Corneal and Conjunctival Sensory Function: The Impact on Ocular Surface Sensitivity of Change from Low to High Oxygen Transmissibility Contact Lenses

Blanka Golebiowski,1,2 Eric B. Papas,1,2,3 and Fiona Stapleton1,2

PURPOSE. Deprivation of oxygen to the ocular surface during contact lens wear has been implicated in the alteration of sensory function. This study investigates whether increasing oxygen availability through discontinuation of contact lens wear or transfer into highly oxygen transmissible (high Dk/t) lenses leads to a change in corneal or conjunctival sensitivity.

METHODS. Twenty-seven long-term extended wearers of low Dk/t soft contact lenses ceased lens wear for 1 week and were refitted with high Dk/t silicone hydrogel lenses. A control group of 25 nonwearers matched for age and sex was also recruited. Central corneal and inferior conjunctival sensitivity were measured using an air-jet aesthesiometer. Threshold was determined using a staircase technique. Measurements were taken during low Dk/t lens wear; after 1 week of no wear; and after 1, 3, 6, and 12 months of high Dk/t lens wear. Measurements were carried out on one occasion on the nonwearers.

RESULTS. Corneal sensitivity decreased 1 week after discontinuation of low Dk/t lenses and no further change in sensitivity occurred with high Dk/t lens wear. Conjunctival sensitivity did not change over the same time frame. Ocular surface sensitivity in long-term low Dk/t soft lens wearers was similar to that of nonwearers. Sensitivity was higher in females than males in the nonwearers, but not in the lens-wearing group. An interaction of sex on change in conjunctival threshold was found in the lens wearers.

CONCLUSIONS. These findings indicate that factors other than oxygen availability alone determine sensitivity of the ocular surface. Silicone hydrogel contact lenses appear to have only a minor impact on ocular surface sensitivity in previous lens wearers. (Invest Ophthalmol Vis Sci. 2012;53:1177–1181) DOI:10.1167/iovs.11-8416

Ocular discomfort induced by contact lenses is the main cause of unsuccessful lens wear. Although as in dry eye, the mechanism is not well understood, it is thought that sensory changes induced by lens wear interfere with the lacrimal functional unit,1,2 thereby altering tear production and inducing changes on the ocular surface. Although perhaps similar to those occurring in dry eye, such changes are more marginal and often transient. Corneal sensitivity changes with contact lens wear have previously been widely reported,5–14 although the mechanism of this change is not known. Several investigators suggest that sensitivity change occurs because of decreased levels of oxygen available to the cornea during lens wear, which may interfere with corneal metabolism.5 Others, however, have put forward a mechanical etiology.8

Numerous studies have demonstrated a reduction in corneal sensitivity with traditional PMMA,5–6 rigid gas permeable (RGP)5,9–11 and conventional hydrogel10,12 contact lenses and a recent study has suggested there may be an effect with silicone hydrogel lenses that are highly permeable to oxygen.13 Conversely, conjunctival sensitivity has been found to increase with short-term silicone hydrogel lens wear in two studies.13,14

Much of the work investigating corneal sensitivity with contact lens wear has focused on the effects of daily or short-term contact lens wear and has not considered long-term or extended wear. No studies have yet been published that examine the effects of long-term or extended wear of silicone hydrogel lens materials on corneal or conjunctival sensitivity.

The aim of this study was to investigate the impact of oxygen availability on corneal sensitivity by comparing the effect of a change to higher oxygen transmissibility (Dk/t, where Dk is oxygen permeability and t is thickness of the lens) contact lens wear in a group of long-term low Dk/t lens wearers, then to follow these changes over short- and long-term wear periods in a longitudinal study and compare with an age- and sex-matched control group with no history of lens wear. In addition, the study aimed to examine the influence on these changes of factors including age and sex previously shown to affect ocular surface sensitivity.

METHODS

Study Design

In this prospective cohort longitudinal study, 27 long-term wearers of low Dk/t hydrogel contact lenses were discontinued from lens wear for 1 week then refitted with high Dk/t silicone hydrogel lenses and followed-up for 12 months. A group of 25 age- and sex-matched subjects, with no previous contact lens wear history, were recruited as a control group. The study was conducted in accordance with the Declaration of Helsinki and all procedures were approved by the University of New South Wales Human Research Ethics Committee. All subjects signed a statement of informed consent before commencing the study.

Study Subjects

Subjects who had worn contact lenses made from etafilcon A (Dk/t = 40 × 10−9 [cm/s][mL O2/mL mm Hg]), Acuvue; Vistakon, Jacksonvile, FL) and/or polymacon (Dk/t = 24 × 10−9 [cm/s][mL O2/mL mm Hg], Seequence; Bausch & Lomb, Rochester, NY) on a 6- or 13-night ex-
tended-wear schedule were recruited. All subjects had no preexisting
ocular disease or history of corneal surgery.

Treatment Protocol
Lotrafilcon A ($Dk/t = 175 \times 10^{-9}$ [cm$^2$/s][mL O$_2$/mL mm Hg], Focus
Night and Day; CIBA Vision, Duluth, GA) and balafilcon A ($Dk/t = 122 \times 10^{-9}$ [cm$^2$/s][mL O$_2$/mL mm Hg], PureVision; Bausch & Lomb)
silicone hydrogel contact lenses were fitted contralaterally and worn
on a 30-night extended wear schedule. Lens type was assigned at
random between the eyes. Lenses were removed and replaced after 30
days of wear. Hydrogen peroxide disinfection was used in the case that
lenses were removed within this period. Ocular surface sensitivity was
measured in contact lens wearers before they discontinued low $Dk/t$
lens wear; after a 1-week washout period of no lens wear; and after 1,
3, 6, and 12 months of high $Dk/t$ lens wear. Ocular surface sensitivity was
measured once in the group of control non-lens wearers. Mea-
surements were made on the eye fitted with lotrafilcon A of each
contact-lens-wearing subject and on one randomly determined eye of
the non-contact-wearing subjects.

Clinical Evaluation
Sensitivity of the central cornea and the inferior conjunctiva (2 mm
below the limbus) was measured using an air-jet aesthesiometer (CR-
CERT-Belmonte Aesthetics [CBA]; Brien Holden Vision Institute,
Sydney, NSW, Australia).14 The stimulus consisted of a 1-second pulse
of medical-quality air delivered at flow rates of 1 to 400 mL/min at a
temperature of 34°C (equivalent to the temperature of the corneal
surface$^{33}$). Sensitivity was measured by determining the threshold of
stimulus detection using a staircasing technique, with a 30-second rest
between stimulus presentations as described previously.$^{16}$ Mea-
surements were carried out between 8:35 AM and 6:20 PM and individual
subjects’ measurement times were kept consistent throughout the
study to mitigate potential effects of diurnal variation. During measure-
ments, the mean ambient temperature was 22 ± 2°C and the mean
ambient humidity was 61 ± 11%. Subjects’ ocular health was examined
at each visit using slit-lamp biomicroscopy.

Statistical Analysis
Threshold changes between ocular sites and over time in the lens
wearers were examined using repeated-measures ANOVA. To mini-
mize the effect of missing values, the effect of 1 to 12 months of high
wear duration on threshold, the mean threshold for 1-, 3-, 6-, and 12-month visits was used in subsequent analyses. Mixed-model
ANOVA was used to examine differences in threshold between the
lens wearers and the control subjects. Post hoc comparisons were
made using a Bonferroni adjustment or the Dunnett $t$-test where ap-
priate. Significance was determined at a confidence level of 95%.

A repeated-measures ANOVA test of between-subjects effects was
used to determine significance of age, sex, lens wear experience, and the
effect of the interaction of these factors with two-way
ANOVA.

RESULTS
Subject Demographics
The demographics of subjects in the lens-wearing ($N = 27$; mean
age = $40 ± 7$ [min, max = 28, 52]; 51.9% female) and the non-lens-wearing control ($N = 25$; 40 ± 7 [min, max = 28, 52]; 56% female) groups were similar. In the lens-wearing group, the mean duration of low $Dk/t$ extended wear experi-
ence was $12.7 ± 3.3$ years (min, max = 8.9, 18) and the range of
lens powers worn was $-1.25$ D to $-7.00$ D.

Corneal Sensitivity
There was a statistically significant increase in corneal thresh-
hold after subjects discontinued low $Dk/t$ lens wear for 1 week (Fig. 1, Table 1). However, there were no further changes in
corneal threshold when these subjects transferred to high $Dk/t$
lens wear ($P = 1.00$). Compared with low $Dk/t$ lens wear, the
mean difference in corneal threshold 1 week after low $Dk/t$
wear was discontinued was $-13.0$ mL/min (95% CI, $-22.3$ to
$-3.8$; $P = 0.004$). There were no significant differences in corneal
threshold for the duration of 1 to 12 months of high
$Dk/t$ lens wear ($P = 0.17$); thus, the mean corneal threshold of
all high $Dk/t$ visits was used for subsequent analyses. Corneal
threshold during high $Dk/t$ lens wear was significantly higher
than that during low $Dk/t$ lens wear (mean difference = $-13.5$; 95% CI, $-17.7$ to $-25.2$; $P = 0.02$) and compared with the
control nonwearers (mean difference = $-14.8$; 95% CI, $-4.2$ to $-25.5$; $P = 0.003$). There was no difference in corneal
threshold between low $Dk/t$ lens wear and the control non-
wearers ($P = 0.98$).

Conjunctival Sensitivity
There was no change in conjunctival threshold after subjects
discontinued low $Dk/t$ lens wear for 1 week or transferred to high
$Dk/t$ lens wear ($P = 0.77$; Fig. 1, Table 1). There were no

![Figure 1. Mean central corneal (CC) and inferior conjunctival (IC) thresholds for control non-lens wearers and for subjects in the lens-wearing group during low $Dk/t$ lens wear, 1 week after lens wear was discontinued (washout), and after 1, 3, 6, and 12 months of high $Dk/t$ lens wear. Error bars represent SD of the mean; *, #, and ‡ indicate significant differences.](https://www.iovs.org/content/iovs/March2012/53/3/1178.full.pdf)
significant differences in conjunctival threshold for the duration of 1 to 12 months of high Dk/t lens wear (P = 0.93); thus, the mean conjunctival threshold of all high Dk/t visits was used for subsequent analyses. Conjunctival threshold during low or high Dk/t lens wear or during 1 week washout was not different compared with the control nonwearers (P = 0.81). Conjunctival threshold was significantly higher than corneal threshold for subjects in the control group of nonwearers and for subjects in the lens-wearing group at all time points (P = 0.001).

Factors Affecting Corneal Sensitivity
There was no significant effect of sex (P = 0.68), age (P = 0.23), low Dk/t extended wear experience (P = 0.68), or the interaction between age and sex (P = 0.65) on corneal threshold in the lens wearers (Table 2). Likewise, there was no significant interaction of these factors on the change in corneal threshold over time in the lens wearers (sex, P = 0.69; age, P = 0.27; low Dk/t extended wear experience, P = 0.88; age × sex interaction, P = 0.98). Results of the analysis of corneal threshold in the lens-wearing group for males and females separately were comparable to those presented for all subjects examined together (Fig. 2A).

In contrast, in the control group of nonwearers, male subjects had significantly higher corneal thresholds than female subjects (P = 0.04; Fig. 2A). Subjects’ age (R = −0.16, P = 0.46), or the interaction between age and sex (P = 0.81), did not have a significant effect on corneal thresholds in the nonwearers.

Factors Affecting Conjunctival Sensitivity
Although male conjunctival thresholds appeared higher than female thresholds in the lens wearers, this difference could be shown only with a reduced level of confidence (P = 0.06; Fig. 2B, Table 2). Conjunctival threshold appeared lower in subjects with more years of experience in low Dk/t extended wear, but this difference could also be shown only with a reduced level of confidence (P = 0.08). There was a significant interaction of sex on the change in conjunctival threshold over time in the lens wearers (P = 0.04). However, the subsequent results of the analysis of conjunctival threshold in the lens-wearing group for males (P = 0.14) and females (P = 0.35) separately were comparable to those presented for all subjects examined together (Fig. 2B). Age did not have a significant effect on conjunctival thresholds in the lens wearers (P = 0.79). There was no significant interaction of age (P = 0.21) or low Dk/t extended wear experience (P = 0.22) on the change in conjunctival threshold over time in the lens-wearing group (Table 2). The interaction between age and sex did not have a significant effect on conjunctival

### Table 1. Mean Group Corneal and Conjunctival Thresholds for Lens Wearers and Control Nonwearers (Mean ± SD)

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>Threshold</th>
<th>Corneal (mL/min)</th>
<th>Conjunctival (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Dk/t</td>
<td>1 Week Washout</td>
<td>High Dk/t (Mean of 1- to 12 Month Visits)</td>
</tr>
<tr>
<td>Corneal (mL/min)</td>
<td>85.2 ± 31.9</td>
<td>97.5 ± 36.4</td>
<td>97.1 ± 35.0</td>
</tr>
<tr>
<td>Conjunctival (mL/min)</td>
<td>130.8 ± 38.6</td>
<td>130.8 ± 50.9</td>
<td>139.4 ± 52.3</td>
</tr>
</tbody>
</table>

Within-subject variations are visit (Low Dk/t, washout, mean High Dk/t), between-subjects factors are sex and low Dk/t extended wear (EW) experience; covariate is age. Values in bold indicate statistical significance.

### Table 2. Summary of Repeated-Measures ANOVA Results for Corneal and Conjunctival Threshold in the Lens Wearers

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>Corneal Threshold P Value</th>
<th>Conjunctival Threshold P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit</td>
<td>0.002</td>
<td>0.77</td>
</tr>
<tr>
<td>Sex</td>
<td>0.68</td>
<td>0.06</td>
</tr>
<tr>
<td>Age</td>
<td>0.23</td>
<td>0.79</td>
</tr>
<tr>
<td>Sex × Age</td>
<td>0.63</td>
<td>0.85</td>
</tr>
<tr>
<td>Low Dk/t EW experience</td>
<td>0.68</td>
<td>0.08</td>
</tr>
<tr>
<td>Visit × Sex</td>
<td>0.69</td>
<td>0.04</td>
</tr>
<tr>
<td>Visit × Age</td>
<td>0.27</td>
<td>0.21</td>
</tr>
<tr>
<td>Visit × Sex × Age</td>
<td>0.98</td>
<td>0.13</td>
</tr>
<tr>
<td>Visit × Low Dk/t EW experience</td>
<td>0.88</td>
<td>0.22</td>
</tr>
</tbody>
</table>

FIGURE 2. Mean corneal (A) and conjunctival (B) thresholds for male and female subjects in the control nonwearer group and the lens-wearer group during low Dk/t lens wear, after lens wear discontinuation (washout), and during high Dk/t wear. Error bars represent SD of the mean; * indicates significant differences.
threshold \( (P = 0.85) \), nor on the differences in conjunctival threshold over time \( (P = 0.13) \), in the lens wearers.

In the nonwearers, male subjects had significantly higher conjunctival thresholds than those of female subjects \( (P = 0.007; \text{ Fig. } 2 B) \). Age \( (R = 0.31, P = 0.15) \), or the interaction between age and sex \( (P = 0.66) \), did not have a significant effect on conjunctival thresholds in the nonwearers.

**Discussion**

Findings from this study showed that corneal and conjunctival sensitivity in long-term extended wearers of low \( Dk/t \) soft contact lenses was similar to those of non-lens-wearing subjects who were matched for age and sex. Although corneal sensitivity in the lens-wearing group decreased 1 week after subjects ceased wearing their lenses, there was no further change once subjects commenced high \( Dk/t \) silicone hydrogel lens wear. In addition, this is the first study to investigate the effects of long-term contact lens wear on the sensitivity of the conjunctiva. No changes in conjunctival sensitivity were detected in low or high \( Dk/t \) contact lens wear or with contact lens discontinuation. Higher corneal sensitivity was found for females in the control group, but not in the contact-lens-wearing group. However, there was some suggestion that contact lens wear may affect ocular surface sensitivity differently in males and females. Overall, our findings suggest that the impact of silicone hydrogel contact lens wear on the sensitivity of the ocular surface appears to be relatively minor.

The reduction in corneal sensitivity that was found to occur after subjects ceased low \( Dk/t \) lens wear for 1 week and transferred into high \( Dk/t \) silicone hydrogel lenses is in contrast to previous work, which has shown an increase in corneal sensitivity after discontinuation of short- and long-term contact lens wear or transfer into a higher oxygen permeable lens type.\(^ {5,6,9-12} \) Likewise, the finding that successful long-term extended wearers of low \( Dk/t \) contact lenses did not have significantly different corneal sensitivity from that of non-contact-lens wearers contrasts with the widely reported reduction in corneal sensitivity with short- and long-term wear of PMMA, RGP, and hydrogel contact lenses.\(^ {5,6,9-12} \) It is notable that only one of these multitude of studies examined extended wear.\(^ {12} \) A number of possible explanations may account for this dissimilarity to previously published findings.

Our findings suggest that deprivation of oxygen due to low \( Dk/t \) contact lens wear did not have a major impact on corneal sensitivity in our group of long-term lens wearers. In addition, the absence of an increase in corneal sensitivity with discontinuation of wear and transfer into high \( Dk/t \) lenses implies that oxygen deprivation is not solely responsible for the changes in corneal sensitivity associated with contact lens wear. Although high levels of hypoxia have previously been demonstrated to play a role in reducing corneal sensitivity,\(^ {15-17} \) it appears that the relatively low levels of hypoxia induced by the soft low \( Dk/t \) lenses worn in this study are not sufficient to induce prominent changes in sensitivity. It is important to note that much of the earlier work in this area has been carried out on non-oxygen-permeable PMMA lenses or on older types of hydrogel lenses, which are thicker, stiffer, and less permeable than those worn in this study.

Differences in the mode of stimulation of the aesthesiometer used here (Cochet-Bonnet) compared with the traditionally used type of aesthesiometer (Cochet-Bonnet) may also help to explain the divergent findings of this study relative to earlier work. We have previously shown that corneal sensitivity measurements made with these two instruments are not easily comparable.\(^ {24} \) Due to dissimilarities in the composition of their stimuli, it is likely that the two aesthesiometers stimulate late different receptor populations and these may be affected by contact lens wear in different ways. The nylon filament of the Cochet-Bonnet type is likely to interact with high-pressure corneal mechanoreceptors, whereas the more complex air jet of the CBA possibly recruits low-pressure mechanoreceptors in addition to polymodal and cold-sensitive units.\(^ {27} \)

Other factors, such as neural receptor sensitization may also explain the present findings. It is possible that sensitization of mechanical and polymodal receptors masks the reduction of corneal sensitivity concurrently induced by lens wear. Such sensitization could be expected to occur due to chronic subclinical inflammation resulting from injury induced by the continuing presence of the lens,\(^ {28-29} \) either due to its mechanical effect or due to metabolic consequences resulting from inadequacy tear exchange during extended wear. The reduction of sensitivity on discontinuation of lens wear could thus be a return to the decreased sensitivity levels expected for this group.

It is also possible that the unexpected reduction in corneal sensitivity found in this study could be associated with other processes that occur concurrently on discontinuation of low \( Dk/t \) lens wear, such as recovery of the epithelial thinning known to be induced by long-term lens wear.\(^ {30} \) Thus, a functional improvement in neuroreceptor sensitivity could be masked by a concurrent increase in epithelial thickness, which places the neural terminals further from the corneal surface, less exposed to stimulation. Although corneal epithelial thickness increased in this study over the same time frame as the reduction in sensitivity (J. Jalbert, personal communication, 2005), there was no association between these two effects on a within-subject level, indicating that the observed sensory decrease is unlikely to be caused by epithelial thickness changes.

It cannot be ruled out that loss of sensitivity due to contact lens wear measured in other studies is a transient effect and that over a long period the subjects in this study have adapted to contact lens wear. It is possible that with sustained wear, corneal sensation returns to near-normal levels, consistent with the reduced oxygen uptake of the corneal epithelium.\(^ {30} \) A similar adaptive recovery in response to long-term contact lens wear has been shown for epithelial thickness and bacterial binding.\(^ {31} \) Adaptation alone, however, does not explain the reduction in corneal sensitivity after discontinuation of lens wear.

Interestingly, no further changes in corneal sensitivity occurred in this study with up to 12 months wear of high \( Dk/t \) silicone hydrogel contact lenses. Ocular surface sensitivity in long-term silicone hydrogel lens wear has not previously been studied. Two studies of short-term wear of these lenses have shown no effect on corneal sensitivity.\(^ {13,14} \) It is possible, therefore, that high \( Dk/t \) lens wear has a minimal impact on corneal sensitivity. Such an explanation would support oxygen availability as a key modulator of corneal sensitivity. Another explanation is that silicone hydrogel lens wear maintains corneal sensitivity at a level below normal, most likely due to the mechanical pressure effects of this relatively stiff lens material on the corneal neuroreceptors.

This study is the first to investigate the effects of long-term hydrogel contact lens wear on the sensitivity of the conjunctiva. No changes in conjunctival sensitivity were detected in low or high \( Dk/t \) contact lens extended wear or with wear discontinuation. However, sex was shown to affect the conjunctival sensitivity response over time with different wear modalities in the lens wear group. The absence of a reduction in conjunctival sensitivity with low \( Dk/t \) hydrogel lenses or a change with transfer into high \( Dk/t \) lenses is not surprising, given that the conjunctiva is unlikely to be markedly affected by an altered oxygen supply. An increase in conjunctival sen-
sensitivity has previously been reported with short-term high Dk/t lens wear, using the same aesthesiometer as that used in the present study.13,14

The sex-related differences in corneal and conjunctival sensitivities found in the non-contact-lens wearers in this study are consistent with our previous findings,17 and with the findings of other investigators using a similar aesthesiometer.18,19 Interestingly, there was no significant effect of sex on corneal sensitivity in the lens-wearing group, suggesting that contact lens wear may in some way eradicate the difference in corneal sensitivity between males and females. However, sex was found to have a significant effect on the conjunctival sensitivity response to contact lens wear. The differing effect of sex on sensitivities of the cornea and conjunctiva is not surprising, given the different physiological makeup of these two tissues. The vascularized conjunctiva may be more susceptible to differences in hormone levels, which in other sensory systems have been suggested to play a role in mediation of sensitivity.52–54

The lens wearers in this study are a select group who have successfully completed a long period of contact lens wear in extended wear, a wear modality known to carry a high risk of discontinuation for physiological reasons; it is thus possible that this group of “survivors” have an altered sensitivity response. They are still, however, very much representative of the effects of long-term contact lens wear.

In summary, this is the first time the impact of low and high Dk/t contact lenses on ocular surface sensitivity has been compared in a longitudinal study and in extended wear, which allows potential confounding effects of contact lens solution to be disregarded. This study is also the first to examine conjunctival sensitivity in long-term wear of any lens type. This work has demonstrated that deprivation of oxygen due to low Dk/t contact lens wear does not have a major impact on corneal sensitivity in long-term wearers. In addition, the absence of a recovery in corneal sensitivity with discontinuation of wear or transfer into high Dk/t lenses has shown that oxygen availability alone does not determine changes in corneal sensitivity associated with contact lens wear. This work has also confirmed the sex differences in sensitivity and shown for the first time that, interestingly, these differences are subjigated by contact lens wear. In addition, this study highlights the importance of the type of instrument used to measure sensitivity because different aesthesiometers may measure the effects of different neuroreceptor populations. Such differences should be taken into account when comparing between studies.

Acknowledgments

The authors thank Thomas Naduvilath for advice on statistical analyses and Serina Stretton for editorial assistance.

References