seen in regenerating cat endothelium. Growth factors have recently been shown to stimulate cellular division in corneal endothelial cells in tissue culture. Perhaps insufficient growth factor leaks into injured cat eyes to stimulate mitosis in the endothelial cells.

The greater increase in protein in rabbit eyes could be due to differences in (1) sensitivities of rabbit and cat eyes to ocular trauma, (2) types or levels of individual proteins, (3) depth or volume of the anterior chamber, or (4) outflow facility. The volume of the aqueous humor in cat is three times that of rabbit, and the outflow facility in cat (1.56 μl/min/mm Hg) is about six times higher than in rabbit (0.21 to 0.34 μl/min/mm Hg). The fluctuations in protein concentration in cat between 4 and 36 hr could be due to high outflow facility, late tissue damage, late alterations in vascular or ciliary process permeability, or temporary blockage of the angle by sloughing endothelial cells. In both species, protein concentration returned to normal by 1 week, indicating that the permeability of the blood-aqueous barrier is only temporarily affected after corneal freezing.

Our purposes in measuring changes in intraocular temperature during transcorneal freezing were to determine if intraocular temperature is lowered sufficiently to explain the breakdown of the blood-aqueous barrier or cause damage or death in tissues other than the cornea. Intraocular temperatures at the angle and ciliary processes never fell below 24° C. In contrast, the temperature of the iris sometimes decreased to near 0° C in both rabbit and cat. It is possible that tissue damage and/or prostaglandin release occurs in the iris at low temperatures, resulting in altered permeability in the iris or ciliary processes.

From the Departments of Ophthalmology and Physiology, The Medical College of Wisconsin, Milwaukee, and Research Service, Veterans Administration Center, Wood, (Milwaukee), Wis. This investigation was supported in part by NEI Research Grant EY-01436 and Ophthalmic Research Center Grant EY-01931, medical research funds from the Veterans Administration, and an unrestricted grant from Research to Prevent Blindness, Inc. Submitted for publication April 19, 1978. Reprint requests: Dr. D. L. Van Horn, Research Service,151, Veterans Administration Center, Wood, (Milwaukee), Wis. 53193.

Key words: aqueous humor, blood-aqueous barrier, cornea, corneal endothelium, corneal injury

REFERENCES

Etiology of corneal sensitivity changes accompanying contact lens wear. KENNETH A. POLSE.

Corneal touch threshold was monitored while corneal edema was experimentally induced by exposing the cornea to either an oxygen-free environment or hypotonic saline. No change in sensitivity occurred during these conditions. Contact lens wearers who were fully adapted to their lenses and did not develop corneal edema during wear showed an increase of 96% in corneal touch threshold. Refitting these subjects with an experimental contact lens which caused a 6% increase in corneal thickness did not further alter the corneal sensitivity. The decrease in corneal sensitivity accompanying contact lens wear is independent of corneal edema and is likely a result of sensory adaptation to a mechanical stimulant.

It is well known that a marked decrease in the sensitivity of cornea and lid margin occurs during and after adaptation to contact lenses. Clinicians have observed that contact lens wear can increase the corneal touch threshold to high
enough levels so that some patients do not experience pain or discomfort, even when the cornea is abraded.

The mechanism which leads to this reduced corneal sensitivity has not been determined. Mechanical impact of the lens against the cornea and lid margins may result in sensory adatation, or the contact lens might disturb the normal corneal physiology, causing a decrease in sensory nerve transmission. Millodot measured corneal swelling and sensitivity on a group of contact lens patients and showed that about 7% increase in corneal swelling and 100% increase in corneal touch threshold occurs after 8 hr of lens wear. He suggests that the reduction in corneal sensitivity is caused by corneal edema. Millodot did not have a control group (contact lens wearers without corneal edema), and therefore the effects of contact lens wear alone on sensitivity cannot be determined.

It therefore still remains uncertain whether the increase in corneal touch threshold accompanying contact lens wear is caused by mechanical stimulation, physiologic disturbance, or a combination of these factors. Clinicians may find it useful to know whether reduced sensitivity during contact lens wear has a metabolic or mechanical basis. However, there are no reports on the effect of either of these conditions on corneal sensitivity. In this study, changes in corneal thickness were used as an indication of disturbed corneal metabolism, and measurements of the effects of corneal edema and contact lens wear on corneal sensitivity were made. Using a modified Cochet-Bonnet esthesiometer, corneal touch threshold was monitored, while corneal edema was experimentally induced by exposing the cornea to either an oxygen-free environment, hypotonic saline, or tightly fitted hard contact lenses. Changes in corneal touch threshold resulting from these conditions were compared to changes when contact lenses that did not produce corneal edema were worn.

**Materials and methods.** Four subjects (three male, one female; mean age 25 years, range 23 to 27) who were free of ocular disease and who were not contact lens wearers participated in the experiment.

Corneal sensitivity was measured using a Cochet-Bonnet esthesiometer, which consists of a 0.12 mm diameter nylon monofilament encased in a cylinder. The esthesiometer was mounted on a triaxis holder so that its position and movement could be controlled in the x, y, and z meridians, in an arrangement similar to that used by Millodot. The length of the monofilament can be varied from 0.5 to 6.0 cm. This range corresponds to pressures of 11 to 20 mg/mm² (the cross-sectional area of the filament = 0.0113 mm²). Two knobs allowed the experimenter to control the vertical and horizontal position of the monofilament relative to the subject's eye so that the same corneal area could be stimulated at each test interval. The sight of impingement of the filament was easily discerned by individual central pinpoint stain. This verified that the touch measurements were made centrally. A third knob controlled movement of the monofilament in the plane perpendicular to the cornea. The subject's head was secured with a headrest aligned with the esthesiometer. A shield was used to block the subject's view of the operator's hand and the body of the esthesiometer holder so that the subject would not know when the instrument was approaching the cornea.

To obtain a measurement, the experimenter viewed the cornea and filament at close range from the side while the esthesiometer holder was moved slowly towards the center of the cornea at a constant velocity until the first perceptible flexure of the filament was observed. The subject was asked to tap on the table if touch was felt. Presence or absence of the blink reflex was also noted. These two signs of sensation are considered equally valid and were used to indicate corneal sensitivity. If the subject reported a sensation,
Corneal thickness was measured using a Haag-Streit pachometer and Mentor slit lamp which had been modified to improve the reliability and validity of the measurements. This apparatus has been described elsewhere.10

Experiment 1. Corneal touch threshold and central corneal thickness were measured for both eyes. Air-tight goggles were then secured to the patient’s head, and 100% nitrogen gas (oxygen-free atmosphere) was passed across one eye while the other eye was exposed to normal atmospheric pressure (partial pressure of oxygen = 155 mm Hg) and served as a control. Neither the observer nor the subject knew which eye was exposed to the nitrogen gas (double masking). After 2.5 hr, the goggles were removed and corneal touch threshold and thickness again measured. The experiment was repeated three times for each subject, for a total of 12 trials for the group.

Experiment 2. Baseline corneal sensitivity and thickness readings were taken on both eyes. Then a pair of tightly fitted plastic goggles was fitted to the subject. Hypotonic saline (0.45 NaCl) was then put into the right goggle until the entire chamber was filled. The goggle was left on 20 min and then removed. Corneal sensitivity and thickness measurements were again made. The experiment was repeated twice on two of the subjects; the observer did not know which eye received the hypotonic saline (single masking).

Experiment 3. The four subjects were fitted with contact lenses made of poly(methylacrylate) (PMMA). In three of the four subjects it was possible to fit lenses which caused less than 1.5% corneal edema after 8 hr of wear. Following adaptation to the lenses (about 3 to 4 weeks), corneal touch threshold and thickness were measured before and after 4 and 8 hr of lens wear. This was repeated three times on each of the three subjects.

Experiment 4. Following the measurements in experiment 3, one eye of each of the three subjects was fitted with an experimental contact lens (tightly fitted) designed to cause corneal edema. Touch threshold and corneal thickness were measured before and after 4 and 8 hr of wear. The experimenter and subject did not know which eye was fitted with the experimental lens. These measurements were repeated three times on each of the three subjects.

Results. When the eye was exposed to an oxygen-free environment, corneal swelling occurred. For the four subjects, the mean increase in central corneal thickness after 2.5 hr of being exposed to an oxygen-free atmosphere was 7.4% ± 2.51%. The control eye (which was exposed to a normal atmosphere) showed a mean increase in corneal thickness of 0.21% (±1.62%). Changes in corneal thickness occurring in the oxygen-free atmosphere condition were significant, but not for the eyes exposed to a normal atmosphere (Walsch test, p = 0.011).

Percent changes in corneal sensitivity were determined by taking differences in pressure (gm/mm²) measured before and after wearing the gog-
threshold, which was not significant (Walsch test, \( p = 0.011 \)). Correlations between changes in corneal thickness and sensitivity were 0 and \(-0.07\) for the experimental and control eyes, respectively (Spearman rank test).

For the two subjects in which the cornea was bathed for 20 min in a 0.45% saline solution, a 6.5% corneal swelling was measured. No differences in corneal sensitivity were observed between before and after bathing the cornea.

Fig. 1 shows the change in central corneal thickness for subject A, wearing either the optimal or tightly fitted lenses (experiments 3 and 4). The mean change in corneal thickness for this subject after 8 hr of wear with the optimal and tight lens was 1.3% and 5.8%, respectively. Slit-lamp examination of the cornea after the optimally fitted lens was worn showed no staining or edema, however, a moderate degree of central corneal edema and light epithelial staining was observed following the wearing of the tightly fitted lens. Subjects B and C showed similar changes.

Fig. 2 shows the mean change in corneal touch threshold for subject A, wearing the optimal and tightly fitted lens (experiments 3 and 4). The mean decrease in corneal sensitivity after 4 hr of wearing the optimal or tightly fitted lens was 17% and 16%, while after 8 hr the corneal sensitivity decreased to 96% and 94% for the two testing conditions. These results were similar for the other two subjects.

Table I is a comparison of the changes in corneal sensitivity and corneal thickness.

**Table I. Changes in corneal sensitivity and corneal thickness**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Duration of wear (hr)</th>
<th>Optimally fitted lenses</th>
<th>Tightly fitted lenses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean decrease in central corneal sensitivity (%)</td>
<td>Mean increase in central corneal thickness (%)</td>
<td>Mean decrease in central corneal sensitivity (%)</td>
</tr>
<tr>
<td>A</td>
<td>8</td>
<td>96.1</td>
<td>1.30</td>
</tr>
<tr>
<td>B</td>
<td>8</td>
<td>93.1</td>
<td>1.96</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>15.3</td>
<td>1.50</td>
</tr>
</tbody>
</table>

baseline levels before the morning of the following day on two subjects and after 1 week on the other wearer.

**Discussion.** Corneal swelling resulting from exposing the cornea to either an oxygen-free environment or a hypotonic solution did not change corneal sensitivity. It was possible, however, to decrease corneal sensitivity by having these same subjects wear contact lenses. During daytime contact lens wear, corneal touch threshold increased whether or not significant amounts of corneal swelling occurred. It was possible to alter corneal sensitivity during contact lens wearing without causing significant corneal swelling. Since sensitivity decreases are related to the time the lens is on, it seems that the change in corneal touch threshold accompanying contact lens wearing is not caused by metabolic disturbance to the cornea, but rather by sensory adaptation as a consequence of continuous mechanical stimulation.

The changes in corneal sensitivity accompanying the wearing of contact lenses observed here are similar to those reported by other investigators. 

Millodot\(^6\) reported a 94% increase in corneal touch threshold and a 6.9% increase in corneal thickness after 8 hr of contact lens wear. The subjects in this present study showed a mean change in corneal thickness of only 1.2% after 8 hr of wear but also had a 96% increase in corneal threshold for touch. Since the principal difference between Millodot’s results and the data reported here is in the degree of swelling, it seems that corneal sensitivity changes during contact lens wear are not related to corneal edema.

These results suggest that measurements of corneal touch threshold will not be useful indicators of disturbed corneal physiology. However, sensitivity measurements may provide a useful guide to the process of adapting to contact lenses. During the adaptive process, there was a slow but steady decrease in corneal sensitivity over a 2 to 3 week period. Once corneal touch threshold had increased approximately 100%, no further changes were noted. This 100% increase in corneal touch
threshold may be a useful indicator of determining when the process of adaption to contact lenses is complete.

Two of the subjects returned to baseline sensitivity after discontinuing lens wear overnight, while one subject required 1 week to regain original threshold levels. Although none of these subjects developed corneal edema or any other adverse signs during lens wear, there apparently are some individual factors which may prolong the corneal desensitization process long after lens wear is discontinued.

From the School of Optometry, University of California, Berkeley, Calif. This study was supported in part by U.S.P.H.S. Grant R01 EY01755-02. Submitted for publication July 7, 1978. Reprint requests: Dr. Kenneth A. Poise, School of Optometry, University of California, Berkeley, Calif. 94720.

Key words: corneal touch threshold, corneal sensitivity, corneal swelling, corneal thickness

REFERENCES


Vitreous fluorophotometry evaluation of xenon photoocoagulation. JAMES M. NOTH, CHARLES VYGANTAS, AND JOSE G. F. CUNHA-VAZ.*

An abnormal increase in the permeability of the outer blood-retinal barrier was induced in the eyes of adult pigmented rabbits after retinal xenon arc photoocoagulation. The alteration of the blood-retinal barrier, which was assessed by vitreous fluorophotometry after systemic administration of sodium fluorescein, followed a well-defined pattern. Higher values, which were recorded during the first three days after photoocoagulation, recovered progressively afterward. The permeability of the blood-retinal barrier returned to near-normal levels between 10 and 14 days after photoocoagulation. A direct correlation was observed between higher initial values and heavier photoocoagulation.

A variety of retinal diseases (vascular retinopathies and macular disorders) associated with breakdown of the blood-retinal barrier are, at some time in their evolution, treated by photoocoagulation. This appears to be somewhat contradictory, in that photoocoagulation has been shown by fluorescein angiography and histologic studies using a variety of tracer materials to induce a breakdown of the blood-retinal barrier.

Further studies were needed to measure the degree of the alteration of the blood-retinal barrier induced by xenon photoocoagulation and its recovery to normal levels. The availability of vitreous fluorophotometry, a new quantitative method of fluorescein analysis of the vitreous that permits the detection of very small amounts of fluorescein penetrating into the vitreous through an altered blood-retinal barrier, enabled us to measure at different intervals the alteration of the blood-retinal barrier after xenon arc photoocoagulation.

Material and methods. Adult pigmented rabbits, principally of the Dutch strain, were used as the experimental animals.

Xenon photoocoagulation. Xenon photoocoagulation was applied to 11 eyes of seven animals. Before treatment all eyes were subjected to ophthalmoscopic examination and fundus photography. Photoocoagulation (Zeiss) with the xenon arc lamp (XBO-2007 Osram), using a 4.5° cone size was selected for all burns. General anesthesia was given to all animals in an ultramuscular injection of acepromazine and ketamine. Xenon photoocoagulation was applied to the posterior pole of the eye in an area immediately inferior to the region of the myelinated nerve fibers. A total of 20 burns were applied to each eye. Although difficult, an attempt was made to evaluate the intensity of the retinal burns by following the system of grading proposed by Tso et al. Five eyes received predominantly grade I photoocoagulations, whereas the other six eyes had heavier grade II and III retinal burns inflicted to their retinas. At the time of the sacrifice, the eyes were enucleated and the retinas were laid flat on slides. The photoocoagulated area