Normal Endothelial Cell Density Range in Childhood

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• Specular microscopy of the in vivo corneal endothelium of 214 clinically normal eyes in children ranging from 5 to 14 years of age showed a regular mosaic of hexagonal cells. The cell population density of individuals presented some variation, as it does in older subjects. Quantitative analysis permitted us to determine the normal range of the endothelial cell count at each age. The mean (± SD) value ranged from 3591 ± 399 cells per square millimeter at age 5 years to 2697 ± 246 cells per square millimeter for the oldest subjects. Our data show a rapid decrease in cell density up to age 10 years. We estimate from our data a decrease in cell density of 13% between ages 5 and 7 years and an additional decrease of 12% by age 10 years.

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It is well known that the human corneal endothelium has a limited repair capacity, and several authors have demonstrated an inverse relationship between age and endothelial cell density in many species.[1-5] The rapid growth and the notable variability from one child to another give rise to the need for establishing a typical range in which the endothelial cell population can be considered normal.

Hiles et al[6] in 1979 reported a normal endothelial cell count range in children. However, they did not specify the selection criteria of the population and they did not provide homogeneous age groups. The aim of this study was to obtain reference values of mean cellular density of the corneal endothelium in subjects aged 5 to 14 years and to assess the possible decreasing trend of the endothelial cell population in childhood.

SUBJECTS, MATERIALS, AND METHODS

We randomly selected 447 subjects from a school population in Milan, Italy; their ages ranged from 5 to 14 years. Our selection criteria excluded the following: (1) subjects who were wearing contact lenses; (2) subjects with a history of ocular surgery or intraocular abnormalities; and (3) subjects with a family history of hereditary corneal disorders. We also excluded subjects with unclear ophthalmologic history and we decided to rule out children with significant refractive errors (which we defined as more than ±3 diopters of spherical equivalent). We also requested informed consent from the parents before the examination.

Following the application of these exclusion criteria, our study consisted of 214 subjects. The reasons for dropping 233 subjects are as follows: 222 subjects did not have parental consent, and all subjects had refractive errors or wore contact lenses. The characteristics and the distribution of the population are reported in Fig 1. Only the right eye was examined in all the subjects. To obtain reliable data we used the same technique in each subject. The horizontal corneal diameter was evaluated and then 15 images were taken for each child using a specular microscope (Pro Koester, CooperVision). The image underwent quantitative analysis using a computerized morphometer (MDO Kontron) to obtain the mean cellular density.

RESULTS

The corneal endothelium in infants is a more regular mosaic of hexagonal cells than is found in adults. This symmetrical organization is more pronounced in children younger than 9 years. In our patients, the horizontal corneal diameter ranged from 11.0 to 11.75 mm; no correlation existed between age and corneal size.

The measurements for 214 subjects are shown in Fig 2. They show that average cell density (solid line) decreases with age in a nonlinear manner with a more rapid rate until age 10 years. The SD at each age is shown by the dashed lines. While there is considerable spread in the measurements, none of the 121 subjects younger than 10 years had densities below 2500 cells per square millimeter and no subject at any age had a density of less than 2000 cells per square millimeter.

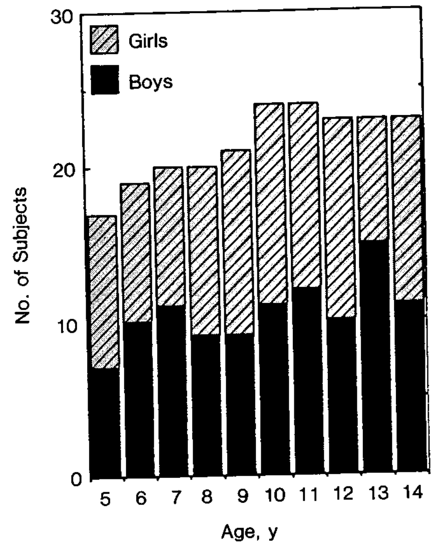
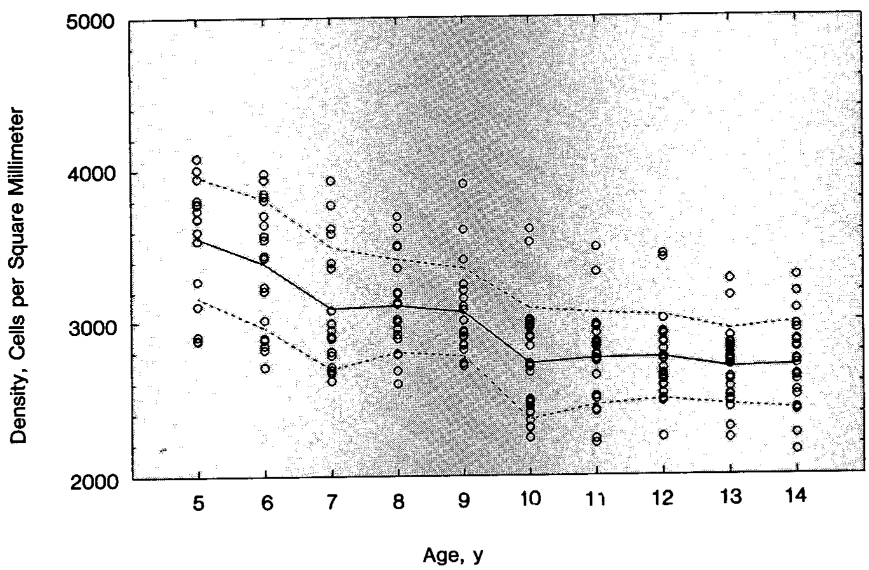


Fig 1.—Sex and age distribution of the population examined.

Fig 2.—Endothelial cell density as a function of age. Each point represents measurements from one eye of one subject. Solid line indicates mean; dashed lines, SD.



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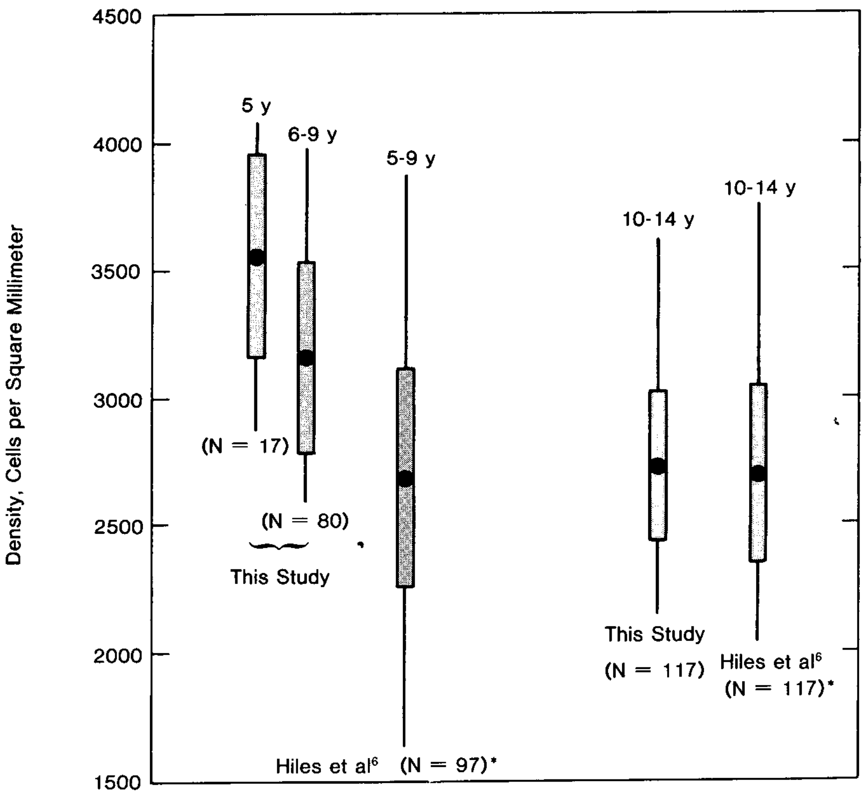

Fig 3.—Endothelial cell density for different age groups in this study compared with data from Hiles et al[6] (1979). Asterisk indicates that Hiles et al considered both eyes in many subjects, while we considered only one eye per subject.

COMMENT

We decided to measure only the right eye of each individual, since Bigar[7] and more recently Speedwell et al[8] reported no significant difference between the eyes in the same individual. Our data are consistent with previous findings reported by Murphy et al[9] and Laule et al[10]. Murphy et al studied the cellularity of two children's enucleated eyes. Both were male, aged 6 to 7 years. By histologic examination they found 3300 cells per square millimeter in the younger child and 3640 cells per square millimeter in the older one. They also reported an age-related decline in cell density starting from the neonatal period. Laule et al reported data obtained in a population ranging from 3 to 25 years old, and the cellularity ranged from 4025 to 2850 cells per square millimeter. Unfortunately, they did not address the change with age, but they treated the entire age range from 3 to 25 years as one group. The only reference values available in the literature from age 5 to 14 years were reported by Hiles et al.[6] Their data are consistent with ours in subjects ranging from 10 to 14 years (mean ± SD, 2695 ± 351 cells per square millimeter [range, 2046 to 3762 cells per square millimeter] compared with our values of 2730 ± 293 cells per square millimeter [range, 2153 to 3613 cells per square millimeter]). Their mean (±SD) measurements for the 5- to 9-year-old group, however, are different from ours (2681 ± 427 cells per square millimeter [range, 1640 to 3869 cells per square millimeter] compared with our values of 3160 ± 351 cells per square millimeter [range, 2597 to 3981 cells per square millimeter]) for the 6- to 9-year-old group. The values are even more discrepant if our 5-year-olds are included (as shown in Fig 3) A comparison between the data of Hiles et al[6] and our observations shows that the difference is due to the lower end of the range for the younger group (Fig 3). Their lowest value was 1640 cells per square millimeter, and many 5- to 9-year-old subjects had cell densities below 2500 cells per square millimeter. Our data for ninety-seven 5- to 9-year-old subjects, however, include no observation below 2597 cells per square millimeter.

Hiles et al[6] stated that from the age of 5 to 20 years there is no significant difference among the age groups. On the contrary, our results show some important differences (Fig 2). The decrease in cell density clearly continues at least until age 10 years, confirming a more rapid decline in endothelial cellularity during the early years of life[8] (23% loss over 5 years; 13% between ages 5 and 7 years, and an additional decrease of 12% between ages 8 and 10 years).

A noticeable difference from the study of Hiles et al[6] is that our population was randomly selected from normal subjects and, as shown by Fig 1, it consists of homogeneous age groups. Hiles et al performed specular microscopy in children selected from their patients, and they did not have homogeneous age groups. It is also important to point out that they collected patients with refractive errors. Hoffer and Kraff[11] report that there are significant differences in the endothelial cell count between subjects with axial hyperopia (<23.40 mm) and axial myopia (>23.90 mm). Moreover, some of the patients with refractive errors could possibly have been wearing contact lenses. This group was not excluded by the selection criteria of Hiles et al.

There are no known growth or endocrinologic reasons to explain the decrease in cell density obtained in our population from age 5 to 10 years. Possibly this decrease can be accounted for by a posterior corneal surface growth in the absence of endothelial mitoses, or, more likely, some relationship between our data and the prepubertal horomonal change can be postulated. Statistical analysis provides clear evidence that this trend of decreasing cell count from age 5 to 10 years is significant ($P < .01$ by a posteriori Scheffé multiple comparison procedure). Our report provides a normal range for endothelial cell counts during the 1½ decades of life, and this enables us to make better judgments about corneal diseases in childhood.

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