Refractive Error, Axial Length, and Relative Peripheral Refractive Error before and after the Onset of Myopia

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PURPOSE. To evaluate refractive error, axial length, and relative peripheral refractive error before, during the year of, and after the onset of myopia in children who became myopic compared with emmetropes.

METHODS. Subjects were 605 children 6 to 14 years of age who became myopic (at least −0.75 D in each meridian) and 374 emmetropic (between −0.25 D and +1.00 D in each meridian at all visits) children participating between 1995 and 2003 in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study. Axial length was measured annually by A-scan ultrasonography. Relative peripheral refractive error (the difference between the spherical equivalent cycloplegic unworn refraction 50° in the nasal visual field and primary gaze) was measured using either of two autorefractors (R-1; Canon, Lake Success, NY [no longer manufactured] or WR 5100-K; Grand Seiko, Hiroshima, Japan). Refractive error was measured with the same autorefractor with the subjects under cycloplegia. Each variable in children who became myopic was compared to age-, gender-, and ethnicity-matched model estimates of emmetrope values for each annual visit from 5 years before through 5 years after the onset of myopia.

RESULTS. In the sample as a whole, children who became myopic had less hyperopia and longer axial lengths than did emmetropes before and after the onset of myopia (4 years before through 5 years after for refractive error and 3 years before through 5 years after for axial length; P < 0.0001 for each year). Children who became myopic had more hyperopic relative peripheral refractive errors than did emmetropes from 2 years before onset through 5 years after onset of myopia (P < 0.002 for each year). The fastest rate of change in refractive error, axial length, and relative peripheral refractive error occurred during the year before onset rather than in any year after onset. Relative peripheral refractive error remained at a consistent level of hyperopia each year after onset, whereas axial length and myopic refractive error continued to elongate and to progress, respectively, although at slower rates compared with the rate at onset.

CONCLUSIONS. A more negative refractive error, longer axial length, and more hyperopic relative peripheral refractive error in addition to faster rates of change in these variables may be useful for predicting the onset of myopia, but only within a span of 2 to 4 years before onset. Becoming myopic does not appear to be characterized by a consistent rate of increase in refractive error and expansion of the globe. Acceleration in myopia progression, axial elongation, and peripheral hyperopia in the year prior to onset followed by relatively slower, more stable rates of change after onset suggests that more than one factor may influence ocular expansion during myopia onset and progression. (Invest Ophthalmol Vis Sci. 2007;48: 2510–2519) DOI:10.1167/iovs.06-0562

The optical role played by the ocular components once myopia has occurred is well understood; axial length exceeds the focal length formed by the refractive elements of the eye. Compared with other ocular components such as the cornea and crystalline lens, axial length is typically regarded as the primary determinant of refractive error. The correlation with refractive error is larger for axial length than for any other component (0.76).1 The correlation between change in axial length and progression of myopia, documented in recent bifocal clinical trials, is also quite high, between 0.77 and 0.89.2,3 Despite playing a primary role in prevalent myopia and myopic progression, the changes in axial length before and at the onset of myopia have not been documented extensively. Goss and Jackson4 found no differences 1 year before the onset of myopia between axial length in 24 children who became myopic compared to 56 children who remained emmetropic.4 However, this finding may be due to a small sample size and limited statistical power. In a study with a larger sample, Zadnik et al.5 have reported that children at greater risk for the onset of myopia by virtue of having two myopic parents have longer axial lengths than do other nonmyopic children with one or no myopic parents. A greater axial length in nonmyopic third-grade children was also a risk factor for the onset of myopia by the eighth grade.6 If an excessively long axial length in children is to be used as a predictive factor, the timing of axial elongation before myopia’s onset is of particular interest. The rate of growth in axial length before, during, and after myopia’s onset has not been documented in detail. Several patterns are possible for growth. Children at risk for the development of myopia may have an excessively long axial length before onset, but display a similar rate of increase compared with that in children who remain emmetropic. As long as axial growth outpaced the loss of dioptric power, there would be the result of a slow, steady loss of hyperopia. Another possibility is for the axial length in
children who become myopic to exhibit a more rapid rate of growth than that in children who remain emmetropic. How consistent this rate may be over time is another open question. The coincidence of any acceleration in growth with respect to environmental exposures such as changing levels of near work or accommodative lag could also shed light on the mechanisms underlying the development of myopia.

In addition to having excessive length, myopic eyes have been reported to have altered shapes relative to emmetropic or hyperopic eyes (i.e., the eye has grown longer axially than equatorially to become either relatively less oblate or prolate in shape). This asymmetry in shape has been detected by x-ray, interferometry, and magnetic resonance scanning. A recent MRI study found that the myopic eye is typically oblate and only rarely prolate, and that the retinal contour becomes less oblate with increasing myopia. Alterations in shape also influence peripheral refractions, with myopic eyes typically having relatively more hyperopic peripheral refractive errors than do emmetropic eyes. Studies consistently have shown considerable variability and overlap in shape as a function of refraction error group. Of note, there are related meridional differences (i.e., peripheral refractive errors were more hyperopic relative to central errors in the horizontal meridian but were more myopic than central errors in the vertical meridian). This corresponds to reports of a greater vertical than horizontal width of the globe, along with more relative oblateness vertically than horizontally, as a function of degree of myopia.

Despite playing a secondary role to axial length in myopia, there is increased interest in peripheral refractive error as a risk factor for the onset of myopia. This interest stems in part from clinical data. A longitudinal study of pilots found that relative peripheral hyperopia in an emmetropic eye was associated with an increased risk of the development of myopia. Animal experiments also support a potential role for peripheral hyperopic defocus in myopia development. Ordinarily, the emphasis is on the central retinal defocus from lenses imposing simulated hyperopic defocus and the compensatory reaction of degree of myopia.

Mechanical factors may also explain the relatively less oblate shape of myopic eyes—factors such as differences in the size of the orbit axially compared with equatorially and anisotropy in the choroid. The crystalline lens may also be a source of equatorial restriction. The pattern of development from infancy through the age of 9 or 10 years is for the crystalline lens to thin, flatten, and lose power. Growth curves for these lens characteristics show departures from this pattern after the age of 10 years, close in time to the peak ages for the onset of myopia. Equatorial stretch, proposed by van Alphen as a factor relating axial growth with decreasing power of the crystalline lens, may be responsible for the thinning and flattening pattern of lens development before the age of 10 years. Restricted growth in the equatorial plane may occur if the ocular size exceeds the ability of the crystalline lens to stretch in response.
contrasts might be drawn between two distinct and unambiguous groups. The number of became-myopic children at each study visit is given in Table 1.

Trained and certified examiners measured central refractive error and peripheral refraction on the right eye of subjects with one refractor (Canon R-1 autorefractor; Canon USA, Lake Success, NY; no longer manufactured) between 1989 and 2000, and another one (WR 5100-K; Grand Seiko Co., Hiroshima, Japan) from 2001 to 2003. Subjects were tested after mydriasis and cycloplegia. When subjects had an iris color of grade 1 or 2, testing was performed 50 minutes after 1 drop of proparacaine 0.5% and 2 drops of tropicamide 1%. When subjects had an iris color darker than grade 2, testing was performed 30 minutes after 1 drop of proparacaine 0.5% and 1 drop each of tropicamide 1% and cyclopentolate 1%. The protocol for measurement has been described in detail previously. Subjects first fixated a reduced Snellen target through a +4.00-D Badal lens in primary gaze. Ten autorefractor measurements were made according to our standard protocol for cycloplegic autorefraction. Immediately after measurement in primary gaze, the track holding the Snellen target was rotated 30° and placed before a front surface mirror on the patient’s right. Five autorefraction measurements were then taken in peripheral gaze. Relative peripheral refractive error equals the spherical equivalent of the average refraction in primary gaze subtracted from the spherical equivalent of the average refractive error in 30° temporal gaze (i.e., the autorefractor axis directed 30° in the nasal visual field of the subject’s right eye). Axial ocular dimensions were measured by A-scan ultrasonography (Model 820; Carl Zeiss Meditec, Inc., Dublin, CA), consisting of five readings with a handheld probe in semiautomatic mode.

Emmetrope Model

Separate growth curves were constructed for emmetropes for refractive error, axial length, and relative peripheral refractive error as a function of age. The best-fitting models as defined by the Akaike Information Criterion were those that incorporated the natural log of age plus the natural log of age squared for all three dependent measures. These methods have been described in detail previously for modeling of emmetropic component development. Gender and ethnicity and the interaction between ethnicity and age were subsequently included in the models. The regression coefficients for ln(age) and ln(age)^2 for each ocular variable, gender, and ethnic group were derived using mixed ANOVA modeling with repeated measures (SAS ver. 9.1; SAS Institute, Cary, NC).

Age-Matched Myopic Data

To be included in the became-myopic group, a subject had to be nonmyopic on at least one visit before a visit during which myopia was diagnosed. The year the became-myopic subject first met the myopia criterion was defined as year 0, the year of onset. The first study year before onset was −1, 2 years prior was −2, and so forth out to −5 years before onset. The number of children in years 0 and −1 in Table 1 are not the same, because some children missed visits between their last nonmyopic visit and their onset visit. Each study year after onset for a given subject was designated +1, +2, and so forth out to +5 years. The age of each became-myopic subject at each study visit was applied to the appropriate emmetrope regression equation. This provided an age, gender, and ethnicity-matched emmetropic value of each ocular variable for every became-myopic data point. Mixed modeling was then used to compare the mean difference between became-myopic data and the emmetrope model values as a function of study visit for each ocular variable. A significance level of P < 0.01 was used in consideration of the large sample size. This level of adjustment is somewhat arbitrary, but represents a compromise between filtering out spurious findings, while allowing small differences to reach significance. Throughout the rest of the text, became-myopic refers to the data from children in that category and emmetrope refers to the values estimated from the model derived from emmetropic children’s data.

RESULTS

Figure 1A displays the average refractive error of became-myopic children compared with emmetropes as a function of years relative to the onset of myopia. Emmetropes had a positive spherical equivalent refractive error of +0.50 D on average that decreased by only −0.25 D throughout the study period. This level of stability among emmetropes is maintained in part by definition in this group. Became-myopic children underwent larger decreases in hyperopia to reach −3.80 D of myopia by +5 years after onset. The amount of difference between the two groups by year relative to onset is shown in Figure 1B. Became-myopic and emmetropic children had similar levels of spherical equivalent refractive error −5 years before onset (P = 0.48). Became-myopic children had less hyperopia or more myopia compared with emmetropes from −4 years before onset through +5 years after onset (P < 0.0001 for each year). The difference between groups increased monotonically, reaching a maximum of −4.10 D in year +5. The difference between the two groups in longitudinal change in refractive error is shown in Figure 1C. The change in refractive error was significantly greater for became-myopic children compared with emmetropes starting between visits −5 and −4 and continuing every year thereafter (P = 0.006 between −5 and −4, P < 0.0001 for each subsequent interval). The magnitude of the difference in the rate of change between groups was largest, −0.81 D, between −1 year before onset and the year of onset, i.e., the time of most rapid refractive change was during the year before onset. This result is in contrast to progression rates of −0.39 to −0.52 D per year for the years after onset (Fig. 1C). We explored whether this finding was the product of varying samples of children in each year by analyzing only those children who had data at each visit from years −2 to +2. Results for these 145 children (represented by the open squares between visits −2 and +2 in panel B of Figs. 1–3) were essentially identical with those when the number of children analyzed varied by visit.

Figure 2A displays the average axial length of became-myopic children compared with emmetropes as a function of years relative to the onset of myopia. The initial axial length in emmetropes was 22.7 mm, increasing at a steady rate of approximately 0.10 mm per year. The axial length of became-myopic children was eventually, but not initially, longer than in emmetropes. The amount of difference between the two groups by year relative to onset is shown in Figure 2B. Became-myopic and emmetropic children had similar axial lengths at −5 and −4 years before onset. Became-myopic children had longer axial lengths compared with emmetropes from −3 years before onset through +5 years after onset (P = 0.0004 for year −3, P ≤ 0.0001 for all subsequent years). This pattern was similar to the time course for refractive error but later in significance by 1 year. The difference between groups increased monotonically, reaching a maximum value of 1.31 mm
longer in became-myopic children in year +5. The difference between the two groups in longitudinal change in axial length is shown in Figure 2C. The changes in axial length taking place between −5 and −4 years before onset were not significantly different between the two groups ($P = 0.057$). The change in axial length was significantly greater in children who became myopic compared with emmetropes, starting between visits

**Figure 1.** Spherical equivalent refractive error as a function of annual visit relative to the onset of myopia (−5 years before to +5 years after, with onset designated as year 0). (A) Data for (■) became-myopic children and (○) emmetropes. Error bars, SEM. (B) The difference between became-myopic and emmetrope data (■). (□) Subset of children with longitudinal data across all five visits from −2 to +2 ($n = 145$). (C) Longitudinal change in refractive error between visits for became-myopic children (note the points occur between years). Significant differences between became-myopic and emmetropic children (i.e., the difference in change between groups is significant relative to 0).

**Figure 2.** Axial length in the became-myopic group (A); difference in axial length between myopes and emmetropes, with the subset of children described in Figure 1 (B); and change in axial length between visits in the became-myopic group (C), as a function of annual visit relative to the onset of myopia. Symbols are as in Figure 1.
Figure 4 presents the difference between spherical equivalent refractive error in the corresponding emmetrope values as a function of ethnic group. There were no differences as a function of ethnicity for any year before onset. At and after onset, Asian became-myopic children tended to have a more negative spherical equivalent refractive error than did Hispanic and African-American (visits 0 through +5) and white (visits +1 through +3) became-myopic children. White became-myopic children were more myopic than Hispanic became-myopic children in year +3 only and more myopic than African-American became-myopic children in years +1 through +5. Hispanic and African-American became-myopic children were not significantly different from each other in any year after onset except for more myopia in Hispanic became-myopic children in year +2.

Figure 5 presents the difference in axial length between became-myopic children and the corresponding emmetrope values as a function of ethnic group. There were no differences as a function of ethnicity for any year before onset, with the exception of Asian became-myopic children, who had a shorter axial length than did white became-myopic children in year −1. Consistent with having more myopia at and after
onset, Asian became-myopic children had longer axial lengths than did Hispanic became-myopic children in years +1 through +5, compared with African-American became-myopic children in years 0 through +5, and compared with white became-myopic children in years +1 through +5 and year +5. White became-myopic children had longer axial lengths than did African-American became-myopic children in years +1 through +5. White and Hispanic became-myopic children were not significantly different from each other in any year after onset. Hispanic and African-American became-myopic children were not significantly different from each other in any year after onset except for longer axial lengths in Hispanic became-myopic children in year +2.

Figure 6 presents the difference in relative peripheral refractive error between became-myopic children and the corresponding emmetrope data as a function of ethnic group. Asian became-myopic children tended to have more relative peripheral hyperopia and African-American became-myopic children tended to have little relative peripheral hyperopia, both before and after onset (difference significant in years −3 through +5). Asian became-myopic children also tended to have more relative peripheral hyperopia than Hispanic became-myopic children in years −1 through +5 and than white became-myopic children, sporadically, in years −3, −1, and +1. African-American became-myopic children had significantly less relative peripheral hyperopia than did Hispanic became-myopic children in years −3 through +3 and than white became-myopic children in years −2 through +4. White became-myopic children tended to have more relative peripheral hyperopia than Hispanic became-myopic children in years +1, +3, and +4. The rank order for relative peripheral refraction after onset generally followed the opposite of the rank order for refractive error seen in Figure 4. Asian and white became-myopic children maintained a significant level of relative peripheral hyperopia before and after onset, in years −3 through +5 and −1 through +5, respectively, whereas African-American became-myopic children showed a significant level of relative peripheral hyperopia only in years −3 and 0. Of note, Hispanic became-myopic children displayed a significant level of relative peripheral hyperopia before, during, and for several years after onset (years −2 through +4) that decreased to become nonsignificant in year +5.

We also explored the relationship between wearing an optical correction and relative peripheral refractive error in became-myopic children. As shown in Table 2, refractive correction was uncommon before visit 0 and was worn by most of the became-myopic children by visit +2. Relative peripheral refractive error was not significantly different between became-myopic children wearing or not wearing a refractive correction at any visit (Fig. 7; P = 0.069). This parallel pattern suggests no effect of correction on relative peripheral refractive error.

### Table 2. Number (%) of Became-Myopic Children Wearing a Refractive Correction or No Refractive Correction by Visit

<table>
<thead>
<tr>
<th>Visit</th>
<th>With Correction n (%)</th>
<th>Without Correction n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−2</td>
<td>31 (7.1)</td>
<td>405 (92.9)</td>
</tr>
<tr>
<td>−1</td>
<td>60 (11.5)</td>
<td>463 (88.5)</td>
</tr>
<tr>
<td>0</td>
<td>176 (33.0)</td>
<td>358 (67.0)</td>
</tr>
<tr>
<td>+1</td>
<td>200 (54.5)</td>
<td>167 (45.5)</td>
</tr>
<tr>
<td>+2</td>
<td>167 (65.5)</td>
<td>88 (34.5)</td>
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</table>
of at least −0.25 D), it is noteworthy that despite this difference in definition, both studies show the fastest rate of change in myopia in the interval between the year before and the year of onset of myopia.4

The choice of criterion level for myopia at onset is somewhat arbitrary. This point may be too late for some children and too soon for others considering 11.5% received a refractive correction 1 year before the 0 visit and 34.5% did not wear a correction even 2 years after. Measurement error is a potential explanation for the faster rate of change before the year 0 visit. The assumption that measurement error is randomly distributed at each visit may not be true between visits −1 and 0. More children may be measured inaccurately as less myopic at visit −1, thereby keeping them from being classified as myopic. These children would then be falsely measured as having a faster rate of progression between visits −1 and 0. This error seems unlikely, however, as the finding of faster change between visits −1 and 0 occurred in independently measured axial length as well as in relative peripheral refraction. Understanding the process underlying this acceleration requires further investigation.

Wearing an optical correction appeared to have no effect on the level of or change in relative peripheral refraction. We have no information on the power of the prescriptions worn by children or the reasons corrections were prescribed. One might reasonably assume that most of the corrections after onset were for myopia rather than for astigmatism, which would be expected to increase the amount of peripheral hyperopia and foveal accommodative lag in children with corrected vision compared with those without correction. Whether this increase was symmetric between periphery and fovea is not known. It may be asked whether correction accelerates myopia progression. Children with corrected vision have shown more lag and more myopia,41 but this result cannot be confounded by the fact that correction is not being randomly applied. More myopic children are more likely to be the ones wearing a correction. Cause and effect of the progression of myopia cannot be distinguished by using these data. The lack of impact of correction on relative peripheral refraction shown in Figure 7 is not expected to be confounded by variation in the strength of refractive corrections needed by children with and those without correction because relative peripheral refraction was largely independent of progression in these early postonset years (with the exception of Hispanics in year +5).

Relative peripheral refractive error displayed a pattern around the time of onset that was similar to refractive error and axial length—namely, more rapid change across visits before onset, with the fastest change occurring at onset. But rather than stabilizing at a moderate rate of change after onset, relative peripheral refractive error showed no change across postonset visits. This pattern suggests a two-phase process in ocular growth, one leading up to onset and a second after onset, assuming that variation in peripheral refraction is due in large part to variation in local ocular shape.12–17,42 An increasingly prolate shape suggests equatorial restriction, whereas a constant shape suggests an overall, more uniform global expansion.43 The suggestion of two phases for shape change raises the possibility that two mechanisms may be at work. Various mechanisms may be proposed for why ocular shape is prolate or less oblate in myopia. If growth occurs preferentially at the posterior pole, axial expansion will outpace equatorial expansion, to create a relatively more prolate shape. This mechanism would produce a monotonically increasing prolate shape, however. Stability of shape could be achieved by cessation of growth, yet the data clearly show continued axial growth during the time shape was stable after onset. External equatorial restriction from extraocular muscles46 or constraints from orbital size48 have also been mentioned as possible causes of a

![Figure 7](http://iovs.arvojournals.org/)

**Figure 7.** Relative peripheral refractive error as a function of visit and whether became-myopic children wore a refractive correction. Error bars, SEM.

**DISCUSSION**

Myopic eyes were clearly different from emmetropic eyes before the onset of myopia in terms of refractive error, axial length, relative peripheral refractive error, and growth rates for these variables. Compared with emmetropes, became-myopic children were less hyperopic on average when nonmyopic as long as 4 years before the onset of myopia. This finding is in agreement with previous longitudinal analyses in which early refractive error was used as a predictive factor.6,40 Axial length followed a similar course—namely, longer than in emmetropic eyes by more than 0.75 D in each meridian is more conservative than that used in this investigation, both studies show the fastest rate of change in myopia in the interval between the year before and the year of onset of myopia.4

The choice of criterion level for myopia at onset is somewhat arbitrary. This point may be too late for some children and too soon for others considering 11.5% received a refractive correction 1 year before the 0 visit and 34.5% did not wear a correction even 2 years after. Measurement error is a potential explanation for the faster rate of change before the year 0 visit. The assumption that measurement error is randomly distributed at each visit may not be true between visits −1 and 0. More children may be measured inaccurately as less myopic at visit −1, thereby keeping them from being classified as myopic. These children would then be falsely measured as having a faster rate of progression between visits −1 and 0. This error seems unlikely, however, as the finding of faster change between visits −1 and 0 occurred in independently measured axial length as well as in relative peripheral refraction. Understanding the process underlying this acceleration requires further investigation.

Wearing an optical correction appeared to have no effect on the level of or change in relative peripheral refraction. We have no information on the power of the prescriptions worn by children or the reasons corrections were prescribed. One might reasonably assume that most of the corrections after onset were for myopia rather than for astigmatism, which would be expected to increase the amount of peripheral hyperopia and foveal accommodative lag in children with corrected vision compared with those without correction. Whether this increase was symmetric between periphery and fovea is not known. It may be asked whether correction accelerates myopia progression. Children with corrected vision have shown more lag and more myopia,41 but this result cannot be confounded by the fact that correction is not being randomly applied. More myopic children are more likely to be the ones wearing a correction. Cause and effect of the progression of myopia cannot be distinguished by using these data. The lack of impact of correction on relative peripheral refraction shown in Figure 7 is not expected to be confounded by variation in the strength of refractive corrections needed by children with and those without correction because relative peripheral refraction was largely independent of progression in these early postonset years (with the exception of Hispanics in year +5).

Relative peripheral refractive error displayed a pattern around the time of onset that was similar to refractive error and axial length—namely, more rapid change across visits before onset, with the fastest change occurring at onset. But rather than stabilizing at a moderate rate of change after onset, relative peripheral refractive error showed no change across postonset visits. This pattern suggests a two-phase process in ocular growth, one leading up to onset and a second after onset, assuming that variation in peripheral refraction is due in large part to variation in local ocular shape.12–17,42 An increasingly prolate shape suggests equatorial restriction, whereas a constant shape suggests an overall, more uniform global expansion.43 The suggestion of two phases for shape change raises the possibility that two mechanisms may be at work. Various mechanisms may be proposed for why ocular shape is prolate or less oblate in myopia. If growth occurs preferentially at the posterior pole, axial expansion will outpace equatorial expansion, to create a relatively more prolate shape. This mechanism would produce a monotonically increasing prolate shape, however. Stability of shape could be achieved by cessation of growth, yet the data clearly show continued axial growth during the time shape was stable after onset. External equatorial restriction from extraocular muscles46 or constraints from orbital size48 have also been mentioned as possible causes of a
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relatively prolate shape. These external sources of compression most likely would result in a continuously increasing, relatively prolate shape that was not seen after onset, unless some plasticity or adaptation reduced their restrictive force.

Several authors have discussed ocular shape in refractive error as either the source or the consequence of local defocus stimulating eye growth.9,19,20,43 Yet it seems counterintuitive that progress toward myopia should involve an increasingly relatively prolate shape. Local control of eye growth suggests that the eye should maintain a roughly uniform spherical equivalent, as do the most emmetropic eyes.20 Relative peripheral refraction did not even reach an absolute hyperopic state in became-myopic children until visit −1 (Fig. 3A), 2 years after axial length exceeded the average for emmetropes. It could be argued that the increasingly relatively prolate shape before the onset of myopia adds to hyperopic defocus on a relative basis and drives the accelerating axial growth. However, stability in peripheral refraction happens when the eye is at its most hyperopic peripherally. A sudden loss of sensitivity to peripheral defocus would create stability, but seems unlikely. Another possible scenario is that peripheral defocus is less effective in driving eye growth compared with defocus at the posterior pole. This could accentuate posterior growth at the pole leading to an increasingly prolative or less oblate shape. As shape becomes less oblate, peripheral hyperopic defocus would increase until some point where low amounts of central defocus and high central sensitivity are equally effective in driving eye growth as the higher amount of peripheral defocus and low peripheral sensitivity. Spherical expansion may then occur when central and peripheral signals are equally effective.

Although this model of differential peripheral and foveal sensitivity seems plausible, it seems reasonable to assume that once a shape with sufficient peripheral hyperopia to drive eye growth both centrally and peripherally is attained at onset, axial length should continue to elongate at the highest rate. However, axial elongation is most rapid in the year before onset and slower after onset. In addition, the idea that a relatively prolate shape and peripheral hyperopia stimulates axial elongation in the periphery would seem only as valid as the evidence that hyperopic defocus drives central ocular growth. Recent evidence of only small effects from bifocal clinical trials,2,3,44 that accommodative lag is elevated only between 0.0 to 1.0 D, with vertical quadrants inconsistently either more myopic or more hyperopic than horizontal quadrants.9,19 Atchison et al. 21 report horizontal–vertical asymmetries are that they are not from children, do not examine incident myopes, and are not longitudinal. Therefore they are not conclusive as to whether the relative changes in each quadrant are symmetric during the development of myopia. The implications of these asymmetries are unclear in either a defocus-based or a restriction-based model. No human investigation has attempted to correlate ocular growth with local defocus. Nasal–temporal asymmetries in ciliary muscle anatomy and lens position are well-known,49 suggesting that restriction-based expansion need not be strictly symmetric. Future studies would be strengthened by longitudinal assessment of multiple quadrants.

Ethnic variation in relative peripheral refraction indicates that neither relative peripheral hyperopia nor an increase in relative peripheral hyperopia are universal features of the myopic eye. African-American became-myopic children in year + 5 are nearly as myopic on average as Asian-American became-myopic children in year + 1 (Fig. 4), yet the African-American group has no significant average relative peripheral hyperopia and the Asian-American group has the largest amount (Fig. 6). This may indicate ethnic variation in the underlying process that leads to excessive axial elongation or merely variation in degree within the same process.

In summary, the current findings suggest that longer eyes, more negative refractive errors, and increased relative peripheral hyperopia occur 2 to 4 years before the onset of myopia and may therefore be potentially useful as predictors of myopia onset. It is problematic, however, that this window of opportun-
faster progression, and a more rapid change toward peripheral hyperopia is also predictive of the onset of myopia, but again, only within a narrow window of time. Because time is arranged relative to onset rather than to age, the analysis may be better suited to pointing out potential predictive factors for future analyses and for evaluating what these patterns near the time of onset indicate about the process of becoming myopic rather than for making specific predictions. Even if not optimized for prediction, the current analysis suggests that the process of becoming myopic is not one of gradually accumulating an excessively long axial length. The acceleration in axial growth, myopia progression, and peripheral hyperopia before the onset of myopia followed by no change in relative peripheral refraction after onset suggest a two-stage process that is not consistent with simple external restriction. Differential sensitivity to defocus in the periphery compared with the fovea is plausible, but does not seem consistent with the timing of axial ocular growth. The current findings may be consistent with a process of resistance to stretching by ocular tissues during growth followed by failure to stretch when growth is excessive, but this hypothesis remains speculative at this stage.

References

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**APPENDIX**

The CLEERE Study Group (as of March 2007)

**Clinical Centers**


**Resource Centers and Executive Committee**

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