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Corneal endothelial changes with rigid contact lens wear

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Abstract
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CORNEAL ENDOTHELIAL CHANGES WITH RIGID CONTACT LENS WEAR

A THESIS PRESENTED TO THE FACULTY OF PACIFIC UNIVERSITY BY SAMUEL C. LO GEORGE E. STONECYPHER IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE DOCTOR OF OPTOMETRY FEBRUARY 1980

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GES
SCL
ABSTRACT

The authors conducted a study of the effects of PMMA contact lens wear on the corneal endothelial mosaic of first-time wearers. A comparison of photographs taken through a slit-lamp at varying magnifications (32X, 50X, and 70X) during pre-fitting, adaptive and full-time wearing stages was made to evaluate changes in the endothelial mosaic.

Qualitative analysis of the mosaic revealed no major changes in cell size, contour, or elevations. However, the clarity of the mosaic was obscured for some subjects due to central corneal clouding. Quantitative analysis showed no statistically significant changes in cell density between the various stages of contact lens wear.

It was concluded for this small sample in the time period studied that PMMA lenses fit to Tabb specifications are not associated with any permanent qualitative or quantitative changes in the endothelial mosaic.
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INTRODUCTION

The corneal endothelium is a single layer of flattened epithelial-like cells making up the most posterior layer of the cornea and is continuous with the anterior iris epithelium at the anterior chamber. The total endothelial population is roughly 935,000 cells at three years of age and declines to 650,000 by age 25 and then to 500,000 by 60 years of age. Normal central endothelial cell densities range from 1600 to 4000 cells per square millimeter, with an average of about 2800 cells per mm². As few as 500 cells per mm² have been recorded in a thin yet clear cornea. Sturrock, Sherrard and Rice give the following regional corneal endothelial cell density relationships: axial count is 2.8% less than the nasal count; axial count is 3.6% less than the temporal count; and the nasal count is 0.8% less than the temporal count. The cell population shows considerable variation in regional cell size and cell density, both of which vary with age. With an increase in age and a normal cellular death rate, the cellular density decreases as the adjacent cells enlarge and shift to fill in the gaps caused by the dead cells. There is little if any cell division in the endothelium. The ability to reestablish endothelial continuity is referred to as spreading potential or healing reserve.

When the corneal epithelium or endothelium is sufficiently damaged stromal swelling follows. Damage to the endothelium
causes much more extensive swelling and loss of transparency than equal damage of the epithelium. Early researchers thought that the endothelium and epithelium were simply water-impermeable barriers to maintain stromal hydration; however, discovery of the limiting layers' permeability to water promoted more searching. Hodson described an endothelial pump which maintains corneal deturgescence by actively pumping bicarbonate ions out of the stroma to balance fluids "leaked" into the stroma.

A variety of endothelial changes are observable when the endothelium is disturbed including buckling, guttata (Fuch's dystrophy if central), bleb formation and cell size change. The extent to which these changes interfere with endothelium function is not entirely clear. Insults to the cornea such as trauma, surgery, drugs, intraocular inflammation, and high intraocular pressure can produce cell damage. Keratoconic patients show reduced cell densities with cells 7 to 8 times the normal size with an indistinct mosaic near the cone.

Transient changes associated with rigid and low water content hydrogel lens wear have been reported by Holden and Zantos. They include an apparent separation of the endothelial cells and the appearance of endothelial blebs that alter the appearance of the endothelial mosaic. These changes occurred in as early as 10 minutes of lens wear and were found to be repeatable in all the unadapted wearers they examined.
Routine endothelial photography indicated these changes are transient and reversible. The etiology is still unclear, but it is suggested that metabolic disturbances in the endothelium could be the cause. These changes are less apparent in the high water content hydrogel lens wearer.a

A careful long-term study needs to be done to see if stress due to contact lens wear disturbs the endothelial integrity by either accelerated cell loss and or mosaic pattern changes. A technique to evaluate the endothelium has been described15, but now needs to be clinically applied to see if there is a significant correlation between changes in endothelial integrity and contact lens wear. It may prove to be an additional prognosticator of successful contact lens wear.

a From a lecture presented by L. J. Coon at Pacific University College of Optometry, April 1979.
METHODOLOGY

The Holden and Zantos\textsuperscript{15} photographic system was used in this study. It consisted of a Nikon F type 35 mm single lens reflex camera with a "C" type focusing screen mounted behind a 20X eyepiece of a Nikon slit-lamp (Figure 1). Photographs were taken at 32X, 50X, and 70X nominal angular magnification (objectives of 1.6X, 2.5X, and 3.5X with a 20X eyepiece). The Nikon slit-lamp photographic flash system, Model MS-1, was used with maximum amount of strob illumination. High resolution film, Ektachrome ASA 200 and ASA 400, was used for the photography. An alignment system described by Barr and Schoessler\textsuperscript{b} was used which allowed repeatable photographs of the same corneal location (Figure 2). It consisted of a fixation lamp set at a constant angle of 25° from straight ahead in relation to the headrest and positioned in front of a telescope through which the eye was observed for accurate repeatable alignment. The head was adjusted until the pupil was centered on a calibrated reticule in the fixed telescope.

The illumination system was set at 90° with respect to the microscope. The angles between the slit-lamp base and the illumination and microscope systems were 30° and 60° respectively.

A series of central corneal endothelial photographs were taken at various stages of adaptation to a clinically acceptable

\textsuperscript{b} From J. T. Barr and J. P. Schoessler's unpublished paper, Corneal Response to Rigid Contact Lens.
Tabb\(^{c}\) lens fit. The "Tabb" lenses are of quadracurve design with diameters averaging 8.4 to 8.8 used in this study. The initial fit is parallel with a slight apical clearance. A gradual blending from the base curve to the peripheral curve generates an approximate aspheric periphery. The long term effects of the contact lens on the corneal endothelial mosaic was primarily evaluated based on cell density with attention given to variations in cell size and mosaic similarities.

Subjects selected had normal ocular health with no previous contact lens wear. They were less than 40 years of age and myopic. With the exception of subject number three, prefit photographs were compared with photographs taken during an intermediate or adaptive time period of 2 to 8 hours daily wear, and after fulltime wear was established with greater than 8 hours daily wear. Photographs of the right eye were taken 5 to 15 minutes after contact lens removal in the intermediate and full-time sessions.

Analysis and counting was accomplished by projecting an endothelial mosaic slide onto a grid (Figure 3). The grid was made from photographs of a hemacytometer slide mounded in approximately the same location as the subjects cornea. Grids were made to match the various powers used for the endothelial photographs (Figures 4, 5, and 6). Each small square in the

\(^{c}\) The lens parameters are described in an unpublished SOA handout titled "Tabb Guidelines for Initial Lens Parameters". The guide is the work of Roger L. Tabb, O.D., Beaverton, Oregon.
constructed grids represents an area of $2.5 \times 10^{-3} \text{ mm}^2$. Therefore when the squares were counted and a mean and standard deviation calculated, they were multiplied times 400 to give the estimated cell density per $1 \text{ mm}^2$.

Since the traditional counting method introduces an edge-effect bias, Sperling and Gundersen's method\textsuperscript{16} was used. Only those cells completely within a square or touching the top and or right-hand lines exclusively were included in the count of a square. Cells touching the left side or its extension upward to the next square and those touching the bottom or an extension downward from the right side into the next square were not counted.
Figure 1. Nikon slit-lamp with photographic set-up.

Figure 2. Telescopic alignment system.

Figure 3. Evaluation of an endothelial slide projected onto a counting grid.
Figure 4. Copy of the 32X hemacytometer grid used to count the corneal endothelium.
Figure 5. Copy of the 50X hemacytometer grid used to count the corneal endothelium.
Figure 6. Copy of the 75X hemacytometer grid used to count the corneal endothelium.
RESULTS

A series of photographs were taken of the subjects at initial, intermediate and full-time stages of contact lens wear. A total of 30 rigid contact lens wearers were photographed between February and November of 1979. Of the original group 12 subjects yielded data sufficient for inclusion in this study with 4 yielding "complete" data. A number of factors worth noting contributed to the difficulty of collecting and analysing the data. There were a number of missed appointments and drop outs. This study utilized many patients from a larger contact lens study. The patients were examined with the cooperative scheduling of both the contact lens fitting clinician and the patient. This did not always function efficiently especially when fitting problems arose or patient time was limited. The attrition rate was affected by stringent criteria in the contact lens fitting study, patients moving from the area, edema prone patients, and patient loss of motivation. There were also technique and equipment difficulties. The continual movement of equipment to and from the photographic site contributed to alignment problems. Although the researchers used the faster Ektachrome ASA 200 film, they were later advised that Kodachrome ASA 64 film gives better contrast and has better photo-enlarging capabilities.

\[d\] From Dr. L. J. Coon's personal conversation with Dr. B. A. Holden, 1979.
Analysis of the slides was done on two levels; qualitative changes in the endothelial mosaic and quantitative changes in cell density.

Qualitatively the endothelial mosaic was unique in its landmarks for each individual over the time period they were photographed. While there were changes in the clarity of the mosaic pattern, subtle variations in contour, cell size variations, and elevations; they did not appear to be significant for individuals or for the group as a whole. Several individuals showed signs of edema with central corneal clouding which made picture taking and analysis difficult. It gave a foggy overlay to the corneal mosaic and forced more peripheral counting.

The quantitative analysis was based on comparisons of endothelial cell density for the various stages of contact lens wear. Table 1 displays the individual subject’s endothelial cell counts per square millimeter with their associated standard deviations. Table 2 shows the changes of each subject’s endothelial cell density from one stage of contact lens wear to another. Six subjects showed an increase in cell density between the initial and intermediate stages while two showed losses resulting in an average increase of \(+289\) cells/mm\(^2\) with an average standard deviation (s.d.) of 132 cells. Between the initial and full-time stages three subjects increased and four decreased giving an average change of \(-39\) cells/mm\(^2\) with an average s.d.
of 146 cells/mm². An average change of -161 cells/mm² with an average s.d. of 182 cells/mm² occurred between the intermediate and full-time stages with two subjects increasing while three subjects decreased in cell density.

Data for the four subjects with complete sets of photographs showed the following average changes: initial to intermediate increased by +357/mm² (average s.d. 182); initial to full-time increased by +161 cells/mm² (average s.d. 130 cells/mm²); and intermediate to full-time decreased by -196 cells/mm² (average s.d. 154 cells/mm²).

The change in endothelial cell density between the various contact lens wearing stages are shown graphically in Figure 7 for each individual subject except subject three. The average changes for the total subject sample and for the subjects with complete sets of photographs are shown in Figure 8.

Analysis of these individual endothelial cell density averages using a treatment-by-subject statistical test gave an F value of 0.913763 with df (1,11) which is significant at less than 20%. When the above statistical test was applied to those with complete sets of data it yielded an F value of 1.52933 with df (2,6) which is significant at less than 20%. Therefore in both cases it can be said that there is no significant changes statistically between the various stages of contact lens wear. Hence in this study with its limited sample, there is no apparent affect on the central corneal endothelial cell density due to contact lens wear over the time period that it was monitored.
Table 1. Subjects' right eye central corneal endothelial cell density mean and standard deviation (cells/mm²) at various stages of contact lens wear.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Initial</th>
<th>Intermediate</th>
<th>Full-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2720±460</td>
<td>3108±592</td>
<td>2472±392</td>
</tr>
<tr>
<td>2</td>
<td>3408±432</td>
<td>3320±488</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>--</td>
<td>3360±280</td>
<td>3340±576</td>
</tr>
<tr>
<td>4</td>
<td>2800±400</td>
<td>--</td>
<td>2584±420</td>
</tr>
<tr>
<td>5</td>
<td>3236±568</td>
<td>--</td>
<td>2992±468</td>
</tr>
<tr>
<td>6</td>
<td>2192±428</td>
<td>2988±484</td>
<td>--</td>
</tr>
<tr>
<td>7</td>
<td>2520±744</td>
<td>2668±428</td>
<td>2928±396</td>
</tr>
<tr>
<td>8</td>
<td>2872±348</td>
<td>3000±420</td>
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<td>9</td>
<td>3256±668</td>
<td>--</td>
<td>2800±284</td>
</tr>
<tr>
<td>10</td>
<td>2528±488</td>
<td>3480±708</td>
<td>2932±460</td>
</tr>
<tr>
<td>11</td>
<td>2996±384</td>
<td>3044±548</td>
<td>--</td>
</tr>
<tr>
<td>12</td>
<td>3284±368</td>
<td>3224±340</td>
<td>3364±476</td>
</tr>
</tbody>
</table>
Table 2. Subjects' right eye change in corneal endothelial cell density mean and standard deviation (cells/mm²) between various stages of contact lens wear.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Initial-Intermediate</th>
<th>Initial-Full-time</th>
<th>Intermediate-Full-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+388±132</td>
<td>-248±68</td>
<td>-636±200</td>
</tr>
<tr>
<td>2</td>
<td>-88±56</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>--</td>
<td>--</td>
<td>-20±296</td>
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<td>4</td>
<td>--</td>
<td>-216±20</td>
<td>--</td>
</tr>
<tr>
<td>5</td>
<td>--</td>
<td>-244±100</td>
<td>--</td>
</tr>
<tr>
<td>6</td>
<td>+796±36</td>
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<td>--</td>
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<td>7</td>
<td>+148±348</td>
<td>+408±316</td>
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<td>11</td>
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</tr>
<tr>
<td>12</td>
<td>-60±28</td>
<td>+80±108</td>
<td>+140±136</td>
</tr>
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Average change all subjects
+289±132
-39±146
-161±182

Average change subjects with complete data
+357±182
+161±130
-196±154
Figure 7. Central corneal endothelial cell density change (cells/mm²) for various stages of rigid contact lens wear, O.D. Subject number 3 is excluded.
Figure 8. Average change in central corneal endothelial cell density, C.D., (cells/mm$^2$) for various stages of rigid contact lens wear.

Solid lines = total subject sample (N=12)

Dashed lines = subjects with complete data (N=4)
DISCUSSION

The effects of contact lens wear on the corneal endothelial mosaic have previously been investigated by Holden and Zantos\textsuperscript{14} and Barr and Schoessler\textsuperscript{e}. The former group studied the effects of soft contact lenses, while the latter group observed the effects of PMMA contact lenses. Transient endothelial bleb formation was reported in both papers to occur approximately thirty minutes after insertion of a contact lens on the eye. They also noted that mosaic changes were reversible with continued contact lens wear and that they were not present in the adapted contact lens wearer.

The distinctively short time course with which the endothelial mosaic changes occur and the absence of any bleb formation in the presence of marked corneal swelling suggests that the stress exerted by the contact lens was the cause of bleb formation\textsuperscript{14}.

The most commonly used criteria for evaluating the appearance of the endothelium include variation in cell size, evenness of contour, clarity of the mosaic pattern, the presence of any elevation or buckling and the percent change in endothelial blebs\textsuperscript{14},\textsuperscript{e}. Since these criteria are difficult to evaluate and only transient in appearance, it was doubtful that they would be entirely suitable for our study. It was felt that

\textsuperscript{e} J. T. Barr and J. P. Schoessler op. cit., p.4.
accelerated cell loss or gain and marked mosaic pattern changes would be better diagnostic criteria to evaluate the long term quantitative and qualitative effects of a contact lens on the endothelium.

The Holden-Zantos photographic technique allowed the photography of the central corneal endothelium without the use of topical anesthetic and direct corneal contact. Repeatable photography of the same corneal location was made possible through the use of the Barr-Schoessler alignment system.

There were qualitative changes of the endothelial mosaic from stage to stage, but they were subtle and considered to be artifacts of lighting changes, magnification changes, or slight fixational changes. Besides focusing problems, the clarity of the mosaic was affected by central corneal clouding on some patients. This forced peripheral counting to get cell density figures and may have contributed to the large means and standard deviations of some of the counts, especially the intermediate counts where adaption and modification procedures were occurring.

Although Table 2 and Figure 8 appear to show central corneal cell densities that increase during the intermediate time period and decrease for the full-time period, it must be remembered that statistically the fluctuations are not considered to be significantly different. Two points of concern may account for the fluctuations seen in the intermediate period: 1) peripheral areas appeared darker and more compact than the central portion of the photograph and may have caused a bias toward higher counts and 2) the angled photograph of the
hemacytometer slide produced a slightly distorted grid which when used to count on the curved cornea may have upped the count especially if used at the periphery.

Considering the limited sample size and being aware of the need of some technique modifications, the researchers conclude that the data indicates that rigid (PMMA) contact lenses fit to "Tabb" specifications are not associated with any significant change in the central corneal endothelial cell density or major mosaic changes in the process of building up to full-time wear (greater than 8 hours).

For those clinicians or researchers who wish to monitor the endothelium the following suggestions are offered:

1) Variation exists in the Barr-Schoessler alignment system so that all of the exact same cells may not show up in repeated photographs. However, this can be minimized by using consistent magnification (50X is recommended) and a constant slit width.

2) Distortion exists when photographs of a curved cornea are measured by photographs of the flat measuring slides. Distortion can be reduced by limiting cell counting to the central area of the photograph.

3) In photographing corneal endothelium, a conventional red fixation light is often found to be invisible when patients are exposed to a high intensity light. An orange or yellow fixation light proved more visible.
4) Occlusion of the nonfixating eye improves the patient's fixation.

5) Kodachrome ASA 64 gives better resolution and photo-enlarging quality than the higher ASA Ektachrome film.

6) For greater accuracy in counting, a permanent record for each slide could be made by dotting the center of each cell on a mimeographed copy of the counting grid.
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