Diurnal Variation of Corneal Thickness in the Cat
Tailoi Chan-Ling, Nathan Efron, and Brian A. Holden

Central corneal thickness of both eyes of seven cats was measured hourly for 72 hr using ultrasonic pachometry. The mean corneal thickness was 569 ± 36 μm (mean ± SD), and the diurnal variation was 49 ± 14 μm (8.6% of corneal thickness). In a separate experiment, the corneal thickness of one eye of each of five cats was measured following 2 hr of natural sleep; 2¼ hr after eye opening, the corneas had thinned an average of 43 ± 22 μm. The authors conclude that corneal swelling induced by eye closure during periods of sleep is the prime determinant of the diurnal variation in cat corneal thickness. In studies where corneal thickness is to be monitored over a period of time, it is possible to control against this large diurnal variation by ensuring that the cat is active for a period of two hours prior to pachometry measurements. Invest Ophthalmol Vis Sci 26:102-105, 1985

The cat is becoming an increasingly popular model of corneal physiology, primarily because its endothelial function is similar to that of humans.1,2 This cooperative, hardy animal is, for example, useful in the study of aspects of corneal transplantation that have direct application to the treatment of human corneal disease.2

Changes in corneal thickness are often used as an index of corneal metabolic integrity. It is therefore necessary to determine the diurnal variation of corneal thickness in the cat if it is to be used as a model for human corneal thickness. Such normative data will aid in the interpretation of studies that present repeated measurements of corneal thickness.

It has been demonstrated in both the human3,4 and rabbit5,6 that eye closure is associated with increased levels of corneal hydration. Such a mechanism may also exist in the cat and thus produce diurnal changes of corneal thickness. The aim of this study was to document the diurnal variation of corneal thickness in the cat and to investigate the possible role of eye closure.

Materials and Methods. A VIDA 55 ultrasonic pachometer with a No. 55-1 hand-held transducer (Visual Instruments Distribution Associates; South Laguna, CA) was used to measure corneal thickness.

This instrument, which yields reliable measurements of corneal thickness in animals,7 was calibrated assuming a speed of sound in cat corneal tissue of 1550 m/s.

The transducer was placed in gentle apposition with the central cornea while the cat was restrained and its lids retracted. Anesthesia was not used, and the animals displayed no visible signs of distress. Corneal thickness was taken as the mean of five consecutive measurements. The average standard deviation for the five measurements was ±4 μm (0.7% of corneal thickness). Examination with fluorescein following this procedure revealed minor punctate staining in 11 eyes, which resolved within 6 hr.

Diurnal variation of cat corneal thickness: Four male and three female healthy adult cats were used in this study (Table 1). The animals were free to roam around an enclosure (maintained at 22°C and 50% humidity) under natural lighting through a large frosted glass window. This experiment was conducted over a period of 3 days in February 1983 in Sydney, Australia; sunrise was at 6:22 AM and sunset at 7:56 PM.

Two investigators (each with an assistant) working alternate 12-hr shifts measured the corneal thickness of each eye of the seven cats every hour for 72 hr. It took approximately 2 min to measure both corneas of a single cat. Prior to each measurement session, the overall level of activity and eyelid status of the cats was rated on an arbitrary scale from 0 to 4: 0—no activity, all eyes closed; 1—no activity, most eyes closed; 2—little activity, most eyes open; 3—moderate activity, all eyes open; 4—active, all eyes open.

To test for errors due to interobserver differences, the corneal thickness of both eyes of a group of 10 cats was determined by each investigator consecutively. The two observers simultaneously assessed the level of activity of the group for 30 sec. This procedure was conducted on 20 occasions over a 3-day period. The mean interobserver difference in determining the corneal thickness of 20 eyes was 5 ± 6 μm (0.9% of corneal thickness). Assessment of the level of activity...
Table 1. Central corneal thickness of the cat

<table>
<thead>
<tr>
<th>Cat</th>
<th>Sex</th>
<th>Age (months)</th>
<th>Weight (Kg)</th>
<th>Corneal thickness (μm)</th>
<th>Mean</th>
<th>Diurnal variation**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RE</td>
<td>LE</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>F</td>
<td>41</td>
<td>2.5</td>
<td>604 ± 15†</td>
<td>600 ± 16</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.5</td>
<td>560 ± 9</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>F</td>
<td>30</td>
<td>3.5</td>
<td>554 ± 7</td>
<td>560 ± 9</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>M</td>
<td>15</td>
<td>2.5</td>
<td>555 ± 17</td>
<td>562 ± 15</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>M</td>
<td>15</td>
<td>3.0</td>
<td>552 ± 18</td>
<td>557 ± 20</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>M</td>
<td>27</td>
<td>3.0</td>
<td>622 ± 12</td>
<td>625 ± 14</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>F</td>
<td>13</td>
<td>2.5</td>
<td>506 ± 12</td>
<td>509 ± 13</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>M</td>
<td>13</td>
<td>2.5</td>
<td>577 ± 11</td>
<td>579 ± 11</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD 22 ± 11* 2.8 ± 0.4* 567 ± 38‡ 570 ± 24 Both eyes: 569 ± 36 § Both eyes: 47 ± 15 ‡ 50 ± 13

* N = 7; †N = 72; ‡N = 504; †N = 1008; †N = 21; †N = 42; and **diurnal variation is the difference between the highest and lowest corneal thickness measurements in any given 24-hr period.

of the cats differed by one scale unit in seven out of 20 estimates and was identical for the remaining 13.

Corneal deswelling following eye closure: Five healthy adult cats, randomly selected from our animal colony, were observed continuously and allowed to fall asleep naturally. After approximately 2 hr of sleep, the cats were awakened and corneal thickness of one eye of each cat was measured at regular intervals for a further 2 ½ hr. The procedures described in this manuscript conform to the ARVO Resolution on the Use of Animals in Research.

Results. Corneal thickness data of each eye of the seven cats is summarized in Table 1. The mean central corneal thickness was 569 ± 36 μm (mean ± SD). The diurnal variation, which is the difference between the highest and lowest corneal thickness measurements in any given 24-hr period, ranged from 23 to 90 μm, with a mean of 49 ± 14 μm. This represents an average diurnal variation of 8.6% of the mean corneal thickness.

The time course of change in corneal thickness of the seven cats, expressed as the change in thickness (μm) relative to the mean corneal thickness of each eye calculated over the 72-hr period, is presented in Figure 1. Data from the 3 days of measurement are superimposed on a single 24-hr scale. Although we observed that the cats would sleep at any time of the night or day, it is evident from Figure 1 that corneal thickness generally was reduced at night (9:00 PM to 7:00 AM), when the activity level averaged 2.1 ± 0.7, and greater during the day (8:00 AM to 7:00 PM), when the activity level averaged 1.1 ± 0.4. An exception to this trend was the transient decrease in corneal thickness between 11:00 AM and 2:00 PM. This followed maintenance of the animal enclosure and introduction of food, which occurred between 10:00 AM and 11:00 AM each day.

A significant negative correlation (r = 5.1, P < 0.002, Spearman’s Correlation Test) existed between corneal thickness and the overall level of activity of the cats; that is, lid closure occurring during periods of reduced activity was associated with increased corneal thickness.

The average decrease in corneal thickness of one eye of each of five cats following 2 hr of sleep is presented in Figure 2. The corneas thinned by an
average of $43 \pm 22 \mu m$ after 135 min; corneal thickness had stabilized approximately 105 min after eye opening.

**Discussion.** The finding in this study of a mean central corneal thickness of $569 \pm 36 \mu m$ in the cat is in agreement with the finding of Bahn et al$^2$ of $580 \pm 50 \mu m$. The average diurnal variation in thickness was $49 \pm 14 \mu m$, which represents 8.6% of mean corneal thickness.

Corneal thickness was found to increase during periods of eye closure and decrease during periods of eye opening. Furthermore, following 2 hr of sleep, the corneas thinned by $43 \pm 22 \mu m$ within 135 min of eye opening. This amount of thinning is only slightly less than the diurnal variation in cat corneal thickness of $49 \pm 14 \mu m$. We conclude that corneal swelling induced by eye closure during periods of sleep is the prime determinant of the diurnal variation of corneal thickness in the cat.

It should be noted that this experiment involved hourly measurements of corneal thickness throughout a 72-hr period; thus, the observed changes in corneal thickness and behavior of the cats may not reflect accurately the changes to be expected under nonexperimental conditions. However, our observation that the cat may sleep at any time during the 24-hr cycle is in agreement with that of Freemont,$^8$ who attributes this behavior to the cat's poorly developed circadian sleep rhythm.
It is not clear why the diurnal variation in corneal thickness of the cat (8.6%) is considerably greater than has been reported in man (3.0%, based on measurements taken immediately upon awakening and at regular intervals throughout the day) and in the rabbit (3.2%, based on morning, noon, and afternoon measurements). Perhaps the limiting layers of the cornea of the cat are less efficient at regulating corneal hydration than in other species. Further studies on the mechanisms controlling corneal hydration in the cat would be necessary in order to explain our finding.

In view of the irregular sleep pattern and the effect of eye closure on corneal thickness of the cat, caution needs to be exercised in studies where corneal thickness is monitored over a period of time. It is possible to control against these variables by ensuring that the cat is active for at least 2 hr prior to corneal thickness measurements; for example, 2 hr after the commencement of feeding. At this time, corneal thickness will be at or near the minimum of the diurnal variation, and changes in corneal thickness due to factors other than diurnal variation will be observed more easily.

Key words: cat, corneal thickness, diurnal variation, eye closure, ultrasonic pachometry

Acknowledgments. The authors thank Daniel O'Leary and Donald Martin for their editorial suggestions and Sue Donahue, Geoff Hearne, and Stuart Ingham for technical assistance.

From the Cornea and Contact Lens Research Unit, School of Optometry, University of New South Wales, Kensington, Sydney, N.S.W., Australia. Supported by the Optometric Vision Research Foundation grant no. 83-27. Submitted for publication: November 2, 1983. Reprint requests: Tai loi Chan-Ling, Cornea and Contact Lens Research Unit, School of Optometry, University of New South Wales, P.O. Box 1, Kensington, Sydney, N.S.W. 2033, Australia.

References


Biosynthetic Human EGF Accelerates Healing of Neodecadron-Treated Primate Corneas

Joseph R. Brightwell,* Steven L. Riddle,* Richard A. Efierman,† Pablo Valenzuela,¶ Philip J. Barr,‡ James P. Merryweather,‡ and Gregory S. Schultz*

Topical administration of biosynthetic human epidermal growth factor (h-EGF), given in combination with an antibiotic and synthetic steroid (Neodecadron) accelerated the rate of corneal epithelial regeneration and significantly increased the strength of full-thickness stromal incisions in primates. The regenerated epithelial cells of EGF-Neodecadron-treated corneas appeared normal on histologic examination and showed no evidence of hypertrophy or hyperplasia. The EGF-Neodecadron-treated stromal incisions were characterized by new collagen formation and a smaller epithelial cell plug than Neodecadron-treated control corneas. These results suggest that biosynthetic h-EGF, which lacks the immunologic potential of nonhuman proteins, may be effective in accelerating healing of corneal epithelial defects and stromal incisions in patients whose healing is suppressed by treatment with steroids. Invest Ophthalmol Vis Sci 26:105-110, 1985

Currently no agent is available for clinical use that, either alone or in combination with corticosteroids, accelerates epithelial regeneration or healing of stromal incisions. There is a need for such an agent that potentially could eliminate persistent corneal epithelial defects or enhance the retarded healing of stromal incisions treated with corticosteroids.1

Other drugs have been tested for accelerating healing of corneal wounds. Parenterally administered ascorbate failed to increase tensile strength of full-thickness...