Central Corneal Thickness in Children

Pediatric Eye Disease Investigator Group*

**Objectives:** To determine the central corneal thickness (CCT) in healthy white, African American, and Hispanic children from birth to 17 years of age and to determine whether CCT varies by age, race, or ethnicity.

**Design:** Prospective observational multicenter study. Central corneal thickness was measured with a handheld contact pachymeter.

**Results:** A total of 2079 children were included in the study, with ages ranging from birth to 17 years. Included were 807 whites, 494 Hispanics, and 474 African Americans, in addition to Asian, unknown race, and mixed-race individuals. African American children had thinner corneas on average than that of both white and Hispanic children \( (P < .001 \) for both) by approximately 20 µm. Thicker median CCT was observed with each successive year of age from age 1 to 11 years, with year-to-year differences steadily decreasing and reaching a plateau after age 11 at 573 µm in white and Hispanic children and 551 µm in African American children. For every 100 µm of thicker CCT measured, the intraocular pressure was 1.5 mm Hg higher on average \( (P < .001 \) for every diopter of increased myopic refractive error, CCT was 1 µm thinner on average \( (P < .001 \).

**Conclusions:** Median CCT increases with age from 1 to 11 years, with the greatest increase present in the youngest age groups. African American children on average have thinner central corneas than white and Hispanic children, whereas white and Hispanic children demonstrate similar CCT.

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The Ocular Hypertension Treatment Study generated clinical interest in the measurement of central corneal thickness (CCT).1 Racial differences in CCT were one of the novel findings. The Ocular Hypertension Treatment Study investigators also found individuals with CCT greater than 600 µm. These data suggest that basing applanation tonometry on average CCT may be inaccurate because it does not account for wide individual variation in CCT. Following the Ocular Hypertension Treatment Study publication, studies in adults confirmed racial differences in CCT between white and African American adults, but not between white and Asian or Hispanic adults. More recently, heredity2 and refractive error3 have been reported to influence CCT. If differences in CCT produce substantial errors in measurement of applanation intraocular pressure (IOP)4 then CCT could have a direct effect on the clinical assessment of glaucoma risk.

There are limited data for CCT among children. Most studies have relatively small sample sizes \( (<100 \) per racial or ethnic group) and few or no subjects younger than 5 years. One study performed among European white subjects found no difference in the mean CCT of children compared with adults.5 However, the study did not include children younger than 5 years. Another study demonstrated that African American children had CCT thinner than that of white children, and both groups showed an increase in CCT after 10 years of age.6 No association between CCT and sex, axial length, or family history of glaucoma was found.6 Dai and Gunderson7 reported similar CCT values in Hispanic and white children but thinner CCT in African American children. This report was also limited in that most subjects were older than 5 years.

Our primary objectives were to determine the CCT of a large cohort of healthy children from birth to 17 years of age and to determine whether CCT varies by age, race, or ethnicity. Secondarily, we sought to determine the age at which childhood CCT stabilizes and to examine associations between CCT and other clinical characteristics, such as refractive error and IOP.

**METHODS**

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health, Department of Health and Human Services, and was conducted by the Pediatric Eye Disease Investigator Group at 36 clinical sites. The protocol and Health Insurance Portability and Accountability Act–compliant informed consent

*Authors/Group Information: The writing committee and a list of members of the Pediatric Eye Disease Investigator Group appear on page 1135.
forms were approved by the institutional review boards at each participating site, and a parent or guardian of each study subject gave written informed consent. The study adhered to the tenets of the Declaration of Helsinki. The protocol is available on the Pediatric Eye Disease Group website (http://pedig.jaeb.org/) and is summarized herein.

ELIGIBILITY CRITERIA AND EXAMINATION PROCEDURES

Major eligibility criteria included age from birth to 17 years, ability to have CCT measured in the clinic setting or under general anesthesia, cycloplegic refraction performed upon enrollment or within 6 months of enrollment, and presence of healthy corneas without ocular or systemic conditions that would influence CCT or IOP measurements. Acceptable ocular conditions included strabismus, nasolacrimal duct obstruction, and refractive error. Major exclusion criteria included anterior segment dysgenesis, congenital cataract, contact lens use, periocular steroid use within 3 months of enrollment or current systemic steroid use,uveitis, corneal structural abnormality, microphthalmia, Marfan syndrome, glaucoma, history of intraocular or refractive surgery, optic nerve edema or other optic nerve abnormality, and history of prematurity (defined as birth <37 weeks postmenstrual age).

The study examination consisted of 3 CCT measurements per eye using a handheld pachymeter (DGH 55 Pachmate; DGH Technology, Inc, Exton, Pennsylvania) and 2 IOP measurements by an application tonometer (Tonopen; Reichert, Inc, Depew, New York) in the right eye. A third IOP measurement with the tonometer was required if the first 2 differed by 2 mm Hg or more. A cycloplegic refraction with dilated fundus examination was performed, if not performed within the prior 6 months. Measurements could be taken in the clinic setting or under general anesthesia. The tonometer and pachymeter were calibrated for use each day prior to the initial subject testing. The accuracy of CCT testing with the pachymeter after successful calibration is within 5 µm.8 For CCT measurements, the pachymeter was placed on the central 3 mm of the cornea after instillation of a drop of proparacaine hydrochloride, 0.5%. Each measurement was an average value recorded by the instrument, taken during a single attempt, which was based on 1 to 25 measurements (98% of averages reported in this study were based on 25 measurements). The CCT average, number of measurements included in the average, and SD were calculated by the instrument. Each average measurement took a few seconds to obtain. Intraocular pressure measurements were taken after instillation of proparacaine, 0.5%, for subjects in the clinic setting. Subjects under general anesthesia had IOP measured within 2 minutes of anesthesia induction, if possible. Time (in minutes) from induction to IOP measurement was documented. The reliability of the IOP measurement was recorded as good, poor, or “could not obtain” to reflect the child’s level of cooperation. Cycloplegic refraction was performed using cyclopentolate hydrochloride, 1% or 2%, or phenylephrine hydrochloride (Cyclomydril) (Alcon Laboratories, Inc, Fort Worth, Texas) per investigator’s routine.

STATISTICAL ANALYSIS

A planned sample size of 70 subjects per age group was chosen to allow mean CCT to be estimated with a half width of a 95% confidence interval of 10 µm within each of 10 age groups, separately by race or ethnicity (white, African American, and Hispanic). There were no specific targets for other racial groups because it was not considered feasible to enroll the necessary numbers in a reasonable time frame. The age groups were as follows: 0 to 5 months, 6 to 11 months, 12 to 23 months, 2 years, 3 years, 4 to 5 years, 6 to 7 years, 8 to 9 years, 10 to 12 years, and 13 to 17 years. Age groups were used to define recruitment goals and to guarantee a greater number of subjects in the age range at which CCT was suspected to be most rapidly changing, on the basis of results of previous studies of CCT in children, but the age groups were not used in analyses; age was analyzed as a continuous factor.

Central corneal thickness measurements with an SD greater than 3.0 µm were excluded from analysis. The median of the CCT measurements for each eye was computed using the number of measurements as a weighting factor, and the medians of the 2 eyes were averaged to obtain a subject-level measurement used for analysis (Pearson product moment correlation for right eye vs left eye medians, 0.95). For subjects with data for only 1 eye, the median for that eye was used as the subject-level measurement.

Subjects were classified into a racial/ethnic group on the basis of parental report of race and ethnicity as follows: white, white race and non-Hispanic ethnicity; Hispanic, white race and Hispanic or Latino ethnicity; African American, African American race, regardless of ethnicity; and East Asian, originating from the Far East or Southeast Asia, regardless of ethnicity. Subjects of other racial/ethnic groups were included in the analyses that were not specific to racial/ethnic group. However, derivation of reference percentiles by race/ethnicity was limited to the 3 groups for which sufficient numbers were enrolled to ensure statistical validity (white, Hispanic, and African American).

Central corneal thickness was compared among age, racial/ethnic (white, Hispanic, African American, and East Asian), and sex groups using a linear model with age as a continuous factor. The Tukey-Kramer adjustment for multiple comparisons was used for racial group comparisons. Central corneal thickness at different ages was compared using linear contrasts. Because the growth curve for CCT was not linear with age, models with higher-order polynomial terms for age were fit, with non–statistically significant higher-order terms eliminated one at a time, to reach a final model that contained a linear and a quadratic term for age. The age of CCT stabilization was defined as the age at which the 95% confidence interval for the slope estimate of the growth curve first contained zero. Data for infants (birth to 11 months) were not included in the model because of the small sample size of this age group. Models including interactions for age by race and sex also were tested to allow for the possibility that the growth curve for CCT differed by these criteria. The same model was used to develop the reference percentiles reported in the tables for the racial/ethnic groups using the method of Altman, except race was treated as a stratification factor rather than a covariate to allow for separate derivation of reference percentiles of African Americans, and data were pooled across sexes and for Hispanic and white subjects. Because of the small sample size in African Americans younger than 4 years, the reference percentile derivation for these subjects was limited to age 4 years and older. A reference range for whites 6 to 11 months of age was derived assuming normally distributed data with constant mean and SD across the age range.

It has been reported that inhalation anesthetics lower IOP within a few minutes of anesthesia induction. Intraocular pressure measurements with poor reported reliability or taken more than 2 minutes after induction of general anesthesia were excluded from analyses. The association of CCT with IOP and spherical equivalent refractive error was evaluated using linear regression models adjusting for age, racial/ethnic group, and sex. The model for IOP also included an adjustment for examination setting. The spherical equivalent model included averaged data from both eyes, whereas the IOP model included data from right eyes only. Infants younger than 6 months with cycloplegic refraction performed more than 30 days before en-
RESULTS

The study enrolled 2199 subjects; 2079 (94.5%) were included in the analysis. Reasons for exclusion from analysis were as follows: subject found to be ineligible after enrollment (29 subjects), procedural deviation when obtaining measurements (11 subjects), SD greater than 5.0 µm or missing for all measurements (79 subjects), and subject cooperation precluding any measurement (1 subject).

After exclusions, the recruitment goal of 70 subjects per age and racial/ethnic group was met for all age groups of white subjects except 0 to 5 months (n=24) and met for all age groups older than 4 years for Hispanic and African American subjects. Two subjects were enrolled on the day of birth. The 132 East Asian subjects enrolled were insufficient for derivation of reference percentiles but were sufficient for comparison of mean CCT with other racial groups. Measurements were made in 407 (19.6%) of the subjects under general anesthesia. A total of 2607 eyes (65.1%) had 3 measurements, and 496 eyes (12.4%) had 1 measurement. Of eyes with at least 2 measurements, the difference between the maximum and minimum measurement was 20 µm or less in 93.2%.

The mean age of the 1672 subjects tested with topical anesthesia in the office was 8.7 years (range, 0-17 years), and the mean age of the 407 subjects tested with general anesthesia was 2.7 years (range, 0-16 years). Fifty-three percent of subjects were female (eTable; http://www.archophthalmol.com). Sixty-four percent of eyes had a spherical equivalent refractive error between −1.00 diop-

ters (D) and +3.00 D. Other than refractive error, common diagnoses included normal findings on the eye examination, strabismus, nasolacrimal duct obstruction, and amblyopia.

Median CCT was derived from a regression model of CCT as a function of age (\(x\)):

\[
CCT = 556.3 + 1.5x - 0.1(x-\bar{x})^2,
\]

where \(\bar{x}=7.7\) (Figure 1); and

\[
CCT = 539.9 + 0.8x - 0.06(x-\bar{x})^2,
\]

where \(\bar{x}=9.5\) (Figure 2).

The coefficients of determination (R²) were 0.03 (Figure 1) and 0.006 (Figure 2). A thicker median CCT was observed with each successive year of age from 1 to 11 years (95% confidence interval on slope of CCT by year of age excluded zero), but was stable thereafter. The median CCT for subjects 12 to 17 years of age differed by 1 µm or less per year. However, there was substantial variability across the age range. Median CCT for subjects 12 to 17 years of age was 573 µm in white and Hispanic subjects and 551 µm in African American subjects (Table 1, Table 2, and Figures 1 and 2).

There was no significant difference in CCT between white and Hispanic subjects, whereas African American subjects had significantly thinner central corneas on average by approximately 20 µm compared with both Hispanic and white subjects of similar age (\(P < .001\)) (Table 3). East Asian subjects had corneas that were significantly thinner on average than white subjects by 10 µm (\(P = .03\)), and thicker than African American subjects by 14 µm (\(P = .001\)) (Table 3). Girls had thinner corneas than boys by an average difference of approximately 5 µm (\(P = .003\)). There was no evidence that the differences observed with age in the median CCT differed by race or sex.

Because of the similarity of CCT for Hispanic and white subjects, their data were pooled for derivation of reference percentiles, whereas reference percentiles for African American subjects were derived separately (Tables 1 and 2). Similarly, data for both sexes were pooled because the small difference between them was judged to
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be clinically irrelevant. White and Hispanic subjects had a median CCT of 561 µm at age 4 years and of 574 µm at age 15 years. African American subjects had a similar increase from 541 to 551 µm during the same age range.

Spherical equivalent refractive error for the cohort ranged from −17.50 D to +13.00 D. A regression analysis showed that mean CCT was 1 µm thinner for every 1.00 D of lower (less hypermetropia, more myopia) spherical equivalent refractive error, although there was considerable variability in CCT unrelated to refractive error (R² = 0.005; P < .001, adjusted for age, race, and sex) (Figure 3). An analysis limited to subjects with a spherical equivalent of −6.00 to +8.00 D was similar, confirming that this result was not due to a small number of subjects with high myopia and thin central corneas or high hyperopia and thick central corneas.

Intraocular pressure ranged from 5 to 29 mm Hg, with most subjects (95.5%) having an IOP 21 mm Hg or lower. A relationship was seen between IOP and CCT, with IOP 1.5 mm Hg higher on average for every 100 µm of thicker central cornea (P < .001) (Figure 4). There was considerable variability in the relationship between IOP and CCT, with CCT explaining only 2% of the variation in IOP on the basis of the partial R².

The median CCT for the 24 white infants younger than 6 months was 563 µm (range, 468-687 µm), and the median CCT for 6 African Americans younger than 6 months was 544 µm (range, 517-666 µm). The median CCT for

| Table 1. Reference Percentiles for White and Hispanic Subjects 1 to 17 Years of Agea |
|-------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Age, y            | 5th            | 10th           | 25th           | 50th           | 75th           | 90th           | 95th           |
| 1                 | 493            | 506            | 528            | 553            | 578            | 600            | 614            |
| 2                 | 495            | 509            | 531            | 556            | 581            | 603            | 617            |
| 3                 | 498            | 511            | 534            | 559            | 583            | 606            | 619            |
| 4                 | 500            | 514            | 536            | 561            | 586            | 608            | 622            |
| 5                 | 503            | 516            | 538            | 563            | 588            | 610            | 624            |
| 7                 | 506            | 520            | 542            | 567            | 592            | 614            | 627            |
| 9                 | 509            | 523            | 545            | 570            | 595            | 617            | 630            |
| 12                | 512            | 525            | 548            | 573            | 597            | 620            | 633            |
| 15                | 513            | 526            | 549            | 574            | 598            | 621            | 634            |
| 17                | 513            | 526            | 548            | 573            | 598            | 620            | 634            |

a Reference percentiles were derived from a regression model of central corneal thickness (CCT) as a function of age (Figure 1). Each cell contains a CCT value in micrometers; CCT for intermediate ages not appearing in the table may be interpolated from adjoining values.

| Table 2. Reference Percentiles for African American Subjects 4 to 17 Years of Agea |
|-------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Age, y            | 5th            | 10th           | 25th           | 50th           | 75th           | 90th           | 95th           |
| 4                 | 483            | 496            | 517            | 541            | 565            | 587            | 600            |
| 5                 | 484            | 497            | 519            | 543            | 567            | 589            | 602            |
| 7                 | 487            | 500            | 521            | 545            | 569            | 591            | 604            |
| 9                 | 489            | 502            | 523            | 547            | 572            | 593            | 606            |
| 12                | 491            | 504            | 525            | 550            | 574            | 595            | 608            |
| 15                | 492            | 505            | 526            | 551            | 575            | 596            | 609            |
| 17                | 492            | 505            | 527            | 551            | 575            | 596            | 609            |

a Reference percentiles were derived from a regression model of central corneal thickness (CCT) as a function of age (Figure 2). Each cell contains a CCT value in micrometers; CCT for intermediate ages not appearing in the table may be interpolated from adjoining values.

| Table 3. Central Corneal Thickness Comparisons by Race/Ethnicity and Sex |
|-----------------|----------------|----------------|----------------|
| Comparison      | Estimated Difference (95% CI), µm | P Valuea |
| Female-male     | −5.1 (−8.5 to −1.7) | .003 |
| White-Hispanic  | 3.4 (−2.2 to 9.0)  | .39 |
| White-African American | 23.2 (17.5 to 29.0) | <.001 |
| White-East Asian| 9.7 (0.6 to 18.8)  | .03 |
| Hispanic-African American | 19.8 (13.7 to 25.9) | <.001 |
| Hispanic-East Asian | 6.3 (−3.0 to 15.6) | .30 |
| African American-East Asian | −13.5 (−22.9 to −4.1) | .001 |

Abbreviation: CI, confidence interval.

a P values for racial group comparisons include the Tukey-Kramer adjustment for multiple comparisons.
74 whites 6 to 11 months of age was 548 µm (range, 471-627 µm; 5th-95th percentiles, 495-601 µm), and the median CCT for 17 African Americans 6 to 11 months of age was 551 µm (range, 483-629 µm). We did not enroll a sufficient number of whites younger than 6 months or African American infants to derive normative percentiles for those groups.

**COMMENT**

Significant changes in axial length, corneal diameter, and refractive state occur with the growth of a child’s eye. We demonstrated that CCT in healthy children also changes modestly with age, with most of the change occurring before age 11 years. This increase with age occurred in the white, African American, and Hispanic racial/ethnic groups. Hispanic and white subjects had similar CCT at each age, whereas African American subjects had significantly thinner corneas at all ages. The range of CCT measurements by the pachymeter at each age was approximately 120 µm and was similar across racial groups. The clinical significance of this range is unknown.

Several studies of CCT among children of varying age have been reported. Hussein et al studied CCT measurements in 108 children and found mean CCT to increase with age, reaching adult thickness by 5 years of age. However, the study had only 18 patients older than 10 years. Consistent with our results, Haider et al found mean CCT to be thicker in both white and African American children 10 to 18 years old compared with that of younger children. Hussein et al reported higher CCT in children 5 to 9 years old, compared with that of children younger than 4 years. These investigators did not have sufficient numbers of older children to determine whether this trend continued beyond age 9 years.

Conversely, other investigators have not found CCT to increase with age. Zheng and colleagues studied 926 children 8 to 16 years of age and found no association between CCT and age. They reported a significant difference in CCT between children (mean, 550 µm) and adults (mean, 537 µm). Nevertheless, they may have missed the age effect in children found in this study and others by excluding children younger than 8 years. Dai and Gunderson analyzed CCT in 106 children of various racial groups and found no age effect, but their sample size was too small to be able to reliably detect an age effect of the size seen in the current study. They also noted that CCT was similar in white and Hispanic children but lower in African American children.

Racial differences associated with CCT found in this study were similar to those reported in adults. White and Hispanic children had similar CCT, whereas African American children had lower CCT than that of white or Hispanic children across all age groups. Although the number of East Asian children enrolled in our study was small, the mean CCT in East Asian children was intermediate between that of white and Hispanic children and that of African American children. The clinical significance of the racial difference is unknown. It is unclear whether thinner corneas in children are associated with an increased risk of glaucomatous optic neuropathy.

Central corneal thickness was found in our analyses to be associated with IOP measured by the applanation tonometer. This relationship was true for subjects in the clinic setting and under general anesthesia. Intraocular pressure was 1.5 mm Hg higher for every 100 µm of increased CCT after combining data from both settings. Biomechanical properties of the cornea may contribute to this observation. Recent research suggests that the effect of CCT on IOP measurements may be increased in eyes with stiffer corneas compared with the effect in eyes with softer corneas.

To understand the clinical importance of this observation, consider the range of CCT in an age group. The range of normal CCT between the 5th and 95th reference percentiles at any age is about 120 µm. For a CCT falling within the 5th and 95th reference percentiles, the effect of CCT would cause variation in IOP of at most 2 mm Hg and should not influence the clinical decision about the presence or absence of glaucoma. Alternatively, if a child’s IOP is 2 mm Hg or more higher than expected and the CCT is within the 5th and 95th

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**Figure 3.** Central corneal thickness (CCT) by spherical equivalent. The average CCT was approximately 1 µm thinner for every 1.00 diopter (D) of spherical equivalent lower. Regression was adjusted for age, race, and sex. Partial coefficient of determination (R²) for spherical equivalent is 0.005.

**Figure 4.** Intraocular pressure by central corneal thickness (CCT). Regression was adjusted for age, race, sex, and examination setting. Partial coefficient of determination (R²) for CCT is 0.02.
percentiles, the measured IOP should not be attributed to normal variation in CCT.

There were 2 statistically significant but not clinically relevant associations. We observed a 1-µm thinner corneal thickness in each 1.00-D myopic shift in refractive error. Girls had CCT that was on average 5 µm thinner than that of boys.

Normative CCT data by age and race in children are shown in Tables 1 and 2. These may be helpful in clinical practice. Healthy children with mildly elevated IOP by tonometry but no other signs of glaucoma may be managed more conservatively if their CCT is found to be substantially higher than normal for their age and race. In contrast, a child with mildly elevated IOP and substantially lower CCT than the normative measurement for his or her age and race may need more vigilant monitoring for signs of glaucoma.

Our study has a number of strengths. We used a single type of corneal pachymeter, the DGH 55 Pachmate, to measure CCT. More than 96% of the children were able to cooperate for measurements. The CCT data obtained in 98% of measurements in this study were based on 25 sequential individual CCT measurements per reading, the highest number of measurements the pachymeter could average to produce a reading, allowing an SD of less than 5 µm for the CCT measurement. The small CCT test-retest difference for most eyes (93.2%) suggests that pachymeter measurements were taken within the same area of the cornea. An additional strength is that the sample included a large number of children across a wide age range for 3 ethnic groups. Nearly all of our age groups had more than 100 patients per group, with older age groups having approximately 300 patients.

Limitations of this study include an inadequate number of infants younger than 6 months, as well as an inadequate number of Asian children in all age groups. Another limitation may be that the CCT measurement obtained in the clinic setting might not have been in the central 3 mm of the child's cornea, depending on patient cooperation and examiner skill. Because our study did not include measurements of axial length, corneal diameter, or corneal hysteresis, we do not know how these specific ocular features might affect CCT during childhood.

In summary, we found higher CCT with age among healthy children from birth to 11 years of age, appearing to plateau after age 11 years. African American children had lower CCT than that of white and Hispanic children. There is a minimal increase in measured IOP with increasing corneal thickness among children with no abnormalities. There is no clinically important association between CCT and refractive error.

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