Overnight Orthokeratology Lens Wear Can Inhibit the Central Stromal Edema Response

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PURPOSE. To investigate the overnight corneal edema response during overnight orthokeratology (OK).

METHODS. Eighteen young adult myopic subjects wore reverse-geometry lenses in Boston XO material (nominal Dk/t 46 × 10−9 cm2 · mL O2/s · mL · mm Hg) on an overnight wearing schedule for 1 month. Another 10 subjects wore conventional rigid gas-permeable (GP) lenses of similar Dk/t in one eye only, on an identical schedule. Corneal stromal thicknesses in the center, midperiphery, and periphery were measured by optical pachometry in the morning after lens removal, after 1, 4, 10, and 30 nights of wear. Changes from baseline for OK, GP and no-lens eyes were compared by repeated-measures ANOVA and protected post hoc t-tests.

RESULTS. The central stroma swelled significantly less in OK than in GP eyes (P < 0.001, ANOVA), and less than with no lens wear (P < 0.001, ANOVA) throughout the study. Overnight edema levels consistent with Dk/t were found on day 1 in the midperiphery (3.5 mm from apex) and periphery (5.0 mm) with both OK and GP lenses. The overnight edema response decreased significantly through the study with both lens types. Recovery to baseline stromal thickness during the day was demonstrated for GP eyes and for OK eyes in the central and peripheral cornea.

CONCLUSIONS. Overnight wear of reverse-geometry OK lenses inhibited the central stromal edema response. Overnight edema levels consistent with Dk/t were found in the corneal midperiphery and periphery. Adaptation of the edema response occurred with continuing overnight lens wear. The results suggest that central pressure exerted by the flat-fitting base curve of the OK lens acts locally as a “clamp” to inhibit overnight central corneal swelling. (Invest Ophthalmol Vis Sci. 2005;46:2334–2340) DOI:10.1167/iovs.04-1162

It is well known that the cornea relies on the supply of atmospheric levels of oxygen to maintain normal metabolic activity and that, if the cornea is deprived of oxygen, it increases in thickness and hydration.1,2 The normal cornea swells slightly during sleep,3,4 due in part to the reduced levels of oxygen available behind the closed eyelid compared with the atmosphere.5 Similarly, contact lenses can act as a barrier to oxygen supply to the cornea, particularly when lenses are worn during sleep. In the closed eye, the supply of oxygen to the cornea through tear circulation behind the lens, driven by blink-activated lens movement, is absent.6 Thus, corneal oxygenation is dependent on the oxygen permeability (Dk) of the contact lens material and the lens thickness (t). Many researchers have demonstrated the clear relationship between lens Dk/t and the amount of corneal swelling induced during closed-eye lens wear, regardless of lens type (rigid or soft).7–9 Indeed, for many years the goal of contact lens materials research has been to develop contact lens polymers with sufficient oxygen permeability that overnight corneal edema can be prevented.10,11 This goal is based on the assumption that corneal health may be compromised if the cornea is chronically deprived of normal levels of oxygenation and that the level of overnight corneal edema provides a reliable indication of the level of corneal hypoxic stress during contact lens wear.

Orthokeratology (OK) is a clinical contact lens–based technique that utilizes specially designed rigid contact lenses to reshape the anterior corneal profile, providing temporary correction of low to moderate degrees of myopia. The reverse-geometry lens designs used in modern OK are thought to apply positive pressure at the corneal center and negative pressure in the midperiphery under the steeper secondary “reverse” curve. This differential postlens tear film pressure profile acts to produce a flattened central treatment zone that corrects the myopic refractive error by reducing corneal power.12 The Food and Drug Administration in the U.S. has recently approved several reverse-geometry lens designs for overnight OK. This modality allows lenses to be worn only during sleep, with lens removal on awakening and clear unaided vision during waking hours. There have been several recent papers reporting good clinical success with this modality of contact lens wear.13–17

We have demonstrated previously that OK lens wear induces central corneal epithelial thinning and midperipheral stromal thickening and that these topographic thickness changes are sufficient to explain the refractive effect of OK.18 In this earlier paper, we reported residual corneal thickness changes found at the end of the day, 8 to 10 hours after lenses had been removed and after any overnight corneal edema had dissipated. However, the overnight corneal edema response with reverse-geometry lens designs was not reported in this earlier paper, despite the typical overnight lens-wearing modality used in modern OK. This information is important to ensure the maintenance of good corneal health during OK lens wear.

In this article, we report on topographical corneal thickness changes measured in the morning soon after eye opening after overnight OK lens wear. The overnight corneal edema response with OK lenses is compared with that found in a control group wearing conventional rigid gas-permeable (GP) lenses of similar Dk/t in one eye only, on an identical lens-wearing schedule, over a 1-month study period.
**MATERIALS AND METHODS**

Materials and methods used in this study have been described in detail elsewhere. The research described in this article followed the tenets of the Declaration of Helsinki (2000), and approval for the study was obtained from the institutional Human Research Ethics Committee. Subjects were required to be non-GP lens wearers with good ocular health. All subjects gave informed written consent before participation and after the risks and benefits of OK and GP lens wear and the study procedures had been fully explained.

Eighteen young adult subjects aged 22 to 29 years (12 men, 6 women) agreed to participate by wearing OK lenses in both eyes. A further 10 young adults aged 22 to 28 years (6 men, 4 women) also participated as control subjects, wearing conventional GP lenses in the right eye only. The left eye acted as a non-lens-wearing control.

The OK group wore BE (UltraVision Pty. Ltd., Brisbane, Queensland, Australia) reverse-geometry lenses (diameter, 10.6 mm) in the land, Australia) reverse-geometry lenses (diameter, 10.6 or 11.0 mm) in the further 10 young adults aged 22 to 28 years (6 men, 4 women) also participated as control subjects, wearing conventional GP lenses in the right eye only.

**RESULTS**

Unless otherwise indicated, the results presented refer to changes in stromal thickness only. Only right eye data are presented for the OK group. Midperipheral and peripheral stromal thickness data represent the mean of nasal and temporal quadrants. Subjects also returned to the clinic in the evening, after 8 to 10 hours of no lens wear, to monitor recovery of the overnight corneal edema response, total corneal and stromal thicknesses were measured across the horizontal corneal meridian, using the Holden-Payor optical pachymeter at baseline and then in the morning after overnight lens wear on days 1, 4, 10, and 30. Baseline measurements were obtained before lens wear commenced, at least 3 hours after eye opening and typically between 11 AM and 1 PM, to minimize potential effects of diurnal variations in corneal thickness. During the study, subjects were asked to attend the clinic wearing their lenses) within 1 hour after eye opening, and pachometry was performed within 5 minutes of lens removal. Corneal thickness was measured across the horizontal meridian at the center, midperiphery (3.5 mm from apex), and periphery (5.0 mm) in the nasal and temporal quadrants. Subjects also returned to the clinic in the evening, after 8 to 10 hours of no lens wear, to monitor recovery of corneal thickness (results reported previously). It has been demonstrated previously that the epithelium does not swell or thicken during hypoxia, and that the overnight corneal swelling response is thus primarily stromal in origin. Furthermore, we have previously reported that OK lens wear induces significant thinning of the central epithelium. Therefore, to avoid confounding our analysis of overnight hypoxic corneal edema by including the (concurrently thinning) epithelium in our considerations, we analyzed only stromal thickness changes for this article.

Right eye data only in the OK group and data from the lens-wearing (right) and non–lens-wearing (left) eyes in the control group were analyzed. Repeated-measures analysis of variance (ANOVA) was used to examine changes from baseline over the study period. Changes from baseline in corneal thickness were also examined with post hoc paired Student’s t-tests. A critical P of 0.05 was chosen for the repeated-measures ANOVA. For Bonferroni protection of post hoc t-tests, a critical P of 0.01 was used to minimize the risks of a type I error.

**Control Group: Non–Lens-Wearing Eyes**

Figure 1 shows the overnight stromal edema response in the non–lens-wearing eyes of the control group over the 1-month study period. The overnight increase in central stromal thickness on day 1 averaged +13.0 ± 4.6 μm (+2.5% ± 0.9%). Central stromal edema was statistically significant on day 1 (P < 0.01, paired t-test) and throughout the 30-day study period (P < 0.001, ANOVA). At day 30, central stromal edema averaged +15.6 ± 4.8 μm (+2.9% ± 0.9%).

Midperipheral stromal thickness also showed a statistically significant overnight increase on day 1 (+16.0 ± 3.2 μm; +2.9% ± 0.6%, P < 0.01, paired t-test), and this overnight edema response remained statistically significant through the study period (P < 0.001, ANOVA). Similarly, peripheral stromal thickness showed a statistically significant overnight increase from day 1 (+19.0 ± 3.9 μm; +3.2% ± 0.7%). The overnight edema response remained statistically significant and consistent throughout the 30-day period.

As previously reported, at the evening measurement sessions after 8 to 10 hours of no lens wear, central, midperipheral, and peripheral stromal thickness had returned to baseline. The difference in stromal thickness from baseline averaged +0.1 ± 2.4, +0.9 ± 2.3, and +1.4 ± 2.4 μm, for central, midperipheral, and peripheral cornea, respectively, on day 30 of the study.

**Control Group: Conventional GP Lens-Wearing Eyes**

Figure 2 shows the overnight stromal edema response in the conventional GP lens-wearing eyes of the control group over the 1-month study period. The increase in central stromal thickness after overnight lens wear was statistically significant over the 30-day period (P < 0.001, ANOVA). Central stromal edema was statistically significant at day 1 (+32.8 ± 5.8 μm, +6.2% ± 1.2%; P < 0.01, paired t-test). At day 10, overnight stromal edema was significantly reduced compared with day 1 (+18.4 ± 3.5 μm, +3.5% ± 0.7%; P < 0.01, paired t-test, day 10 vs. day 1), and by day 30 the overnight change in central stromal thickness averaged +15.5 ± 2.5 μm (+2.9% ± 0.5%). This was equivalent to the edema response found in the contralateral non–lens-wearing eyes.

Midperipheral stromal thickness showed a statistically significant increase after overnight lens wear through the 30-day study (P < 0.001, ANOVA). Midperipheral stromal edema reached statistical significance on day 1 (+33.0 ± 2.1 μm; +6.1% ± 0.4%; P < 0.01, paired t-test). However, the edema...
response at day 30 was significantly reduced compared with day 1 (+17.2 ± 2.1 μm, +3.2% ± 0.4%; P < 0.01; paired t-test, day 30 vs. day 1). Similarly, the overnight increase in peripheral stromal thickness averaged +34.8 ± 4.4 μm (+5.8% ± 0.9%) and +17.9 ± 4.0 μm (+3.0% ± 0.6%) on days 1 and 30, respectively.

At the evening measurement sessions conducted 8 to 10 hours after lens removal, stromal thickness had recovered to baseline, averaging +0.5 ± 2.8, +1.1 ± 2.4, and +1.4 ± 2.4 μm relative to baseline in the central, midperipheral, and peripheral stroma, respectively, on day 30 of the study.

**OK Lens-Wearing Group**

Figure 3 shows the overnight stromal edema response in the OK group over the 1-month study period. Central stromal edema averaged +6.6 ± 2.9 μm (+1.2% ± 0.6%; P < 0.01, paired t-test) on day 1 of the study. At days 10 and 30, the overnight central stromal change from baseline averaged +2.5 ± 3.7 μm (+0.5% ± 0.7%), and −0.3 ± 2.1 μm (−0.1% ± 0.4%), respectively; these differences from baseline were no longer statistically significant (P > 0.05, paired t-test). Central stromal edema in the OK group was significantly lower than in the GP and non-lens-wearing eyes of the control group throughout the study (OK < no lens ≤ GP; P < 0.01, unpaired t-tests).

Midperipheral stromal thickness after overnight OK lens wear showed an overall increase from baseline over the 1-month study period (P < 0.001, ANOVA), reaching statistical significance on day 1 (+35.1 ± 6.0 μm, +6.1% ± 1.2%; P < 0.01, paired t-test). However, by day 30, stromal edema, although still statistically significant, was significantly reduced compared with day 1 (+24.4 ± 4.2 μm, +4.3% ± 0.9%; P < 0.01, paired t-test, day 30 vs. day 1).

Peripheral stromal thickness also showed an increase after overnight OK lens wear over the 1-month study period (P < 0.001, ANOVA). The peripheral stromal edema reached statistical significance on day 1 (+41.8 ± 5.4 μm, +6.5% ± 0.8%; P < 0.01, paired t-test), and showed a significant reduction by day 30 (+26.7 ± 6.8 μm, +4.1% ± 1.1%; P < 0.01, paired t-test, day 30 vs. day 1).

At the evening measurement session on day 1, stromal thickness averaged −0.1 ± 2.1, +1.2 ± 3.6, and 0.8 ± 3.5 μm in the center, midperiphery, and periphery respectively, indicating complete recovery to baseline. Thereafter, although central and peripheral stromal thickness continued to show complete daytime recovery to baseline, gradual residual stromal thickening was found in the stromal midperiphery. This phenomenon was reported and discussed in detail in an earlier paper.18

**DISCUSSION**

**Inhibition of Central Stromal Edema**

Our results show that the central overnight stromal edema response was significantly reduced in OK subjects wearing reverse-geometry lenses, to a level lower than in the conventional GP and non-lens-wearing eyes in the control group. On the first night of lens wear, central overnight stromal edema, measured within 1 hour of eye opening, averaged 1.2% ± 0.5% in the OK group, compared with 6.2% ± 1.2% in the GP eyes and 2.5% ± 0.9% in the non-lens-wearing eyes of the control group.

It is widely assumed (and many previous publications have confirmed) that, because tear circulation behind a contact lens is essentially absent during sleep,6 the overnight corneal edema response is dependent primarily on the level of oxygen that reaches the anterior corneal surface through the lens, and thus on lens oxygen transmissibility (Dk/t).7,9,11 This relationship between overnight edema and lens Dk/t holds irrespective of contact lens type (hydrogel, silicone hydrogel or GP). Where there is substantial variation in the lens-thickness profile, such as occurs with high-powered contact lenses, then the average lens thickness must be considered when determining the lens Dk/t.21,22 The expected overnight corneal edema response can be estimated with a formula presented by Holden and Mertz,11 which calculates the percentage edema based on lens Dk/t. This formula was derived from overnight corneal edema responses measured immediately after eye opening after overnight wear of hydrogel lenses:

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\text{Corneal edema} = 23.9 - 4.44 \ln(Dk/t_{avg}) 
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**Figure 3.** Overnight stromal edema (%) across the horizontal corneal meridian in the right eyes of subjects wearing reverse-geometry OK lenses, over the 1-month study period. Measurements were obtained within 1 hour of eye opening and 5 minutes of lens removal. Error bars, SD.
According to the manufacturer (Polymer Technology—a Bausch & Lomb Company, Rochester, NY) the Boston XO material used for lenses in this study has a nominal Dk of 100 × 10\(^{-11}\) cm\(^2\) · mL O\(_2\)/s · mL · mm Hg. The BE reverse geometry lenses worn by the OK group have a nominal center thickness of 0.22 mm, whereas the J-Contour conventional GP lenses have a nominal center thickness of 0.18 mm. Both lens types have close to parallel thickness in the low powers used in this study (plano for the BE lenses, −3.00 D for the J-Contour lenses), allowing an assumption that lens Dk/tavg is approximately equivalent to the Dk/t at the center of the lens. The nominal Dk/tavg of the BE lenses is thus 45.5, and the J-Contour lenses 55.6 × 10\(^{-10}\) cm · mL O\(_2\)/s · mL · mm Hg. According to the Holden-Mertz formula, overnight corneal edema of approxi- mately 6.9% and 6.1% would thus be expected for OK and GP groups, respectively. Assuming that overnight edema is stromal and not epithelial in origin and using baseline corneal and stromal thicknesses in the two groups, these estimates convert to anticipated overnight \textit{stromal} edema levels of 7.5% for the OK group and 6.7% for the conventional GP group.

In this study the GP group showed central overnight stromal edema levels (6.2%) consistent with the Holden-Mertz prediction on the first night of lens wear. Midperipheral and peripheral stromal edema responses in the OK group (averag- ing 6.1% and 6.5%, respectively) and the GP group (averaging 6.1% and 5.8% respectively) were also consistent with Holden- Mertz predictions, allowing for some corneal deswelling due to the slight delay in measurement (up to 1 hour) after eye opening.

In contrast, the central overnight stromal edema response in the OK group (1.2%) was significantly reduced or inhibited compared with the 7.5% edema response predicted on the basis of lens Dk/t. Furthermore, throughout the study the central edema response in the OK group was not only significantly lower than with conventional GP lenses of slightly higher Dk/t, but also lower than in the non-lens-wearing eyes of the control group. We speculate that the positive pressure exerted by the reverse-geometry lens against the central cornea acts in some way to inhibit the normal overnight stromal edema response. It has been demonstrated, using anoxia in gas-goggle experiments, that the extreme periphery of the cornea is physically prevented from swelling due to the clamp- ing effect of the tightly packed limbus.\(^{23,24}\) In a similar way, we hypothesize that, during overnight wear of reverse-geometry lenses, the cornea may be “clamped” between the central contact lens-induced pressure and intraocular pressure. This appears to either prevent the influx of water that would nor- mally occur into the central stroma in response to the contact lens-induced hypoxic challenge, or alternatively force this water laterally toward the midperipheral stroma.

The central epithelium has been shown to thin under reverse-geometry lenses as a result of central contact lens-in- duced pressure. Alharbi and Swarbrick\(^{26}\) found central epithe- lial thinning 8 to 10 hours after lens removal after overnight OK lens wear, with no change in central stromal thickness. Their finding confirmed an earlier report by Swarbrick et al.\(^{20}\) of central epithelial thinning with daily wear of reverse-geometry lenses, and this is now supported by evidence from indepen- dent studies.\(^{14,16}\)

The corneal epithelial layer is believed to play an important role in the stromal edema response due to an increase in lactate production by the hypoxic epithelium.\(^{25,26}\) With the reduction in central epithelial thickness with reverse-geometry lenses wear, a consequent reduced production of lactate may reduce the central stromal swelling response. Recent evidence from his- tologic studies in the feline model, however, suggests that, at least in an 8-hour time frame, the OK lens–induced epithelial thinning is due to epithelial cell compression, rather than to loss of epithelial cell layers (Choo J, et al. \textit{IOVS} 2004;45:ARVO E-Abstract 1552). Further work is needed to determine whether this compression in itself affects the oxygen requirements of the central epithelium. However, if all cell layers are present and functioning, it is reasonable to assume that they will show similar metabolic effects of hypoxia as the epithe- lium beneath a conventional GP lens of similar Dk/t. Our results therefore suggest that the reverse-geometry lens can suppress the consequences of epithelial hypoxia (i.e., stromal edema), but does not prevent epithelial hypoxia per se. In other words, the reduced central overnight corneal edema response under reverse-geometry lenses does not mean that the central epithelium avoids hypoxia during overnight OK lens wear.

It is generally accepted that the amount of local corneal epithelial hypoxia is dependent on the local Dk/t of the lens over that particular corneal location.\(^{27,28}\) It has also been shown that the corneal edema profile does not necessarily mirror the regional Dk/t of the lens. For example, central stromal edema is higher in eyes wearing high minus lenses, and lower in those with high plus lenses, than would be predicted by the Dk/t at the lens center.\(^{8,29}\) and the concept of “average Dk/t”\(^{21,22}\) has been applied to explain the resultant central edema response. Because of the absence of tear mixing under contact lenses in the closed eye\(^{30}\) and the assumption that lateral movement of water (or edema itself) in the stroma is min- imal,\(^{30}\) the most likely explanation for this apparent “aver- aging” of the edema response in overnight hydrogel lens wear is lateral diffusion of lactate in the stroma.\(^{27,28}\)

The results presented herein provide a new perspective on the corneal edema response in contact lens wear. To our knowledge, there have been no previous reports suggesting that the overnight corneal edema profile can be modulated in vivo by contact lens-induced pressure. The lenses worn in this study did not show significant regional variations in lens thick- ness and thus would have been expected to provide similar epithelial oxygenation across the corneal areas covered by the lens. Nevertheless, the edema response in the central cornea was inhibited by reverse-geometry lens wear, presumably due to the pressure exerted by the flat lens base curve, through the postlens tear film, against the central cornea. This indicates that contact lens–induced pressure can modulate the overnight corneal edema response. Since this work was first presented at the 2003 ARVO conference (Alharbi A, et al. \textit{IOVS} 2003;44: ARVO E-Abstract 3704), the reduced overnight central corneal edema response under reverse-geometry lens designs has been confirmed by others.\(^{31}\)

It is thought that corneal edema occurs primarily in a posterior direction.\(^{22,32}\) The way in which anteriorly applied pressure in OK modifies this posteriorly directed response requires further study. Such studies will involve relatively complex modeling of the corneal topographic changes induced by reverse-geometry lenses in corneal elevation and correlation of this profile with the edema response profile. This ongoing analysis will be the subject of a future paper.

The central stromal edema response on day 1 (within 1 hour of eye opening) in the non-lens-wearing eyes of our control group (2.5%; equivalent to total corneal edema of 2.3%) is consistent with previous reports of non-lens-wearing overnight corneal edema levels ranging from 1.5% to 4.5%.\(^{3,4,9,34}\) The edema response was similar across the horizontal meridian out to a 10-mm chord (Fig. 1) and remained consistent over the 30-day study period.

**Adaptation of the Stromal Edema Response**

The second major finding in this study is the apparent reduc- tion or adaptation of the overnight stromal edema response.
with continuing overnight wear of both OK and conventional GP lenses. This gradual reduction in the overnight edema response over time was noted in the central, midperipheral, and peripheral cornea and reached statistical significance by day 10 of the study. No such reduction in overnight edema was noted in the non-lens-wearing eyes of the control group. Figure 4 illustrates these progressive changes in the overnight stromal edema response, for the central, midperipheral, and peripheral cornea respectively, in the non-lens-wearing, GP, and OK groups over the 30-day study period.

Within 30 days of commencement of lens wear, overnight edema levels were equivalent in the lens-wearing and non-lens-wearing eyes in the control group. In the OK group, overnight edema declined to zero in the center of the cornea after 10 nights of lens wear and approached non-lens-wearing levels in the midperiphery and periphery after 1 month of overnight lens wear. Such complete adaptation of the overnight edema response may be specific to this study, in which lenses were removed during the day, and moderately high Dk/t lenses were worn overnight. The pattern and time course of edema adaptation may be slower when lenses are worn continuously (night and day) or if low closed-eye oxygen levels and thus high overnight edema responses are involved.

Early studies of corneal edema with open-eye PMMA lens wear demonstrated apparent adaptation of the edema response over the first few days to weeks of lens wear. This was explained on the basis of hypotonic reflex tearing in novice lens wearers, which decreased gradually as the patients adapted to lens discomfort, leading to a reduction in osmotically induced edema. However, in our study OK and GP lenses were worn overnight only, minimizing the contribution of reflex tearing to the edema response. Comfort levels with closed-eye lens wear are much higher than in the open eye, because lens discomfort arises primarily from interactions between the lens edge and the eyelid margins during blinking. Furthermore, there was no evidence of a reduction in edema levels over time in the non-lens-wearing eyes in the control group, despite contralateral GP lens wear. This finding suggests that osmotic edema due to reflex hypotonic tearing did not play a significant role in the overnight edema response and its apparent adaptation in this study.

A reduced overnight corneal edema response in adapted contact lens wearers compared to novice subjects has been reported previously for both GP and hydrogel lenses. In hydrogel lens wear the potential impact of lens discomfort, particularly during closed-eye lens wear, is also difficult to reconcile with an explanation of edema adaptation based on reduced hypotonic reflex tearing.

There are several alternative explanations for the apparent adaptation of the overnight edema response found in this study. Because optical pachometry was performed up to 1 hour after eye opening in this study, one might argue that an increasing interval between eye opening and corneal thickness measurement as the study progressed may provide an explanation. However, although this interval was not explicitly recorded, the delay between eye opening and pachometry was consistent throughout the study period. Alternatively, it is possible that there is an increased rate of corneal deswelling from overnight edema with increasing lens exposure. There is no evidence to support such a hypothesis. Indeed, very little difference in corneal deswelling rates has been found between novice and long-term contact lens wearers.

In the classic study by Holden et al., after an average of 5 years of unilateral hydrogel lens extended wear, lower levels of daytime corneal edema were found in the lens-wearing eyes than anticipated based on lens Dk/t, giving the appearance of adaptation of the edema response. However, after lenses had been removed for a week to allow complete recovery from

![Figure 4](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933438/ on 11/19/2018)
lens-induced edema, the stroma in the lens-wearing eye was found to be significantly thinner than in the fellow non-lens-wearing eye. Holden et al. argued that there had been no adaptation of the edema response and that the normal corneal swelling response was obscured by gradual stromal thinning.

Although our study was conducted over a much shorter time than the study by Holden et al., we found no evidence that the apparent adaptation of the edema response in our study could be explained by stromal thinning. There was no evidence of residual stromal thinning at the end of the day, after lenses had not been worn for 8 to 10 hours. As reported in detail elsewhere, there was complete recovery of stromal thickness to baseline levels during the daytime over the 30-day study period in the GP lens-wearing eyes and in the corneal center and periphery in the OK group. Midperipheral stromal thickness in fact showed a gradual residual thickening in the OK group at the evening measurement sessions with continuing overnight OK lens wear. It is unlikely that the edema induced by overnight lens wear was still unresolved at the evening measurement sessions, 8 to 10 hours after lens removal, given the relatively low levels of overnight edema and the fact that no lenses were worn during the day with the eyes open and exposed to atmospheric oxygen levels.

Recent work by Bonanno et al. (JOVS 2003;44:ARVO E Abstract 1369) provides another possible explanation for the apparent adaptation of the edema response demonstrated in our study. Corneal epithelial cells in culture were preadapted to hypoxic conditions and were subsequently shown to have downregulated their response to hypoxic challenge in terms of reduced lactate production, compared with unadapted cells. Differences in the in vivo corneal response to hypoxic stress were also demonstrated between novice and preadapted subjects in terms of stromal pH change but not oxygen consumption. Bonanno et al. hypothesized that corneal epithelial cells repeatedly exposed to hypoxic challenge may become more efficient at metabolizing the oxygen that they do receive.

**CONCLUSIONS**

In summary, the results of this study clearly demonstrate that the overnight central stromal edema response can be suppressed during overnight wear of reverse-geometry contact lenses designed for OK. Normal levels of stromal edema, as predicted by lens Dk/t, were found in the corneal midperiphery and periphery in the OK group and at all corneal locations in the control group wearing conventional GP lenses. We hypothesize that positive pressure generated behind the center of the reverse-geometry lens, together with intraocular pressure, acts as a "clamp" to restrict overnight central corneal hypoxic edema in OK lens wear.

We also documented gradual adaptation of the overnight stromal edema response with continued overnight wear of conventional and reverse-geometry GP lenses. Levels of overnight corneal edema approached those recorded in the non-lens-wearing control eyes after 50 nights of lens wear. This apparent adaptation of the overnight edema response could not be explained by residual stromal thinning after resolution of the edema during the day and may represent true adaptation of epithelial cells to hypoxic challenge. The time course and pattern of adaptation of the edema response may differ for different lens types and wearing schedules and warrant further study.

Although lens Dk/t is arguably the most significant factor in determining the stromal edema response to overnight contact lens wear, this study demonstrates that the overnight corneal edema response can be modulated by lens-induced pressure and by experience in lens wear.

**References**