Purpose. To examine whether corneal hydration control is impaired in corneas with endothelial morphologic changes (increased variation in cell size and cell angularity) due to long-term low gas-permeable contact lens wear.

Methods. Twenty-one long-term wearers of low gas-permeable contact lenses (mean age, 41 years ± 8 SD) and 18 age-matched controls (mean age, 42 years ± 8 SD) were studied. To assess endothelial morphology, endothelial photographs were taken, enlarged 400X, scanned into a computer, and evaluated. Hydration control was assessed by a corneal stress test. Corneal swelling was induced by applying low gas-permeable soft contact lenses for 2 hours during eye closure. After the lenses were removed, the rate of deswelling was determined using optic pachometry.

Results. Morphologic analysis of the endothelial photographs showed a significant increase of polymegethism ($P < 0.01$) and pleomorphism ($P < 0.01$) in the group wearing contact lenses compared with the control group. The percentage of recovery of corneal thickness per hour (PRPH) from induced swelling proved to be significantly lower ($P = 0.03$) and the induced swelling proved to be significantly lower ($P < 0.01$) in the group wearing contact lenses than in the control group. Multiple regression analysis showed that the PRPH decreased as the morphologic alterations increased. However, this trend appeared not to be significant at the 5% level. A significant relationship was found between morphologic parameters and induced swelling, indicating that induced swelling decreased as the morphologic alterations increased.

Conclusions. The results of this study indicate that increased endothelial polymegethism and pleomorphism may be accompanied by a decreased corneal hydration control in people who wear contact lenses. Invest Ophthalmol Vis Sci. 1994;35:3071–3077.
differences in endothelial permeability to fluorescein between contact lens wearers and controls.

The increased degrees of polymegethism and pleomorphism are thought to be induced by chronic hypoxia of the cornea under the contact lens. This hypothesis is supported by the finding that high gas-permeable rigid and silicone lenses do not induce these changes in the corneal endothelial morphology.14,15

Whether corneal functional deterioration does exist in corneas with endothelial polymegethism is not yet clear from the research. The study described here was, therefore, performed to contribute to determining whether corneal function is decreased in corneas with increased polymegethism and pleomorphism due to long-term low gas-permeable contact lens wear and whether corneal function is related to endothelial morphology.

MATERIALS AND METHODS

Subjects

Twenty-one long-term (>10 years) wearers of low gas-permeable contact lenses (mean age, 42 years ± 8 SD, range 26 to 51 years; 19 women, 2 men), who were known at the contact lens department, and 18 controls of similar age (mean age, 41 years ± 8 SD, range 25 to 52 years; 9 women, 9 men) were included in this study. Both groups were free of ocular disease or treatment.

The contact lens group was composed of 17 wearers of polymethyl methacrylate (PMMA) lenses and four wearers of soft contact lenses, all of whom wore their contact lenses on a daily wear basis. All subjects were currently wearing contact lenses except two PMMA lens wearers, who discontinued contact lens wear 2 and 3 years, respectively, before the start of this study because of increased endothelial polymegethism. At the time of the measurements, two subjects wore PMMA lenses and three subjects wore soft lenses. Fourteen of the 19 current contact lens wearers had been refitted with rigid high gas-permeable contact lenses. The years of this high gas-permeable contact lens wear (range, 2 to 5 years) were not added to the number of years of low gas-permeable (PMMA or soft) lens wear.14,15 All but one subject wore only one low gas-permeable lens type; the remaining subject wore PMMA lenses for 24 years and soft lenses for 3 years. The mean wearing time of low gas-permeable contact lenses was 19.5 years (range, 12 to 29 years).

This study followed the tenets of the Declaration of Helsinki, and permission to perform the study was obtained from the Medical Ethics Committee of the Academic Medical Center of Amsterdam. Informed consent was obtained from each subject after the nature and the possible consequences of the study were explained.

Morphology

The corneal endothelium was photographed with a Nikon (Tokyo, Japan) noncontact specular microscope, using Kodak (Rochester, NY) T-max 400 ASA film. The approximate location of the specular photographs was the center of the cornea. The area covered by one photograph was approximately 0.04 mm². About 15 photographs were taken of each cornea. Based on cell boundary clarity, the best three were selected for further evaluation. The total linear magnification of the final enlargements was 400X.

The contours of the endothelial cells on the enlarged photographs were obtained by digitizing the photographs and selecting the coordinates of the cell apices with the aid of a mouse. For each photograph, a pattern of 50 contiguous cells was digitized. Thus, 150 cells per eye were measured.

For each cornea, a number of parameters describing cell size and cell shape were determined. With regard to cell size, the mean cell area and the coefficient of variation (CVAREA) were determined. Cell shape was quantified with the number of sides of each cell (angularity). For each cell pattern, the mean number of sides, the coefficient of variation of the number of sides (CVANG), and the percentage of six-sided cells (%SIX) were determined. CVAREA was used as a measure of the variation in cell size (polymegethism), and CVANG and %SIX were used as measures of the variation in cell shape (pleomorphism). Reliability and accuracy of the method were discussed previously.15

Function

Contact lens wearers discontinued their lens wear the evening before the corneal thickness measurements were performed. To eliminate any possible effect of contact lens wear on the outcome of the corneal thickness measurements, it has been advised16 in extended wear to observe a longer lens-free period before the measurements. A longer lens-free period, however, was not acceptable for the subjects in this study. A contact lens-free period of 12 hours was expected to be sufficient because subjects only wore their lenses on a daily wear schedule.

Central corneal thickness was measured with a Haag-Streit (Bern, Switzerland) pachometer that was equipped with fixation and alignment lights to increase reproducibility.17,18 The pachometer was attached to an electronic recording system and linked to a personal computer, which allowed simultaneous calculation of corneal thickness. On each measuring day,
Effects of Long-Term Contact Lens Wear

the pachometer was calibrated with eight polymethylmethacrylate contact lenses of known thickness (300 μm to 650 μm). Each corneal thickness measurement, at a certain time point, was obtained as two sets of 10 readings, carried out within 4 minutes. Each set of 10 readings was averaged; hence, at every time point, 2 means of 10 readings were obtained.

To assess corneal hydration control, corneal swelling was induced and, subsequently, the deswelling was measured. Swelling was induced by applying a low gas-permeable soft stress contact lens on both eyes for 2 hours, during which time the eyes were kept closed with a patch. A low water content (40%) hydrogel contact lens, having a thickness of 0.45 mm and a diameter of 15 mm, with an oxygen permeability (Dk) of 7 ((X10-11)(cm²/s)(ml O₂/ml X mm Hg)) was used. The lenses were available in the posterior curve radii 8.1, 8.3, 8.5, 8.7, 8.9, and 9.1 mm.

Before applying the stress contact lens, at least 10 duplicate thickness measurements were performed during 2 hours to establish the baseline corneal thickness. These baseline measurements were performed after the subjects were awake for at least 2 hours to avoid possible thickness changes after eye closure during the night.10

Corneal swelling was subsequently induced by applying the stress contact lenses for 2 hours during eye closure. During this period, no measurements were made. After 2 hours of lens wear, the lenses were removed and thickness measurements were performed at 15-minute intervals during 5 hours. A representative example is shown in Figure 1.

An exponential curve was fitted to the experimental recovery data by the least squares method.

![Figure 1](example.png)

**FIGURE 1.** Example of the corneal stress test to determine hydration control. Each point represents the mean of two eyes of one individual. PRPH of this individual is 49.5%.

### Table 1. Morphologic Parameters of the Corneal Endothelium After Long-Term Contact Lens Wear

<table>
<thead>
<tr>
<th>Contact Lens Wearers</th>
<th>Controls</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 21</td>
<td>n = 18</td>
<td></td>
</tr>
<tr>
<td>Cell area (μm²)</td>
<td>343.6 ± 57.8</td>
<td>349.6 ± 54.4</td>
</tr>
<tr>
<td>CVAREA (%)</td>
<td>39.6 ± 6.9</td>
<td>27.1 ± 4.0</td>
</tr>
<tr>
<td>Cell angularity</td>
<td>6.0 ± 0.2</td>
<td>6.0 ± 0.2</td>
</tr>
<tr>
<td>CVANG (%)</td>
<td>12.3 ± 1.5</td>
<td>9.7 ± 1.1</td>
</tr>
<tr>
<td>% SIX</td>
<td>56.1 ± 7.1</td>
<td>67.8 ± 6.1</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

CVAREA = Coefficient of variation of the mean cell area; CVANG = coefficient of variation of the number of sides; % SIX = percentage of six-sided cells.

\[
\text{th}(t) = a + b \cdot e^{-c \cdot t_0}
\]

\(\text{th} = \) thickness at time t (in hours)
\(a = \) baseline thickness
\(b = \) induced swelling
\(c = 1/\text{time constant}
\(t_0 = \) time of removal of contact lens

From this, the percent recovery per hour (PRPH) after induced swelling was calculated according to the following formula:

\[
\text{PRPH} = (1 - e^{-c}) \times 100\%
\]

### Statistical Analysis

For comparison of the parameters describing morphology and function between the patient and the control groups, the Mann-Whitney test was used. To quantify the relationship between morphologic and functional parameters and the relationship between those parameters and the duration of low-gas permeable contact lens wear, multiple regression analysis was used. Averages of the parameters of left and right eyes were used for the analyses.

### RESULTS

To examine the effect of long-term low gas-permeable contact lens wear on endothelial morphology and on corneal hydration control, a group of long-term wearers of contact lenses and an age-matched control group were investigated.

The parameters that describe the endothelial morphology are summarized in Table 1. The mean area per cell and the mean number of sides per cell were approximately equal for both groups. CVAREA and CVANG of the group wearing contact lenses were significantly increased compared with those of the control group (P < 0.01). %SIX in the group wearing con-
TABLE 2. Functional Parameters of the Cornea After Long-term Contact Lens Wear

<table>
<thead>
<tr>
<th></th>
<th>Contact Lens Wearers (n = 21)</th>
<th>Controls (n = 18)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline thickness (µm²)</td>
<td>537.9 ± 34.5</td>
<td>555.0 ± 28.5</td>
<td>0.10</td>
</tr>
<tr>
<td>Induced swelling (%)</td>
<td>11.6 ± 1.5</td>
<td>12.8 ± 1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PRPH (%)</td>
<td>52.1 ± 7.0</td>
<td>56.7 ± 5.8</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Contact lenses was decreased compared with the control group (P < 0.01). Thus, increased polymegathism and pleomorphism were found in the contact lens wearing group.

The parameters describing corneal hydration control are summarized in Table 2. Corneal baseline thickness showed no significant difference between the group wearing contact lenses and the control group. On the other hand, the percentage of induced swelling caused by 2 hours of stress-lens wear was significantly smaller in the contact lens wearing group than in the control group (P < 0.01). PRPH of the contact lens wearing group was significantly decreased compared with the control group (P = 0.03), indicating a slower recovery from induced swelling and, thus, a deterioration of corneal hydration control in the contact lens wearers.

Multiple regression analysis was used to determine whether corneal hydration control was related to corneal endothelial morphology. The contact lens wearers and the controls were grouped together for this analysis. A downward trend was found between the parameters describing endothelial morphology (CVAREA, CVANG) and the functional parameter PRPH, indicating that PRPH decreased as morphologic alterations increased (Fig. 2). This trend was not significant at the 5% level (P = 0.11 and P = 0.13, respectively). Both groups were also analyzed separately. No correlation was found between morphology and PRPH within the groups. Because the parameters describing pleomorphism (CVANG and %SIX) have similar outcomes, only CVANG was analyzed for determining relationships.

![Figure 2](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933405/)

**FIGURE 2.** Relationship between morphologic parameters and PRPH. □ = Contact lens wearers; ▲ = controls.

![Figure 3](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933405/)

**FIGURE 3.** Relationship between morphologic parameters and induced swelling. □ = Contact lens wearers; ▲ = controls.
TABLE 3. P Values Describing Relationship Between Duration of Contact Lens Wear and Morphologic and Functional Parameters

<table>
<thead>
<tr>
<th>CVAREA</th>
<th>CVANG</th>
<th>PRPH</th>
<th>Swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact lens wearers and controls</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Contact lens wearers</td>
<td>0.45</td>
<td>0.95</td>
<td>0.77</td>
</tr>
</tbody>
</table>

The same analysis was performed to determine whether a relationship existed between the morphologic parameters (CVAREA, CVANG) and corneal swelling response caused by the 2 hours of stress-lens wear. A significant relationship was found between morphologic parameters and swelling when the contact lens wearers and controls were grouped together, indicating a decrease of induced swelling as the morphologic alterations increase ($P = 0.03$ and $P = 0.04$, respectively) (Fig. 3). This relationship was not detectable in the separate groups.

We also investigated whether the morphologic and functional changes were related to the duration of low gas-permeable contact lens wear. When contact lens wearers and controls were grouped together, a significant correlation was found for almost all parameters. When the contact lens wearing group (duration of wear 12–29 years) was analyzed separately this correlation was not found (Fig. 4). P-values are provided in Table 3.

**DISCUSSION**

In this study a long-term low gas-permeable contact lens wearing group and an age-matched control group were investigated in order to determine whether corneal hydration control was decreased in corneas with increased polymegathism and pleomorphism, and if so, to determine whether the degree of loss in function was related to the extent of the morphologic changes.

The parameters describing variation in cell size (polymegethism) and variation in cell angularity (pleomorphism) were increased in our long-term contact lens wearing group as compared with the age-matched control group. These findings correspond with earlier findings reported by other groups.1–6

Recently, Pole and coworkers developed a method for in vivo assessment of overall corneal hydration control in which the recovery of corneal thickness from induced swelling is determined.19 In our study, a decreased rate of recovery was present in the group of long-term wearers of contact lenses com-

![Figure 4](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933405/)
pared with the age-matched control group. This finding supports the hypothesis that the long-term wear of low gas-permeable contact lenses is accompanied by functional impairment.

If contact lens wearers and controls were grouped together, a significant correlation between the degree of morphologic changes (increased polymegethism and pleomorphism) and the degree of swelling response was found: Increased polymegethism and pleomorphism was accompanied by a decrease in swelling response. Furthermore, a downward trend between the degree of morphologic changes and the thickness recovery rate was demonstrated. These results indicate a possible relationship between endothelial morphologic alterations and corneal function deterioration as a result of hypoxic contact lens wear. If both groups were analyzed separately, correlation between morphology and function was not found. Within the control group, such an outcome, indicating a normal range, was to be expected. However, within the group wearing contact lenses, morphology and function appeared not to correlate as well, indicating that other as yet unknown factors may also be responsible for corneal hydration control in contact lens wearers.

Another problem involves the fact that the specular microscopic photographs we used to assess the endothelial morphology only show the posterior surface of the endothelium. Bergmanson used scanning electron microscopy to evaluate the endothelium of contact lens wearers after death and found an oblique reorientation of the lateral walls of the endothelial cells, indicating that a cell with a large posterior surface might have a small anterior surface or vice versa and that polymegethous cells may not vary in overall volume.

After inducing corneal edema from 24 hours of PMMA contact lens wear, Bergmanson observed morphologic changes of the corneal keratocytes. He also found that stromal edema began posteriorly and then advanced anteriorly, indicating endothelial dysfunction.

Possibly stromal keratocytes and their proteoglycan production also play an important role in the corneal hydration control. Kangas showed that proteoglycans are lost from the stroma in short-term edema, induced by the disruption of endothelial intercellular junctions. Chronic edema might lead to more pronounced loss of proteoglycans. This supposed diminished capacity of the cornea to contain water might, in part, also be responsible for the finding that the degree of induced swelling by stress lens wear appeared smaller in the contact lens wearers than in the controls.

In our study, corneal baseline thickness showed no significant difference between the group wearing contact lenses and the control group. Holden found a stromal thinning of 2 μm per year in wearers of extended hydrogel contact lenses and ascribed this phenomenon to the chronic corneal edema due to chronic hypoxia under the contact lens.

A correlation between years of contact lens wear and degree of deterioration of both endothelial morphology and corneal hydration control was found when controls and contact lens wearers were grouped together. This is in agreement with a study by Polse et al in which a dose-dependent decrease of morphologic and functional parameters was suggested. Most subjects in that study, however, had worn their lenses for less than 10 years. When only the contact lens wearers were analyzed in our study (duration of wear 12 to 29 years), no significant correlation was found. These findings are in agreement with a recent publication of McMahon. A possible explanation might be that most morphologic and functional changes may be introduced during the first 10 years of contact lens wear and that these changes remain more or less stable when contact lens wear is continued. However, there also might be individual variability with regard to the corneal response to chronic hypoxia induced by low gas-permeable contact lens wear. Individual metabolic requirements might be different or the hypoxic dose received by the cornea might depend not only on the gas-permeability of the contact lens but also on factors like contact lens fitting, tear pumping rates, and individual wearing time per day.

After the subjects in our study were awake for at least 2 hours, we measured the baseline thickness during 2 hours before applying the stress contact lens (see Materials and Methods). These baseline thickness measurements were analyzed in all subjects to detect any downward trend from possible overnight swelling that could influence the recovery data. Chi-square analysis demonstrated no downward trend. Based on the above findings, the 2 hours of wakefulness was expected not to cause any systematic errors in the data analysis.

Previous studies and this study indicate that both the endothelium and the stroma appear to play an important role in hydration control in short-term and long-term contact lens wear. However, the precise effects of chronic hypoxia on the corneal function are not yet clear. This study provides evidence that the long-term wear of low gas-permeable contact lenses may lead to functional impairment. Emphasis should be put on the need to prescribe contact lenses that guarantee high gas permeability to avoid hypoxic influence on the cornea.

**Key Words**

corneal endothelium, morphology, hydration control, contact lenses, long-term wear
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Acknowledgment

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References