Effect of Long-Term Contact Lens Wear on Corneal Endothelial Cell Morphology and Function

Keith H. Carlson, William M. Bourne, and Richard F. Drubaker

Anterior segment fluorophotometry (topical) and central endothelial cell photography were performed on 40 long-term (2–23 years) contact lens wearers (four groups of ten each: hard, soft, gas permeable, and gas permeable plus prior lens usage) and 40 non-contact lens wearers of similar ages. Morphologically, the endothelial cells of contact lens wearers showed greater variability in size and shape compared to controls. The mean endothelial cell size in contact lens wearers (307 ± 35 μm²) was smaller than that of controls (329 ± 38 μm², P < 0.01). There was an increase in the coefficient of variation of cell size of the contact lens group (0.35 ± 0.06 versus 0.25 ± 0.04 for controls, P < 0.0001). The endothelial cell mosaic contained a smaller percentage of hexagonal cells in contact lens wearers (66 ± 8) compared to controls (71 ± 7, P < 0.01). There was a compensatory increase in five-sided cells. Functionally, there was no difference in corneal clarity, central corneal thickness or endothelial permeability to fluorescein (3.78 ± 0.57 x 10⁻⁴ cm/min versus 3.85 ± 0.55 x 10⁻⁴ cm/min for controls) between the two groups. Aqueous humor flow was increased 7% in contact lens wearers. We found no correlation between oxygen transmissibility, estimated underlying oxygen tension, or duration of wear of the contact lenses and any morphologic or functional variable. We also found no differences between the four groups of contact lens wearers except that the gas permeable lens wearers had more hexagonal and less pentagonal cells. Long-term contact lens wear induces morphologic changes in the corneal endothelium. These changes, however, do not result in functional abnormalities detectable by the methods of this study. Invest Ophthalmol Vis Sci 29:185–193, 1988

Contact lens usage for the correction of refractive error is widespread. These lenses, in their various forms, have been available for over 30 years. In 1981, Schoessler and Woloschak described morphologic changes in the corneal endothelium which they attributed to chronic contact lens usage; since that time, numerous reports have confirmed and extended their findings.

The corneal endothelium is a single cell layer of neural crest origin that forms the most posterior layer of the cornea. The integrity of this layer is crucial for maintenance of normal corneal transparency. Its main function is to keep the cornea in a relatively dehydrated state for optimum clarity. This is accomplished by means of an energy-dependent metabolic pump and a relative barrier to fluid flow between the endothelial cells. Loss of endothelial function results in prompt corneal swelling.

The endothelium appears to have limited regenerative potential. If human or primate endothelial cells are damaged, the remaining cells in the area respond by enlargement and migration to cover the defect. Mitotic activity is minimal.

Several studies have shown that with increasing age there is a decrease in endothelial cell density and a concurrent increase in the variability of cell size. Numerous insults including infection, trauma or intraocular surgery can damage and destroy endothelial cells and thereby hasten the “aging” process. Given this limited endothelial regenerative potential, as cell loss occurs a point may be reached where the remaining cells are not in sufficient number to enlarge and cover the entire posterior corneal surface, producing corneal decompensation.

A number of studies have shown statistically significant alterations in the endothelium of young, long-term contact lens wearers. Although the mean cell size is normal, there is a wide variability of individual cell sizes which is out of proportion to age-matched controls. The cellular variability seen in these young contact lens wearers is similar to that seen in much
older non-contact lens wearing populations. This gives the impression of an "accelerated" aging process.

Several interesting questions arise. Do these morphologic changes in the endothelium translate into functional changes? Are endothelial permeability and central corneal thickness affected in contact lens wearers? Do changes in endothelial cell morphology or function vary with the type of contact lens worn? Are such changes transient or permanent and progressive? In this study we addressed the first three questions.

### Materials and Methods

Forty long-term (at least 2 years) contact lens wearers age 17 to 42 years (28 ± 6 years, mean ± standard deviation) were recruited from the Mayo Clinic contact lens practice. All subjects had a negative ophthalmic history and examination, ie normal visual acuity, intraocular pressure and slit lamp appearance. The corneas of all subjects were clear and without edema. There were four subject groups often end of the control group was 12 to 48 years (mean ±11 years). We obtained written informed consent for the study from all subjects.

The study consisted of two parts: endothelial cell photography and anterior segment fluorophotometry. All of the subjects had five to ten photographs taken of the central 3-4 mm of each cornea with a contact specular microscope (Heyer-Schulte Medical Optics Center, Irvine, CA). The microscope had a rectangular field of view of approximately 0.04 mm² of endothelial area. The central corneal thickness of each eye was also measured with the specular microscope.

Photographic measurements of the volumes of the anterior chambers were recorded.

The photographic negatives were projected at a magnification of ×500, and the areas of the individual cells were measured with an electronic planimeter (Numonics, Inc., Lansdale, PA). For each eye, 100 cells were traced from several negatives by a masked observer. This technique of measurement has a precision of 2% and a reproducibility (different photographs of the same cornea) of 7% if only 50 cells are traced. The mean and standard deviation of endothelial cell size, as well as the coefficient of variation of cell size (standard deviation/mean), were recorded for the 100 cells traced from each eye. In addition, the cell shape or polygonality was determined by counting the number of vertices (or sides) of each traced cell. Polygonality was expressed as the percentage of cells with n sides for n = 5, 6, 7, etc.

On a separate day, 30 hr after contact lens removal, the subject instilled Fluress® (0.25% fluorescein and 0.4% benoxinate; Barnes-Hind Inc., Sunnyvale, CA) into both eyes every 5 min for 20 min starting at 2:00 AM. Three fluorophotometric measurements were performed at 4 hr intervals with a scanning ocular fluorophotometer beginning at 8:00 AM. The measurements were made through the central 5 mm of the cornea and anterior chamber. The lids and lashes were carefully rinsed to remove any dried deposits of fluorescein prior to the first measurement.

The concentration of fluorescein in the mid-horizontal plane of the anterior segment was measured each time. The autofluorescence of the corneal stroma, measured before application of fluorescein, was subtracted from the total fluorescence. The mass of fluorescein in the corneal stroma (M_c) was calculated as the product of the mean concentration of fluorescein in the stroma (C_c) and the geometric volume of the cornea (V_c) (assumed to be 70 μl for all eyes). The mass of fluorescein in the anterior chamber (M_a) was calculated as the product of the mean concentration of fluorescein in the anterior chamber (C_a) and the geometric volume of the anterior chamber (V_a) measured for each eye photogrometrically.

The rate of clearance of fluorescein from the anterior chamber by diffusion and flow was calculated for

### Table 1. Characteristics of contact lens subgroups

<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup Description</th>
<th>n=</th>
<th>Manufacturers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Standard hard contact lenses</td>
<td>10</td>
<td>—poly(methyl)acrylate (10)</td>
</tr>
<tr>
<td></td>
<td>—five males, five females</td>
<td></td>
<td>—five males, five females</td>
</tr>
<tr>
<td>2</td>
<td>Daily wear soft contact lenses</td>
<td>10</td>
<td>—Hydron® (2), Hydron 04® (2), Soflens® (4), Ciba Clear® (1), Ciba aqua® (1)</td>
</tr>
<tr>
<td></td>
<td>—five males, five females</td>
<td></td>
<td>—five males, five females</td>
</tr>
<tr>
<td>3</td>
<td>Gas permeable hard contact lenses</td>
<td>10</td>
<td>—Polycon I® (2), Polycon II® (4), Boston II® (2), Paraperm® (2)</td>
</tr>
<tr>
<td></td>
<td>—three males, seven females</td>
<td></td>
<td>—three males, seven females</td>
</tr>
<tr>
<td>4</td>
<td>Gas permeable hard contact lenses plus prior hard or soft lens wear</td>
<td>10</td>
<td>—Polycon I® (1), Polycon II® (6), Paraperm® (1), Optacryl 95® (1), Optacryl K® (1)</td>
</tr>
<tr>
<td></td>
<td>—five males, five females</td>
<td></td>
<td>—five males, five females</td>
</tr>
</tbody>
</table>

Manufacturers:
- Hydron and Hydron 04: American Hydron, Woodbury, NY.
- Soflens: Bausch and Lomb, Rochester, NY.
- Ciba Clear and Ciba aqua: CIBA Vision Care, Atlanta GA.
- Polycon I and II: Sola-Syntex Ophthalmics, Phoenix, AZ.
- Boston II: Polymer Technology Corporation, Wilmington, MA.
- Paraperm: Paragon Optical Inc., Mesa, AZ.
- Optacryl 95 and K: Optacryl Inc., Inglewood, CO.
each temporally spaced pair of measurements of fluorescence in the eye:

\[
\text{rate of clearance} = \frac{(\Delta M_c + \Delta M_a)}{\bar{C}_a \Delta T} \tag{1}
\]

\(\bar{C}_a\) is the "average" concentration of fluorescein in the anterior chamber during the time interval, calculated from the formula:

\[
\bar{C}_a = \frac{C_a(1) - C_a(2)}{\ln [C_a(1)/C_a(2)]} \tag{2}
\]

Ten percent of the clearance of fluorescein was assumed to be due to diffusional losses and 90% due to the flow of aqueous humor through the anterior chamber: rate of flow of aqueous humor = rate of clearance \times 0.9.

We calculated the cornea-to-anterior chamber transfer coefficient \(k_{c-a}\) from the same measurements of fluorescein concentration using the relationships defined by Jones and Maurice. The endothelial permeability to fluorescein was calculated from the transfer coefficient as follows: Permeability = \(k_{c-a} \times CT/0.64\) in which \(CT\) is the central corneal thickness as measured with the specular microscope, and 0.64 is the anterior chamber-to-cornea equilibrium distribution ratio determined by Ota et al. Polarization of fluorescence in the corneal stroma and anterior chamber was measured fluorophotometrically using modifications in the scanning fluorophotometer as described by Herman et al. The polarization is related to the proportion of the emitted light that is linearly polarized parallel to the same plane as the polarized excitatory light. The polarization of fluorescence gives an indication of binding of the fluorescein molecule in tissue or solution.

For each subject, the following contact lens information was recorded: brand name, number of years worn, hours of daily wear, water content, oxygen permeability (Dk), central lens thickness (L) and estimated oxygen tension under the lens.

The manufacturers provided the oxygen permeability (Dk) for each specific lens, except for the polymethylmethacrylate lenses (group 1), for which we used the permeability value reported by O'Neal et al. The central lens thickness (L) was determined by direct micrometer measurement for the hard and gas permeable lenses and from the manufacturers' specifications for the soft lenses. The oxygen transmissibility (Dk/L) was calculated for both lenses of each subject using the central lens thickness for L. The oxygen tension under each lens was estimated by the method of Fatt and Lin using a blink period of 5 seconds, a tear film thickness of 32 \(\mu m\), and a tear mixing efficiency of 0.05 for the soft lenses and 0.15 for the hard and gas permeable lenses.

Analysis of Data

We recorded the following values for both eyes of each subject: (1) Endothelial permeability to fluorescein; (2) Central corneal thickness; (3) Aqueous humor flow; (4) Mean endothelial cell size; (5) Coefficient of variation of cell size; (6) Relative frequency of cell shapes; (7) Polarization of fluorescence in the cornea; and (8) Polarization of fluorescence in the anterior chamber.

First, we compared the data (values 1–8) of all contact lens wearers (n = 40) with that of the control group (n = 40). Second, we compared each contact lens subgroup separately with the control group. Third, we looked for significant differences between the four contact lens subgroups. Fourth, we looked for sex differences in the contact lens wearers. Fifth, we looked for correlations with oxygen transmissibility of the lenses, estimated oxygen tension under the lenses, and duration of lens wear. A two-sample t-test and Wilcoxon test were performed for each variable analyzed. Correlations were tested with a Spearman coefficient of correlation. A probability of 0.05 was considered statistically significant.

Results

Table 2 summarizes the combined data from all four contact lens-wearing groups and the control group. The data listed in Tables 2 and 3 are mean values from both eyes. The data from the right and left eyes were also analyzed separately, and the results were similar. Endothelial permeability to topically applied fluorescein was not statistically different between the two groups. We found average values of 3.78 ± 0.57 \(\times 10^{-4}\) cm/min for the contact lens group and 3.85 ± 0.55 \(\times 10^{-4}\) cm/min for the control group. In a study such as this, a statistically significant difference \((P \leq 0.05, \text{two-sided})\) would be found 90% of the time (90% power) if the true difference in permeability were at least 4.1 \(\times 10^{-4}\) cm/min (11%) and the population from which the samples were drawn were distributed normally. In other words, we can be 90% confident that long-term contact lens wearers, as a group, differ by less than 11% in endothelial permeability from non-contact lens wearers. Central corneal thickness was similar for both groups.

A slight increase in aqueous humor flow was found in contact lens wearers, 2.84 ± 0.51 \(\mu l/min\) compared to 2.65 ± 0.52 \(\mu l/min\) for the controls. This was of borderline statistical significance (Wilcoxon: \(P < 0.05, \text{t-test: } P < 0.10\)).
Table 2. Summary data: all contact lens wearers versus controls

<table>
<thead>
<tr>
<th></th>
<th>Contact lens wearers (mean ± SD)</th>
<th>Controls (mean ± SD)</th>
<th>Probability (Wilcoxon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endothelial permeability to fluorescein (×10⁻⁴ cm/min)</td>
<td>3.78 ± 0.57</td>
<td>3.85 ± 0.55</td>
<td>&gt;0.58</td>
</tr>
<tr>
<td>Central corneal thickness (mm)</td>
<td>0.54 ± 0.03</td>
<td>0.54 ± 0.03</td>
<td>&gt;0.78</td>
</tr>
<tr>
<td>Aqueous humor flow (µl/min)</td>
<td>2.84 ± 0.51</td>
<td>2.65 ± 0.52</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Endothelial cell size (µm²)</td>
<td>307 ± 35</td>
<td>329 ± 38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Coefficient of variation of cell size</td>
<td>0.35 ± 0.06</td>
<td>0.25 ± 0.04</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relative frequency of cell sides (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 sides</td>
<td>20 ± 4</td>
<td>16 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 sides</td>
<td>66 ± 8</td>
<td>71 ± 7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>7 sides</td>
<td>12 ± 3</td>
<td>11 ± 3</td>
<td>&gt;0.61</td>
</tr>
<tr>
<td>8 sides</td>
<td>2 ± 1</td>
<td>1 ± 1</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Polarization of fluorescence (cornea)</td>
<td>0.19(n = 18) ± 0.02</td>
<td>0.18(n = 38) ± 0.02</td>
<td>&gt;0.15</td>
</tr>
<tr>
<td>Polarization of fluorescence (anterior chamber)</td>
<td>0.03(n = 18) ± 0.03</td>
<td>0.03(n = 38) ± 0.03</td>
<td>&gt;0.38</td>
</tr>
<tr>
<td>Fluorescein concentration (ng/ml)†</td>
<td>752 ± 400</td>
<td>646 ± 402</td>
<td>&gt;0.15</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>28.1 ± 6</td>
<td>29.1 ± 11</td>
<td>&gt;0.10</td>
</tr>
</tbody>
</table>

* P < 0.10—t-test. † Initial concentration of fluorescein in corneal stroma, 6 hr after topical application.

Morphologic analysis of the endothelial cells showed a decrease in mean cell size in contact lens wearers compared to the controls, 307 ± 35 µm² and 329 ± 38 µm² respectively. In addition, there was an increase in the coefficient of variation of cell size among contact lens wearers (0.35) compared to controls (0.25).

Contact lens wearers showed a decrease in the relative frequency of endothelial cells with six sides, 66% compared to 71% for controls, and a corresponding increase in five-sided cells.

Polarization of fluorescence, an indication of protein binding, was measured in 18 of the 40 contact lens wearers (Table 2). No significant difference was found between the contact lens and control groups with respect to cornea and anterior chamber polarization of fluorescence. The initial concentration of fluorescein in the corneal stroma was not statistically different between the two groups (Tables 2 and 3). Finally, we found no differences by sex in any of the variables analyzed in either the contact lens or control groups.

Table 3 summarizes the data of each subgroup of contact lens wearers compared to the control group. Endothelial permeability and central corneal thickness were relatively constant across all four contact lens groups as well as the control group. Wilcoxon rank sum analysis showed no differences between the groups.

The relative frequency of five and six-sided endothelial cells was found to differ across the four contact lens groups. Gas permeable lens wearers had a higher proportion of six-sided cells and a lower proportion of five-sided cells (72% and 16% respectively) than the other three groups (P < 0.01 and P < 0.001).

The oxygen transmitissibility (Dk/L) and estimated oxygen tension of each lens were compared to the mean endothelial cell size, the coefficient of variation of cell size and the percentage of hexagonal cells associated with it. No statistically significant correlations were found. The preceding correlations were also not significant when each contact lens group was tested separately. Aqueous humor flow, central corneal thickness, polarization of fluorescence, endothelial permeability to fluorescein and the percentage of...
Table 3. Subgroups of contact lens wearers vs control group

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 40)</th>
<th>Hard</th>
<th>Soft Corneal</th>
<th>Gas Permeable Plus</th>
<th>Gas Permeable</th>
<th>Continuous Wear</th>
<th>Continuous Wear Gas Permeable plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability (%)</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
<td>100.0 &gt; 144.02</td>
</tr>
<tr>
<td>Contact lens subgroup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
<td>2.9 ± 0.74</td>
</tr>
<tr>
<td>Central Corneal Thickness (μm)</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
<td>0.4 ± 0.35</td>
</tr>
<tr>
<td>Endothelial permeability</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Mean ± standard deviation.

† From Table 2.

§ Initial concentration of fluorescein in corneal stroma, 6 hours after topical application.

# Contact lens subgroup compared to control group (Wilcoxon).
Table 4. Contact lens data

<table>
<thead>
<tr>
<th>Water content (%)</th>
<th>Hard</th>
<th>Soft</th>
<th>Gas permeable</th>
<th>Gas permeable* plus other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.5</td>
<td>39.0</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Range</td>
<td>1.5</td>
<td>37.5-45.0</td>
<td>&lt;1-&lt;2</td>
<td>&lt;1-&lt;2</td>
</tr>
<tr>
<td>Years worn</td>
<td>14.1</td>
<td>4.9</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Range</td>
<td>5-23</td>
<td>2-11</td>
<td>2-7</td>
<td>2-8</td>
</tr>
<tr>
<td>Hours per day worn</td>
<td>13.4</td>
<td>14.2</td>
<td>14.5</td>
<td>14.7</td>
</tr>
<tr>
<td>Range</td>
<td>8-16</td>
<td>12-16</td>
<td>5-17</td>
<td>12-16</td>
</tr>
<tr>
<td>Oxygen transmissibility (Dk/L) (\times 10^{-9})</td>
<td>Mean</td>
<td>0.17</td>
<td>12.1</td>
<td>11.0</td>
</tr>
<tr>
<td>cm ml (O_2/\text{sec ml mm Hg})</td>
<td>Range</td>
<td>0.1-0.3</td>
<td>5.4-16.5</td>
<td>4.6-17.3</td>
</tr>
<tr>
<td>Estimated oxygen tension under contact lens (mm Hg)</td>
<td>Mean</td>
<td>15.0</td>
<td>37.3</td>
<td>49.9</td>
</tr>
<tr>
<td>Range</td>
<td>—</td>
<td>16.0-54.0</td>
<td>26.0-76.0</td>
<td>17.0-95.0</td>
</tr>
</tbody>
</table>

* Data are for gas permeable hard contact lenses currently worn. Subjects had previous hard or soft contact lens usage.

cells with sides other than six also showed no significant correlations with DK/L or estimated oxygen tension.

Table 4 summarizes additional contact lens data. Percent water content of lens, number of years worn and hours worn per day are listed for each contact lens group. We found no statistically significant correlations between wearing time (either years or hours/day) and any morphologic or functional variable. This was true across all subgroups of contact lens wearers.

Discussion

This study agrees with the results of other investigators in showing that contact lens wear affects the corneal endothelium. There is an increased variation of endothelial cell size and shape in the eyes of contact lens wearers. The ratio of the standard deviation of cell size divided by the mean cell size, termed the coefficient of variation of cell size, is a useful measure of the variability of endothelial cell size in a given subject. Numerous studies, including this one (Table 2), show an increased coefficient of variation in contact lens wearers. In addition, the percentage of hexagonal cells making up the endothelial mosaic decreases in contact lens wearers, and there is a compensatory increase in cells of other than six sides (Table 2). Contact lens-induced hypoxia is thought to be responsible for these endothelial changes.1-6 It is noteworthy that the gas permeable lens wearers had a statistically significantly higher proportion of hexagonal cells (\(P < 0.01\)) and lower proportion of five-sided cells (\(P < 0.001\)) than the other three groups (Table 3). It has been reported that cellular hexagonality is a more sensitive indicator of endothelial damage or instability than is the coefficient of variation of cell size.34

If corneal hypoxia is responsible for these morphologic changes, then a contact lens which provides the greatest amount of oxygen to the cornea should produce the least amount of endothelial change. Schoessler et al7 have shown that lenses of extremely high oxygen transmissibility (Silicone Elastomer—Silsoft® (Bausch and Lomb, Rochester, NY): DK/L = \(340 \times 10^{-9}\) cm ml \(O_2/\text{sec ml mm Hg}\) for a lens 0.1 mm thick) produce no morphologic changes in the corneal endothelium. O’Neil et al32 and Holden and Mertz35 found that a minimum lens oxygen transmissibility (DK/L) of 75-87 \(\times 10^{-9}\) cm ml \(O_2/\text{sec ml mm Hg}\) is needed to prevent contact lens-induced corneal edema with overnight wear. The contact lenses used in the present study had substantially lower oxygen transmissibilities (Table 4). Because we used central lens thickness rather than average thickness36 to calculate DK/L, the true oxygen transmissibilities of the lenses may be somewhat different, but this should not affect our conclusions.

We found no significant correlation between oxygen transmissibility, estimated oxygen tension or duration of lens wear and any morphologic or functional variable, even when each contact lens group was considered separately. It is possible that these values do not mirror corneal oxygenation closely because of other factors such as lens movement and tear exchange and our inability to measure them accurately.

Whereas others1-11 have shown either no change or an increase in the mean endothelial cell size of contact lens wearers, we recorded a decrease in size that
was present across all subgroups (Tables 2, 3). Because we analyzed 100 different cells from several small-field photographs, it is possible that proportionally more large cells than small cells were untraceable (and therefore not measured) because they crossed the margins of the photographs. If this error in sampling had occurred, however, we probably would not have observed a much larger coefficient of variation of cell size in the contact lens group. Nevertheless, our results need to be confirmed by studies with wide-field photography. In our contact lens group, despite the large variation in size and shape, a substantial proportion of endothelial cells were much smaller than the mean cell size of the control group. Why a larger proportion of small endothelial cells should be present in contact lens wearers is puzzling. It has been shown that mean endothelial cell size increases with age.\textsuperscript{20-24} In our study, however, there were no age differences between the contact lens and control groups (Tables 2, 3). One explanation is the possible faulty sampling mentioned above, which we feel is unlikely. A second unsupported explanation is that endothelial cells are dividing in response to metabolic stress. Hirst et al,\textsuperscript{6} observing clusters of small cells in endothelial cell photographs, suggested the possibility of active endothelial mitosis despite evidence to the contrary after other types of injury.\textsuperscript{13-19}

Aqueous humor flow was slightly increased in contact lens wearers (Tables 2, 3). The change in flow was quite small (7\%) and probably is unimportant. We hesitate to speculate about its cause (increased lactate in the cornea\textsuperscript{37} or aqueous humor,\textsuperscript{38} for example) until the finding is confirmed.

We looked for differences between the groups that could account for the changes in flow observed. Contact lens wearers removed their lenses 30 hr prior to the study to allow the corneal epithelium to return to a baseline state. Accordingly, we found no difference between the initial fluorescein concentration within the corneal stroma of contact lens wearers and controls (Tables 2, 3). There was no evidence of increased binding of fluorescein within the stroma of either group as shown by the similar values of the polarization of fluorescence (Table 2). Had increased binding been present, it could have quenched the fluorescent signal from the corneal stroma and, thereby, influenced the flow calculation. The anterior chambers of myopic contact lens wearers may have been larger than the controls, but no correlation was found between the anterior chamber volume and aqueous flow.

With these morphologic changes in the corneal endothelium, is endothelial function impaired? Corneal clarity and central corneal thickness were the same in both groups. Likewise, endothelial permeability to fluorescein was not statistically different; with the techniques used in this study, we can state with 90\% confidence that the true difference in endothelial permeability between contact lens wearers and controls is not greater than 11\%. By the techniques of this study, it appears that the endothelium of contact lens wearers functions as well as that of non-contact lens wearers. However, as Holden et al\textsuperscript{10} have shown, epithelial and stromal thickness decrease following contact lens removal. They found that stromal thickness was 2.5\% greater in the lens-wearing eye than in the control eye immediately following lens removal, but decreased to become thinner than the control eye by the second day. Stromal thickness continued to decrease and reached a constant level in 1 week. Our subjects removed their lenses 30 hr prior to the study. Perhaps our corneal thickness measurements were made during the period of transition from increased stromal thickness to stromal thinning, and thus we were unable to record a difference in corneal thickness between controls and contact lens wearers.

The changes in the endothelial cell morphology seem to develop early and regress slowly, if at all, after abandoning contact lens wear. Santos and Holden\textsuperscript{39} and others\textsuperscript{40-45} have shown that the earliest endothelial cell changes (endothelial bleb response) appear minutes after initial exposure to contact lenses. Holden et al\textsuperscript{10,46} observed that increased variation in endothelial cell size is apparent within 2 weeks of commencing extended soft lens wear. In addition, they observed patients 1 month after discontinuing contact lenses and found only a slight reduction in the variability of endothelial cell size that was not statistically significant. MacRae et al\textsuperscript{41} studied former hard contact lens wearers who discontinued lens wear for an average of 4.3 years. These individuals showed persistent endothelial alterations compared to controls. From our data, patients with prior hard or soft contact lens wear and subsequent gas permeable lens wear showed no improvement in endothelial cell morphology. However, the oxygen transmissibility in the gas permeable lenses was not substantially greater than that of the soft lenses (Table 4). Moreover, subjects with gas permeable lenses and no prior lens wear showed endothelial changes similar to that of soft and hard contact lens wearers.

Stocker and Schoessler\textsuperscript{4} noted a significant increase in polymegathism (coefficient of variation of cell size) with increased wearing time in 15 hard contact lens wearers. We did not demonstrate a significant correlation between these factors, although we studied only ten subjects in each group. The range of ages of our subjects was less than that in their study. The effect of age, which is also correlated with polymegathism,\textsuperscript{20-24} on the regression between wearing time...
and polymegathism was not evaluated by Stocker and Schoessler.8 The average age of the control subjects and contact lens wearing subjects in our study was young (29 ± 11 years and 28 ± 6 years, respectively). We have recently observed that endothelial permeability to fluorescein increases by a factor of 23% from age 5 years to 79 years.47 At the same time, endothelial cell morphology becomes more variable with advancing age. The increased variability in endothelial cell size and shape in older individuals is similar to that seen in much younger contact lens wearers. Time will tell if contact lens wearing plus advancing age have additive effects on the corneal endothelium and thereby lessen its functional reserve in times of stress.

In summary, the use of daily wear soft, standard hard or gas permeable hard contact lenses induces morphological changes in the corneal endothelium. Contact lens wearers show greater variation in the size and shape of endothelial cells compared to non-contact lens wearing controls. By the methods used in this study, however, no differences in endothelial function were found between these contact lens wearers and controls. Endothelial permeability to fluorescein, central corneal thickness and corneal clarity were the same for both groups.

Key words: contact lens wear, specular microscopy, fluorophotometry, endothelial morphology, endothelial function

References