Corneal Endothelial Polymegathism Induced by PMMA Contact Lens Wear

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Central corneal endothelial photographs were taken for 15 persons who had worn polymethylmethacrylate (PMMA) contact lenses for 7-15 yr and for a nonwearing control group matched for age and sex. An individual cell area analysis was made from the cell tracings. Significant endothelial polymegathism was noted for each member of the contact lens wearing group. PMMA wearers showed an average coefficient of variation of 0.445 for central corneal endothelial cell area compared to 0.245 for nonwearers (81.6% increase in polymegathism). The average maximum/minimum cell size ratio was 8.06 for the PMMA wearers vs 3.42 for the nonwearing control group. The frequency distributions for the cell areas reveal that the contact lens wearer develops cells that are much smaller and larger than normal. Invest Ophthalmol Vis Sci 26:857-863, 1985

Two types of corneal endothelial changes have been noted in response to the wearing of hard polymethylmethacrylate (PMMA) contact lenses. The first was described by Zantos and Holden and is a transient change that occurs when a contact lens of low oxygen transmissibility is placed on an eye unadapted to contact lens wear. Changes in the endothelial mosaic soon appear and reach a peak in 25-30 min. These so-called "blebs" then begin to disappear in about 2-3 hr.

The second type of endothelial change can be described as a pleomorphic change which occurs during the course of wearing hard PMMA lenses on a daily basis. A large variation in cell size (termed polymegathism by Rao et al) is the characteristic feature of this phenomenon. The purpose of this report is to explore some of the quantitative aspects of this second type of endothelial transformation.

Materials and Methods

Fifteen PMMA contact lens wearers who had worn contact lenses for more than 5 yr and a group of control subjects of the same age and sex as the individuals in the experimental group were chosen at random from the clinics of the Ohio State University College of Optometry. Informed consent was obtained from each individual prior to photography. Twenty women and 10 men, ranging in age from 21 to 52 yr, participated in the study.

The central corneal endothelium of each eye for all subjects was photographed with the Nikon Endothelial Camera (Nikon; New York, NY). The endothelium was viewed at ×60 magnification and photographed at ×10 magnification in the film plane. The slides obtained were projected for tracing, resulting in traces ×426 linear magnification. A grid located in the film plane and superimposed on the endothelial cells allowed for accurate assessment of magnification.

All cell tracings were then entered into a Zeiss Videoplan Computer (Carl Zeiss; Thornwood, NY) by means of a digitizing tablet so that an individual cell analysis of cell area could be obtained. Several tests were performed to assess the reliability and accuracy of this technique and of the computer program for determining cell area. First, a precision grid was photographed at the same angle (30°) and under the same conditions as the corneal endothelial photographs. The grid photographs were then analyzed exactly as for corneal endothelial cells, that is, projected, traced, and entered into the computer for determination of individual areas of the grid. Results showed that the areas determined by the computer were within 1% of the known grid values. To further test the computer program, numerous known polygons of various sizes were traced onto the computer digitizing tablet for area computation. An extremely high correlation (R = 0.999) was found for measured area vs known area.

Since this report deals with cell size variation, which is best expressed by the coefficient of variation of cell area of the sample, it is important to know the repeatability of such determinations made from endothelial cell micrographs. On 10 different occasions, 50 cells from a photograph of polymegathous corneal endothelium were traced and then entered...
onto different locations on the computer graphics tablet for individual cell analysis and subsequent determination of coefficient of variation of cell area. The mean coefficient of variation for these 10 determinations was 0.397 with a standard deviation of 0.012, thus indicating a high repeatability of the technique (standard deviation = 3.0% of mean value). The error of measurement for individual cell areas was ±9%. Interobserver contributions to this error were negligible. The differences in endothelial cell patterns for contact lens wearers cited in this report are well beyond experimental error and should be considered as real effects.

Fifty central cells from each eye of the subject were analyzed and combined to present a distribution of 100 cells for each individual. A variance components analysis performed on the data of 12 subjects had earlier shown that photographs taken from various corneal locations all around the central area did not contribute to the variance of the data, indicating that a photograph of one central location is representative of the general central corneal area. This analysis also indicated that there was no difference in photographs taken from the right or left eyes, thus providing the rationale for combining the data. Also, for all of these 12 subjects, the mean cell area and coefficient of
variation of cell area were not significantly altered if more than 50 cells were analyzed. This is in agreement with previous studies.6

Results

Examples of endothelial photographs from two contact lens wearing subjects and two control subjects are found in Figures 1-4. Comparative cell tracings from these subjects are seen in Figures 5 and 6. Inspection of the photographs and tracings readily reveals differences in the endothelial mosaic patterns between individual lens wearing and control subjects.

Figures 7 and 8 display the histograms for the endothelial cell area distributions for the 15 control subjects and 15 PMMA wearers, respectively. The horizontal axes are conformed to common limits for easy comparison.

Table 1 lists the mean cell area, coefficient of variation, and maximum/minimum cell area ratio for each of the PMMA wearers and for the matched control subjects. Cell density (cells/mm²) can be calculated by taking the reciprocal of the mean cell area for each subject. The mean endothelial cell area for all 15 PMMA wearers was 0.000404 mm² compared to 0.000375 mm² for the matched control
group. These means are not significantly different for the two populations ($P > 0.05$, t-test).

Two possible methods of estimating the degree of polymegathism in the endothelial mosaic are to examine the coefficient of variation of the cell areas and the ratio of maximum cell size/minimum cell size for each subject. Holden has suggested the term "percentage increase in polymegathism" to denote the increase in cell size variation due to contact lens wear. This index is the ratio of the coefficients of variation for the wearing and nonwearing matched subjects.

Table 2 displays the correlation of several variables for all subjects in the study. Highly significant correlations ($P < 0.0005$) are seen for wearing time vs standard deviation of cell area, coefficient of variation of cell area, minimum and maximum cell area, and maximum/minimum cell area ratio.

**Discussion**

The endothelial cell area distributions for PMMA contact lens wearers and for nonwearers of the same age and sex are clearly different ($P < 0.0005$, chi-square test). Inspection of the cell area distributions for these two groups (Figs. 7, 8) show two major differences. First, contact lens wearers develop greater numbers of small cells than are found in nonwearers. Secondly, contact lens wearers develop cells which are much larger than those found in the nonwearing population producing a large spread in distribution.
Fig. 4. Endothelial photograph of matched subjects 4C (Fig. 3) and 4X (Fig. 4). The smallest grid mark in the photograph equals 0.1 mm.

Fig. 5. Corneal endothelial cell tracings for matched subjects 1C and 1X.

Fig. 6. Corneal endothelial cell tracings for matched subjects 4C and 4X.
No cells larger than 0.000855 mm² were found in the control subjects, whereas cells as large as 0.00136 mm² were found among the PMMA wearers.

Two ways in which cell size variation can be quantified are by the coefficient of variation of the cell area and by the maximum/minimum cell area ratio. Comparing the coefficients of variation between the two subject groups shows that there is an 81.6% increase in polymegathism for the PMMA wearers. This increase is highly significant ($P < 0.0005$) and establishes the fact that polymegathism is an early manifestation of adverse effects on the endothelium in contact lens wearers. Greater polymegathism in contact lens wearers has also been confirmed from studies using unilateral contact lens wearers in which the nonwearing eye is used as the control (Woloschak M and Schoessler J, unpublished data).

There are significant correlations between contact lens wearing time and several variables related to polymegathism. Figure 9 shows this correlation for wearing time and coefficient of variation of endothelial cell area (amount of polymegathism). Apparently, as
the duration of lens wear increases, so does the probability of having an unusually large range of individual cell areas. Additionally, there is a strong correlation between mean cell area and standard deviation of cell area for both the control subjects \((r = 0.66)\) and for the PMMA wearers \((r = 0.71)\). Sawa and Tanishima\(^6\) demonstrated a similar correlation in a study of 103 normal subjects (these may have included contact lens wearers).

The consequences of corneal endothelial polymegathism may be a loss of endothelial functional capacity.\(^5,9,10\) This may result in postsurgical edema complications as found by Rao et al, and perhaps help explain the so-called "corneal exhaustion phenomenon" (whereby contact lenses cannot be tolerated after many years) frequently associated with long-term PMMA wear.

It has been noted in this study and in others\(^4,11,12\) that the coefficient of variation for cell area in persons free of corneal disease and who do not wear contact lenses is almost always less than 0.30 and that the maximum/minimum ratio is less than 5.0. We therefore suggest that values above these figures represent endothelial cell patterns that do not normally appear in the age group of 20–60 yr of age, and are indicative of an increased amount of polymegathism.

It must also be pointed out that previous investigations, which have described normal corneal endothelial cell distributions and characteristics, may contain inaccuracies if the subject population used included contact lens wearers.

The mechanism by which polymegathism occurs with contact lens wear is probably related to corneal hypoxia. The degree of polymegathism seems to be dependent upon the transmissibility of the lens and the wearing time. Polymegathism is significantly associated with wearing time in this study, but investigations using persons wearing silicone elastomer lenses (with high oxygen transmissibility) show no increased polymegathism over a matched control population.\(^12\) This result suggests that PMMA represents the worst case in contact lens wear for producing endothelial changes while highly transmitting lenses such as silicone elastomer represent lenses least likely to alter the endothelium. It can be inferred that hard or hydrogel gas permeable lenses will produce endothelial changes but at a slower rate than for PMMA.

Endothelial cell loss with contact lens wear as found by Caldwell et al\(^{13}\) is not confirmed in this report.

**Key words:** contact lenses, corneal endothelium, endothelial photography, polymegathism

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### References


### Table 2. Table of correlations

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SD: standard deviation; max: maximum; min: minimum.