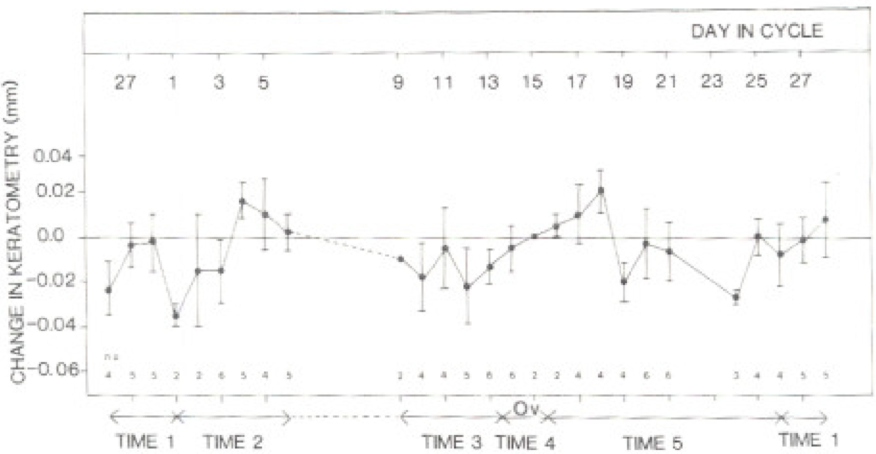

FIG. 3. Variation of vertical corneal radius of curvature (from keratometry) during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day; positive values indicate corneal flattening.

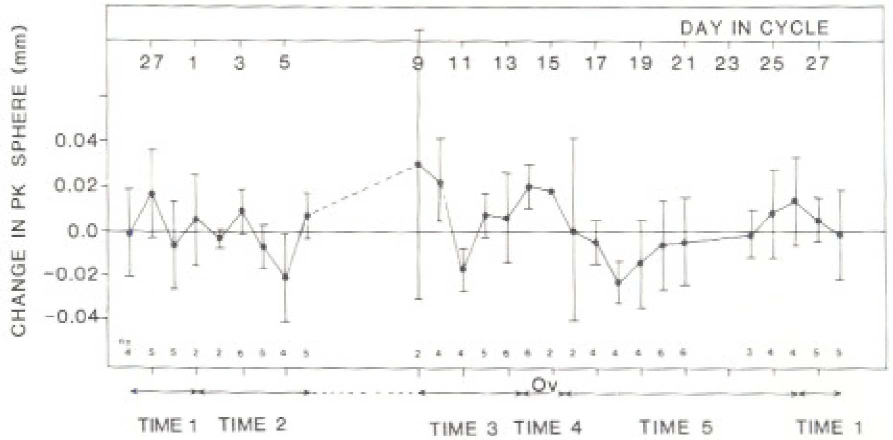

FIG. 4. Variation of photokeratoscope sphere radius during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day; positive values indicate corneal flattening.

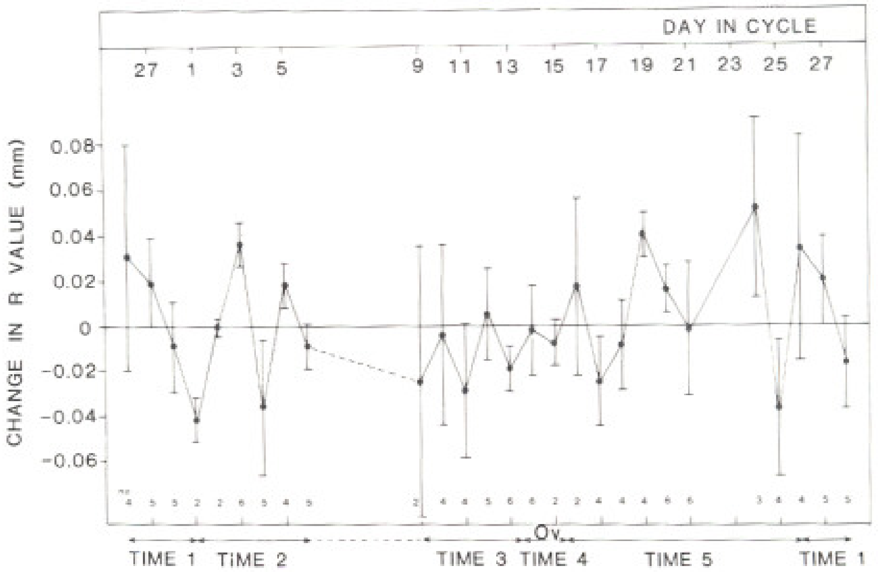

FIG. 5. Variation of R (radius value from the rotationally symmetric mathematical model to the cornea) during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day; positive values indicate corneal flattening.

before the beginning of the next cycle,[10] approximate times can be determined and are labelled "Ov" in the graphs. For subject 2, the times of ovulation could be more easily determined. For the mean data of both eyes of subject 2 (Fig. 10), there is approximately a 5.6% increase in corneal thickness from day 15 to day 16. This is slightly more than the average corneal swelling observed overnight by Mertz[13] and exceeds the range of accuracy of pachometry readings[7] (± 0.002 mm or ± 0.4%).

Some of the observed changes correspond to those found for the means of the six subjects followed in the first study. For both groups, corneal thickening occurs before menstruation; changes occur around ovulation, and a change also occurs about 5 to 7 days before the commencement of the next cycle. However, these results are still inconclusive. Billings and Westmore[10] report that 6 to 11% of cycles in healthy women are anovular. All cycles for the second subject in the second study were ovula-

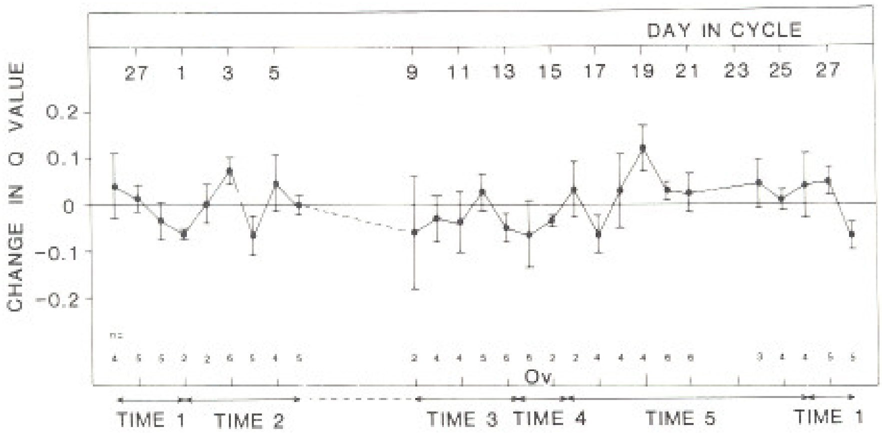

FIG. 6. Variation of Q (asphericity value from the rotationally symmetric mathematical model to the cornea) during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day.

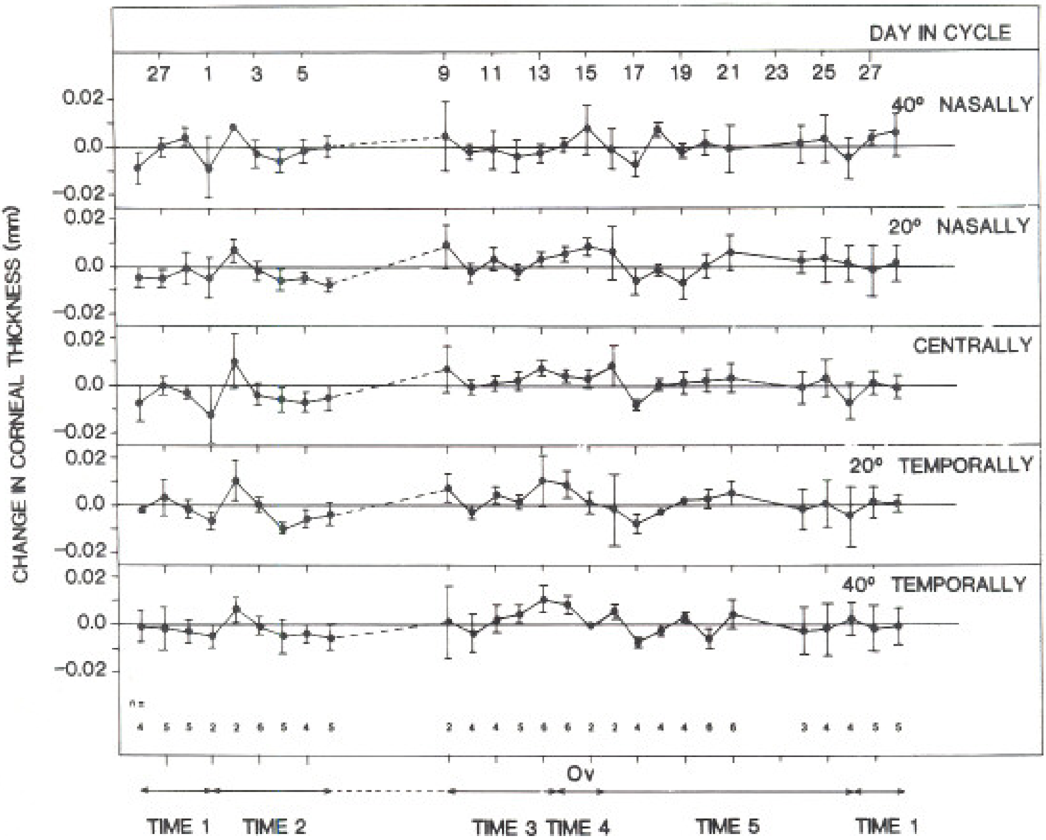

FIG. 7. Variation of central and peripheral corneal thickness during the female menstrual cycle for the six subjects in the first study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of subjects contributing to the result on any day; positive values indicate corneal thickening.

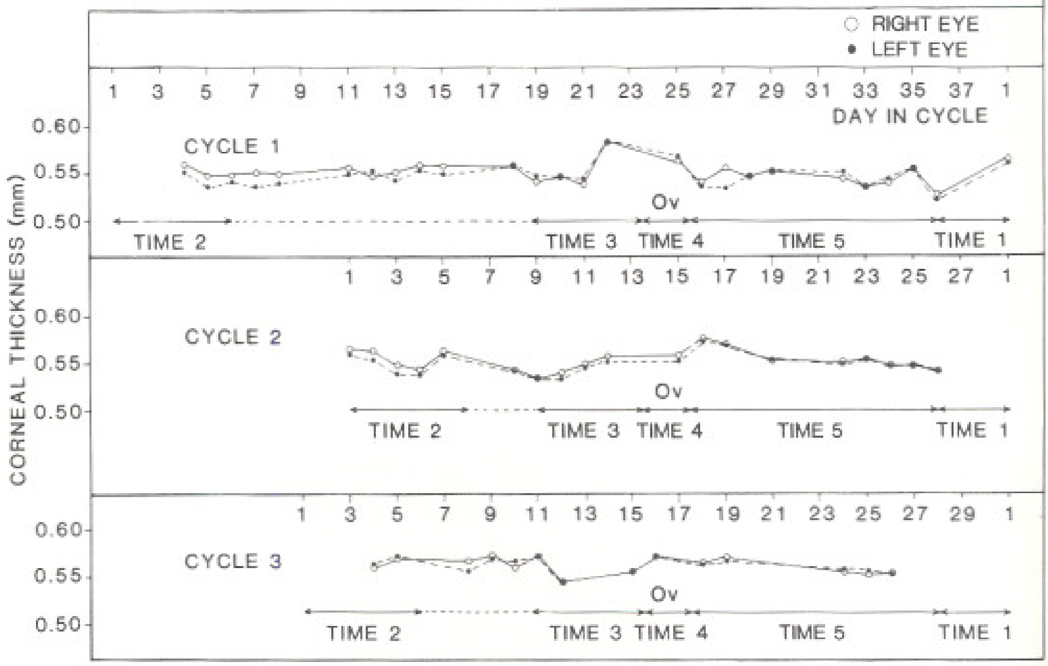

FIG. 8. Variation of central corneal thickness during the female menstrual cycle for subject 1 in the second study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. Positive values indicate corneal thickening.

tory, and so the most accurate description of corneal change can be achieved from a summary of her results:

1. during the menses, corneal thickness is very stable (here, urine levels of estrogen and pregnanediol are constant[11, 12])
2. corneal thickness increases on the first 2 days after menstruation (small, gradual increase in estrogen)
3. then follows a decrease in corneal thickness, then constant thickness, then an increase in thickness at ovulation (urine estrogen peaks at ovulation)
4. increase in corneal thickness 4 days after ovulation (this was the maximum thickness observed for subject 2, and accompanies increases or peaking of urine estrogen and pregnanediol; this is the second, but lower estrogen peak)
5. decrease in thickness, then fluctuations with two further peaks—the first 7 days after ovulation, and the second before menstruation (urine estrogen and pregnanediol decrease 6 to 7 days before menstruation)
6. corneal thickness increases on the last day of the cycle (sharp decreases in urine estrogen and pregnanediol).

DISCUSSION

These results show some similarities to those of other authors;[2, 5, 6] corneal thickening before the onset of menstruation was observed by Feldman et al.[5] and Soni,[6] but in the results of Soni this was the time when the cornea was at its thickest value. However, there are a number of discrepancies between the results of all these studies, and these inconsistencies can be attributed, at least in part, to the methods of analysis. For example, Hirji and Larke[4] divided their subjects' cycles into nine parts and Soni[6] normalized cycles to a 28-day cycle. These methods of analysis may not necessarily correlate comparable times in the cycle between subjects. If we consider that the time from ovulation until the end of the cycle is fairly constant at approximately 14 days, and there are two subjects, one with a 23-day cycle, the other with a 35-day cycle, the subject with the 23-day cycle would be expected to ovulate in the fourth of her nine groups (about day 9), whereas the subject with the 35-day cycle would ovulate in the sixth of her groups (about day 21). Soni's[6] normalization of data would create similar problems.

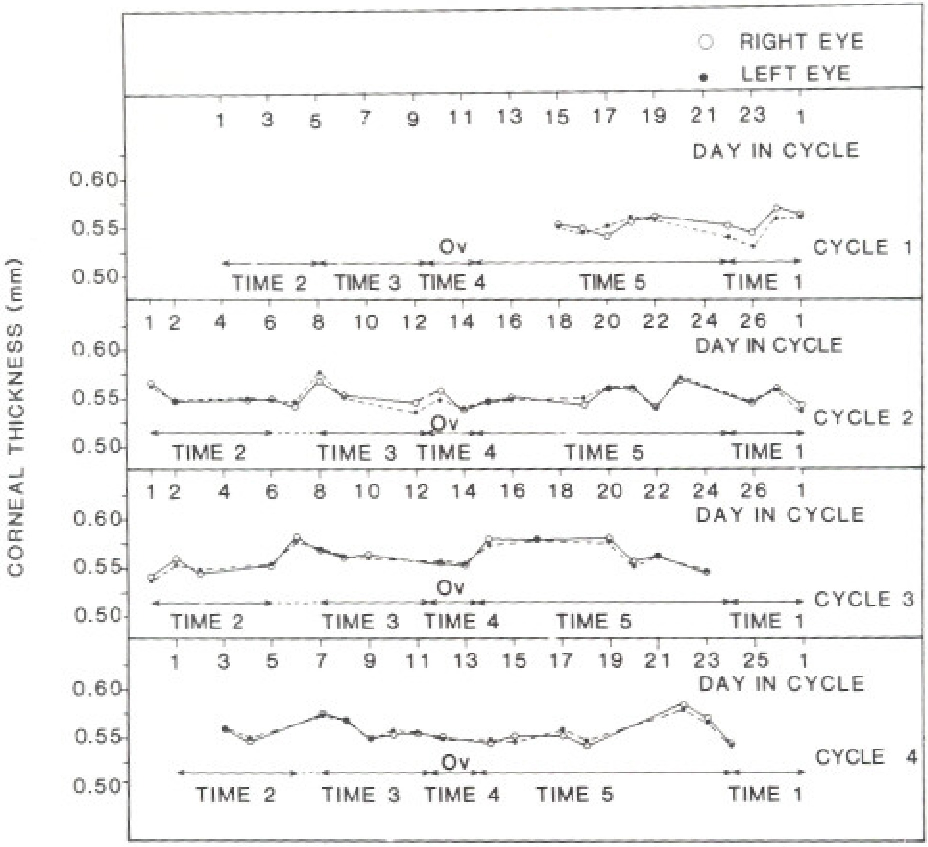

FIG. 9. Variation of central corneal thickness during the female menstrual cycle for subject 2 in the second study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. Positive values indicate corneal thickening.

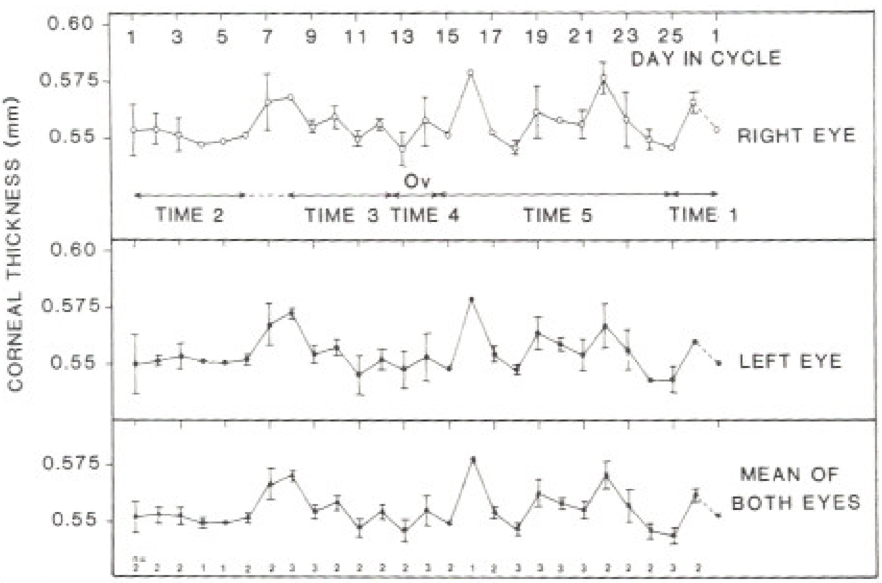

FIG. 10. Mean variation of central corneal thickness from three menstrual cycles of subject 2 in the second study. Definitions of "Time 1" to "Time 5" and "Ov" are described in the text. n, the number of cycles represented by each point; positive values indicate corneal thickening.

From these observations and results, it appears that corneal thickness, and possibly shape, do alter during the female menstrual cycle, and that these changes are often concurrent with changes in estrogen levels; at most times when urine estrogen rises, corneal thickness also increases.

It is noteworthy that the increase in corneal thickness that occurs with increased estrogen may be associated with other effects of estrogen. The main action of estrogen is on the state of hydration of tissues and on sodium and chloride balance.[14] Estrogens cause an increase in weight of the tissues of the uterus by an increase in extracellular fluid,[15] and large doses of estrogens enhance reabsorption of sodium leading to water retention and edema.[16]

It is clear, however, that for any given subject, the timing of corneal variations will be intimately related to landmarks in her menstrual cycle and generalizations about the responses are not possible. Because of the individual nature of these cycles, the effects reported above need to be considered more by qualitative assessment than rigorous statistical analysis. The difficulties associated with further data collection are numerous. First, subjects must not be taking oral contraceptives or be pregnant. Second, subjects must not be contact lens wearers or exhibit any corneal pathology. Third, subjects must be willing to attend daily throughout at least one cycle, and be able to assess basal body temperature or cervical mucus or both to determine times within a cycle.

In general, the changes observed in corneal thickness and curvature observed in this study extend our knowledge of biological rhythms. They may also have clinical significance in the contact lens situation where changes in corneal curvature or shape could alter the fit of a contact lens; additionally, the changes in corneal thickness which are normal during a cycle, when compounded by possible changes in thickness due to contact lens wear, may cause significant problems.

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