A Longitudinal Investigation of Adult-Onset and Adult-Progression of Myopia in an Occupational Group

Refractive and Biometric Findings

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Purpose. To investigate the refractive and biometric changes associated with adult-onset and adult-progression of myopia in an occupational group.

Methods. The sample population consisted of 251 clinical microscopists aged 21 to 63 years. Subjects had their refraction and ocular dimensions measured on four occasions during a 2-year period, and a total of 166 subjects (332 eyes) completed the longitudinal aspect of the study. Refraction was measured objectively with a Canon R-1 autorefractor and subjectively by an optometrist using standard procedures. Corneal curvature and axial ocular dimensions were measured with a keratometer and A-scan ultrasonography, respectively.

Results. Of eyes emmetropic at the start of the study, a total of 39% underwent a myopic change in refraction greater than 0.37 diopter (D), with a mean change of -0.58 ± 0.04 D (mean $\pm$ standard error of the mean; $n = 37$). This was associated with an elongation of the vitreous chamber of 0.26 ± 0.05 mm ($P < 0.01$). Eyes emmetropic at the start of the study that did not undergo a refractive change >0.37 D ($n = 58$) during the 2-year study period had a mean change in refraction of 0.02 ± 0.03 D ($P = 0.69$) associated with a change in vitreous chamber depth of 0.05 ± 0.02 mm. Changes in corneal curvature, anterior chamber depth, or lens thickness between the initially emmetropic groups were not significant. The median age of onset of myopia in initially emmetropic eyes was 26.3 years. Of eyes that were myopic at the start of the study, 48% progressed further into myopia by 0.37 D or more during the 2-year period. The mean increase in myopia for the "myopic progressor" group was 0.77 ± 0.03 D ($n = 108$ eyes) compared to -0.01 ± 0.02 D ($n = 115$ eyes; $P = 0.49$) for myopes who did not undergo a refractive change >0.37 D during the study period. The only significant difference in ocular component dimension changes during the study period for these two initially myopic groups was elongation of the vitreous chamber depth (0.24 ± 0.04 mm versus 0.03 ± 0.03 mm, $P < 0.01$). The average age of the myopes who progressed further into myopia during the study was 29.3 years. Axial length–corneal radius ratio at the start of the study was not significantly different between initially emmetropic eyes in which adult-onset myopia developed or emmetropic eyes that remained refractively stable. The incidence of adult myopia development during a 2-year period in this occupational group was 45%.

Conclusions. The structural cause of adult-onset and adult-progression of myopia is vitreous chamber elongation. Invest Ophthalmol Vis Sci. 1997;38:321–333.

For the majority of the population (approximately 65%), the eye's growth is regulated so precisely as to produce a sharp image of a distant object on the photoreceptor layer of the retina without the need for accommodation, thus producing an emmetropic eye. However, in a significant minority of the population, there is a breakdown of this regulated growth and refractive errors develop, particularly that of myopia. The prevalence of myopia in developed countries is reported to be between 25% and 30%,[1,2] with higher levels reported in certain Asian populations.[3]

The prevalence of myopia can be broken down further with respect to the age of onset of the myopia,

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with approximately 2% congenital-onset (age, 0 to 6 years), 18% youth-onset (age, 6 to 20 years), and 10% adult-onset (age, 20 years or older). This classification of myopia was proposed by Grosvenor[4] to distinguish youth-onset myopia, which develops during normal adolescence, cessates around 15 to 16 years of age,[5] and is suggested to have a hereditary influence,[6] from truly adult-onset myopia, which occurs in the third and fourth decades of life and for which an environmental cause has been suggested.[7] This classification is based purely on age and does not make any assumptions on the causes of myopia and also avoids the contentious area of adolescent-onset of myopia (age, 16 to 20 years), also termed college age-onset myopia or late-onset myopia, which may be confounded by normal ocular growth.

It is well documented that the structural cause responsible for youth-onset myopia is vitreous chamber elongation.[8] As the axial growth of the eye is reported to have reached adult emmetropic length by the age of 13 years,[9,10] it has been speculated that adult-onset myopia may not be axial in origin. Studies have suggested a lenticular cause[11] and also a corneal contribution.[12] Cross-sectional studies of late-onset myopia (i.e., onset after 16 years) in university students have, however, indicated vitreous chamber elongation as the ultimate structural cause,[13,14] a finding substantiated more recently by a report of a longitudinal study of a similar adolescent-onset (age, 16 years and older) myopic group.[15] However, the choice of 16 years or older as an age of onset for adult myopia has been questioned by studies, suggesting continued axial growth of the emmetropic eye up to 18 years of age.[16,17] Evidence indicating continued axial growth of the emmetropic eye until 18 years of age makes it difficult to determine if the elongation of the vitreous chamber in late-onset myopic eyes is just an extension of normal growth or the result of some new environmental stimulus, as suggested previously.[11] Also attempting to delineate youth-onset and young adult-onset myopia in adolescence might be confounded further by individual variation in reaching physical maturity if body growth is related to myopia development and progression.[18]

The suggestion of an environmental stimulus to the causation of adult-onset myopia has gained support because of substantial epidemiologic evidence that some aspect of the nearwork associated with formal education can lead to myopia.[19,20] However, as indicated above, the findings are difficult to interpret in adolescent populations because of the concurrent normal growth of the eye. A clearer indication of the association between nearwork and myopia comes from studies on the prevalence of refractive errors in particular occupations, showing a positive correlation between amount of nearwork and myopia.[11,21] These studies do not prove a cause and effect relation. However, work on animal models of refractive development has provided direct evidence that restricting vision to close viewing results in the development of myopia.[22–24]

In an attempt to address definitively the structural cause of adult-onset myopia, the present longitudinal study investigated the development of refractive errors in an occupational group with a minimum age of 21 years. By using such an occupational group, it was possible to avoid the confound of previous studies that have used student populations and the more contentious criterion for myopia-onset of 16 years or older. The occupational group under investigation has been reported to have a substantially higher prevalence of myopia than that observed in the general population and also a higher prevalence of adult-onset or adult-progression of myopia.[25]

MATERIALS AND METHODS

Subjects

The occupational group that formed the subject population was clinical microscopists. Subjects were drawn from clinical microscopy departments throughout Great Britain. The population initially was identified from results of a postal questionnaire on eye problems experienced by this particular type of clinical microscopist. The results of the questionnaire indicated a prevalence of myopia of 61%, considerably higher than that reported for most other graduate-educated populations.[26–28] Of particular interest, 54 of the 247 replies reported onset of myopia after entry into clinical microscopy (36% of all myopic subjects). The results of the questionnaire were used only to identify this particular occupational group and not individual subjects. No further reference was made to the postal questionnaire results after identifying that the population was likely to be an informative group on which to conduct a prospective study on adult-onset and adult-progression of myopia. The data reported in this article were from direct personal interview and measurement taken during the study duration.

The 20 largest regional centers for this branch of clinical microscopy in Great Britain were chosen. Selection was based purely on size of center with no reference to questionnaire responses. At each center, all clinical microscopists were requested to participate irrespective of age, race, refractive state, or gender to avoid any selection bias. Only three subjects asked not to be included, and in each case this was because of previous ocular disease. A total of 251 subjects (90 men, 161 women) were seen on the first set of visits. The median age was 29.7 years (range, 21 to 63 years) at the start of the study.

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This group constitutes approximately 75% of this type of clinical microscopist in Great Britain. Although every attempt was made to see subjects at each of the subsequent visits, 38 (15%) changed occupations or moved to a center not in the study, so they were not available for any follow-up. Also, because of various reasons (e.g., illness, maternity leave), a total of 40 subjects (16%) missed 1 subsequent visit and 7 subjects missed 2 subsequent visits.

This type of clinical microscopist is educated to degree level or above and works principally within National Health Service or health trust hospitals. Their work typically involves long periods (more than 20 hours per week) of high magnification microscopy (×800 to ×1250) interspersed with lower magnification microscopy (×125). Other tasks include histologic and histochemical preparatory techniques. The microscopes used were high-quality binocular microscopes (e.g., Zeiss, Leitz) with infinity-based optics, which were serviced regularly.

All measurements were conducted at the subject's place of work. Subjects at each center were seen a total of four times during a 2-year period. The intervals for each set of visits was 6 months between the first and second visits, 9 months between the second and third visits, and again 9 months between the third and fourth visits. At each subsequent visit to a center, no records were available to the experimenter concerning previous findings, and all analysis was conducted using codes rather than subjects' names to avoid any possibility of bias on subsequent measures. All procedures performed in the study adhered to the Declaration of Helsinki. Informed consent was obtained from all subjects after they were given an explanation of the study and ethical committee approval was obtained.

At each visit, detailed history and symptoms were taken on all subjects, which included details on working practices as well as more visually related information. Particular emphasis was placed on obtaining information of previous refractive history, and wherever possible, the subject's own optometrist or ophthalmologist was contacted to obtain more quantitative information. Information on the number of changes in prescription requiring a change in refractive correction since entering clinical microscopy and also the number and type of refractive changes in the 5 years before entry was requested. Family history of refractive errors also was obtained by personal interview.

Measurement of Refractive State

Refractive error was measured both objectively and subjectively. A Canon (Tokyo, Japan) Autoref R-1 infrared autorefractor was used to take objective measures of the subject's refraction. This instrument has been shown to give a valid and reliable estimate of refractive state.[29,30] A full binocular-subjective refraction with an endpoint of maximum positive sphere consistent with best vision was carried out on all subjects by the same examiner. Subjects were categorized into refractive groups based on criteria described previously.[31] Briefly, emmetropes were classed as subjects whose subjective refractive error was between −0.25 and +0.625 diopter (D), hyperopes were subjects whose refractive error was ≥ +0.75 D, and myopes were subjects whose refractive error was −0.375 D or greater.

The repeatability of the subjective refraction routine was assessed on a total of 30 subjects. The examiner started from the objective findings (obtained from the Canon R-1). All trial case lenses had their value covered and the examiner simply asked the assistant for a stronger- or weaker-powered lens. The second refraction routine for each subject was carried out on a separate day. The 95% confidence interval for the subjective refraction was 0.37 D. The nearest clinical step to this value (0.375 D) was taken as the criterion for a refractive change in this study. All measures of refractive error were converted from spectacle refraction to ocular refraction at the corneal apex. All refractive data reported are ocular refraction or change in ocular refraction. Analysis of change in refraction was based on the mean equivalent sphere (sphere power + $^1/_2$ cylinder power). However, to analyze accurately any changes in astigmatism between groups, both in degree and direction, a recently reported[32] vectorial analysis of refractive errors also was undertaken.

Refractive Classification of Subjects

Previous criteria on which myopes have been classified has been based on several factors (e.g., etiology, age, degree), and this has led to considerable confusion in the literature. In an attempt to clarify the situation, Grosvenor[4] proposed a classification of myopia based on age of onset that did not make any assumptions on the causes of the myopia. In this classification, adult-onset myopia was defined as myopia with onset after the age of 20 years, thus avoiding the contentious area of adolescent-onset of myopia (age, 16 to 20 years) that may be confounded by normal ocular growth. In the present study, a similar classification was adopted. Subjects in whom myopia developed after the age of 20 years were classified as adult-onset myopes, and subjects in whom myopia developed before 20 years of age were classed as youth-onset myopes. For the cross-sectional analysis, youth-onset myopes were segregated into onset before 16 years and onset between 16 and 20 years to allow comparison with previous university student-based studies. For cross-sectional biometry analysis, only the right eye of subjects was included and classification was based on the refraction of this eye. Subjects who could not recall

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accurately (±1 year) the age of onset of myopia were excluded from the cross-sectional biometry analysis.

Ocular Biometry Measures

To obtain information on structural correlates to any observed changes in refractive state during the study period, measurements of the ocular component dimensions were taken using keratometry and A-scan ultrasonography. Corneal curvature was measured with a calibrated Javal-Schiotz (Keeler, Windsor, UK) keratometer. Three measures were taken in the horizontal and vertical meridians. Calibrations were performed before each set of visits using ball bearings of known curvature.

Axial ocular component dimension measures were obtained using a Storz A-scan alpha 20/20 biometer, equipped with a 10-MHz focused transducer and soft probe tip to prevent corneal compression. The instrument has been found to give valid and reliable results,[33] and the measurement procedure has been described in detail previously[13] and will only be described here briefly. The patient's corneas were anesthetized with one drop of 0.4% benoxinate hydrochloride in each eye. The subject's full refractive correction for the eye not under measure was placed in a Halberg clip situated 12 mm in front of the eye, and the subject was instructed to view a letter on the 6/9 line of a distant Snellen letter chart. A minimum of 10 acceptable measurements of anterior chamber depth, lens thickness, and vitreous chamber depth were collected and the procedure then repeated on the other eye. To be accepted, measurements had to have a standard deviation of <0.1 mm (the standard deviation of 480 measures taken by the Storz 20/20 in approximately 0.5 second) and a soft probe compression of <1 mm. Waveforms also were viewed to ensure that each waveform had four clean ultrasound peaks. If this was not the case, the waveform was removed before any analysis and additional readings were taken. Before each center was visited, the ultrasound biometer was calibrated against a temperature-controlled fluid-filled block. Twenty subjects had ultrasound repeated on an eye to assess the repeatability of ultrasound measures. The second set of 10 waveforms was collected after the water standoff had been refilled and the probe tip distance recalibrated. The difference between repeated measures was 0.01, 0.01, and 0.05 mm for the anterior chamber depth, lens thickness, and vitreous chamber depth, respectively. The 95% confidence limits were 0.16, 0.11, and 0.09 mm for the same ocular dimensions, which equate to <0.25 D for any component.

Measurement of anterior and posterior crystalline lens curvature using video ophthalmophakometry[34] also was completed on subjects. Recorded Purkinje images from the fiber optic light sources were digitized, measured, and converted to lens power using corneal curvature and axial ocular dimension findings, using an assumed refractive index of 1.4163. Because of logistic constraints, this measurement was, unfortunately, only taken at the third (15 months) and fourth (24 months) measurement sessions.

This article is concerned principally with biometric changes associated with the development of adult myopia. Therefore, findings on accommodation and occupational factors, which also were collected, will be presented and discussed in a separate article.

Statistical Analysis

Data for all subjects from all measurement sessions were transferred from individual record sheets to a statistical spreadsheet package on a mainframe computer (SPSS, Detroit, MI). Results of differences in ocular components are presented as mean ± standard error of the mean unless otherwise stated. Analysis of variance was performed for between-group differences, with multiple comparison tests (Duncan) used to compare individual differences. Where required, appropriate statistical procedures were employed to take account of fellow eye correlation.[35] Dependent and independent t statistics were also utilized for within group analysis. Nonparametric tests were used where appropriate.

RESULTS

Cross-Sectional Findings

The prevalence of refractive errors in this population, at the start of the longitudinal study, have been reported previously[25] and will only be discussed here briefly. It was found that of the 502 eyes in the study, 66% of eyes were myopic, 28% emmetropic, and 6% hyperopic. In terms of subjects, 70.5% of clinical microscopists had at least one myopic eye. If subjects who were myopic were classified with regard to their report of when myopia-onset occurred (where this could be determined accurately; n = 171 myopes), 37% of subjects were youth-onset myopes (i.e., onset between 6 and 20 years of age) and 33% were adult-onset myopes (i.e., onset of myopia after 20 years of age) with congenital myopes accounting for 1%. There was no significant difference in onset or progression of myopia in adulthood between men and women (P = 0.66).

Table 1 presents the cross-sectional biometric data on axial ocular component dimensions from the first visit. Subjects were classified with respect to age of onset of myopia, based on their own reporting and, where possible, confirmed by their own practitioner's records. Because of the inconsistency among previous studies on the criteria adopted for classifying adult-onset myopia, the present study has divided the myo-

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TABLE 1. Cross-Sectional Refractive and Biometric Findings Taken at the First Measurement Session of the Longitudinal Study

	Hyperopia	*Emmetropia*	*Adult Onset Myopia*	*Youth Onset Myopia*	*Myopia Onset 15 to 20 years*
Number of subjects	14	68	78	47	38
Ocular refraction					
Mean	+1.51	+0.10	−1.68	−3.74	−2.46
SEM	±0.22	±0.03	±0.13	±0.31	±0.27
Corneal radius (mm)					
Mean	7.861	7.892	7.849	7.847	7.854
SEM	±0.085	±0.033	±0.034	±0.048	±0.048
Anterior chamber depth (mm)					
Mean	3.55	3.51	3.69	3.76	3.67
SEM	±0.10	±0.04	±0.05	±0.07	±0.08
Lens thickness (mm)					
Mean	3.91	3.96	3.88	3.91	3.98
SEM	±0.14	±0.05	±0.05	±0.07	±0.09
Vitreous chamber depth (mm)					
Mean	15.81	16.23	17.14	17.80	17.24
SEM	±0.28	±0.08	±0.12	±0.16	±0.19
Axial length (mm)					
Mean	23.26	23.69	24.71	25.47	24.89
SEM	±0.26	±0.08	±0.12	±0.17	±0.18
Age (years)					
Median	29.72	30.83	31.04	30.39	28.77
Range	(22–50)	(21–61)	(22–53)	(21–46)	(21–64)

Subjects are separated into groups based on their reported age of onset of myopia. Refractive and biometric data are presented from the right eye only of each subject. Subjects who could not accurately (±1 year) recall the age of onset of myopia were not included in this cross-sectional analysis.

pic subjects into three groups (for reporting the cross-sectional biometric results) based on reported age of onset: Adult-onset myopes (i.e., onset after 20 years of age), youth-onset myopes (i.e., onset before 15 years of age), and late adolescent-onset (i.e., onset between 15 and 20 years of age). This gives a clear separation between adult- and youth-onset myopes while treating the somewhat contentious age range of 15 to 20 years separately. This takes into account the conflict among studies indicating that normal emmetropic axial growth is complete by 13 years[9,10] and data suggesting that normal ocular growth in emmetropic eyes continue up to 18 years.[16,17]

The cross-sectional findings from this large non-university-based adult population showed that the major structural difference between adult-onset myopes compared to that of emmetropes was vitreous chamber depth (Table 1). Emmetropes had significantly shorter vitreous chamber depths than all three groups of myopes (analysis of variance $F = 23.9$, $P < 0.001$). The difference in refractive error between emmetropes and each of the myopic groups was almost fully accounted for by the difference in vitreous chamber depth based on schematic modeling. Youth-onset myopes had significantly more myopia and deeper vitreous chamber depths than did adult-onset myopes (Duncan Multiple Comparison Test $P < 0.05$). There were no significant differences in corneal radius between any of the five groups ($F = 0.26$, $P = 0.9$). Anterior chamber depth was significantly deeper in both youth-onset and adult-onset myopes when compared to that of emmetropes (analysis of variance $F = 3.04$, $P < 0.02$; Duncan Multiple Comparison Test $P < 0.05$). No significant differences were observed in lens thickness between any of the groups ($F = 0.46$, $P = 0.76$). There was no significant difference in age between the five cross-sectional groups in Table 1 ($P = 0.49$). The median age of reported onset of myopia in the adult-onset group was 26.3 years.

However, what cannot be determined from the cross-sectional data is whether any of the observed structural differences between the groups were present before the development of the adult-onset myopia. Also, no information concerning the chronologic sequence of structural changes in ocular component dimensions was available. A primary aim of the present study was to monitor the structural changes in the eye that accompany changes in refractive state from emmetropia toward myopia and to determine what factors may influence this change.

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TABLE 2. Classification and Dioptric Thresholds for Groups in the Longitudinal Study

Group	*Eyes (n)*	*Starting Refractive Range (D)*	*Final Refractive Range (D)*	*Change in Equivalent Sphere (D)*
Adult-onset myopic	23	+0.62 to −0.25	−0.37 to −1.25	≥−0.37
Emmetropic changing	14	+0.62 to −0.25	+0.25 to −0.25	≥−0.37
Emmetropic stable	58	+0.62 to −0.25	+0.62 to −0.25	<−0.37
Myopic progressing	108	−0.37 to −7.87	−0.75 to −8.37	≥−0.37
Myopic stable	115	−0.37 to −6.25	−0.37 to −6.37	<−0.37

In this study, ≥−0.37 D signifies myopia greater than −0.37 D or an increase in myopia of 0.37 D or greater, whereas <−0.37 D means a refraction less myopic than −0.37 D or change less than −0.37 D.

Longitudinal Results

A total of 166 subjects (median age, 29.9 years; range, 21 to 55 years) were seen for at least 3 of the 4 data collection visits, including the first and last measurement session. For the analysis of the longitudinal data, subjects were classified based on their refractive error at the start of the study and whether this changed during the study (Table 2). Emmetropic subjects were divided into those who underwent a change in refractive error of <0.37 D and were termed "emmetropic stable" and those who underwent a change in refraction of ≥0.37 D. Emmetropic subjects who underwent a refractive change of ≥0.37 D in one or both eyes were further subdivided into those who became clinically myopic (manifest refractive error > −0.37 D) and were termed "adult-onset myopes" and those who, although undergoing a myopic change ≥0.37 D, did not reach our criterion of clinical myopia (e.g., changed from +0.50 D to plano) and who were termed "emmetropic change." Subjects myopic at the start of the study also were divided into those undergoing a refractive change in at least one eye (myopic progressors) and those who were stable (myopic stable) throughout the study period. Because one of the primary aims of this study was to determine the structural correlate responsible for observed refractive changes within eyes, the analysis of refractive and biometric changes was conducted with respect to individual eyes and not subjects. Where both eyes of a subject were included in the same group, the values for the two eyes were averaged and analyzed as a single data point[35] to account for the correlation between fellow eyes. Analysis of possible risk factors or indicators of refractive change were carried out with respect to subject.

Refractive and Biometric Changes in Subjects Initially Emmetropic

Of the 166 subjects (332 eyes) that were observed for the duration of the longitudinal study, a total of 45% of eyes (n = 151) showed a refractive change toward myopia of greater than 0.37 D, whereas 55% of eyes (n = 181) were refractively stable. Of subjects observed throughout the longitudinal study period, a total of 95 eyes were emmetropic at the start of the study, of which 37 (39%) underwent a refractive change of ≥0.37 D (all in the myopic direction). The mean change in refraction during the 2-year period of the study in initially emmetropic eyes showing a refractive shift of ≥0.37 D was (mean ± standard error of the mean) −0.58 ± 0.04 D (n = 37; P < 0.001). In emmetropic eyes that underwent a significant refractive change but did not reach our clinical criterion of myopia (≥ −0.375), the mean change was −0.43 ± 0.02 D (n = 14, P < 0.001). In initially emmetropic eyes that onset into clinical myopia during the course of the study, the mean change was −0.68 ± 0.04 D (n = 23; P < 0.001). In initially emmetropic eyes that did not undergo a refractive change of ≥0.37 D, the mean change during the 2-year period was 0.02 ± 0.03 D (n = 58; P = 0.69). Significant differences in refractive change between the three initially emmetropic groups were found (F = 47.6, P < 0.001), with significant differences between the emmetropic stable group and both the adult-onset group (P < 0.01) and emmetropic change group (P < 0.01; Duncan MCT). There also was a significant difference (P < 0.01) in refractive change between the adult-onset myopic group and the emmetropic change group (Fig. 1A). Vectorial analysis of refractive change also found significant changes in the equivalent sphere component (M vector) for adult-onset myopic eyes and emmetropic change eyes compared to the emmetropic stable eyes. However, neither the J_0 nor J_{45} component of the astigmatic error showed any significant change for all three groups during the 2-year period (P ≥ 0.20).

In adult-onset myopic eyes, the refractive change was associated with a corresponding drop in unaided visual acuity during the study period of 0.21 (Snellen decimal equivalent).[36] No change in unaided visual

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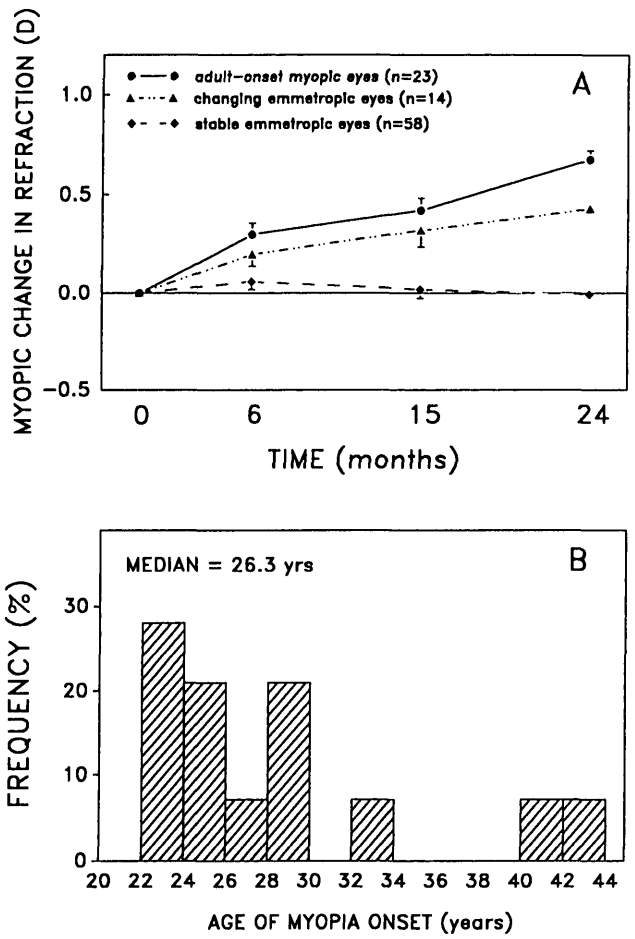

FIGURE 1. (**A**) Change in noncycloplegic ocular refraction in eyes emmetropic at the start of the longitudinal study. Time 0 is when the first measurements were collected. Subsequent measures were taken at 6, 15, and 24 months after this. "Adult-onset" myopic eyes ($P < 0.01$) and "emmetropic changing" eyes ($P < 0.01$) underwent significant myopic changes in refraction during the 2-year period. Error bars = 1 SEM. (**B**) Age of onset into clinical myopia for those subjects classified as having adult-onset myopia develop during the study.

acuity was observed during the study period for stable emmetropic eyes. There was no significant difference in the mean age of the three groups of initially emmetropic subjects ($P = 0.07$). The average (median) age of onset of myopia in the emmetropes in whom adult-onset myopia developed was 26.3 years with a range of 22 to 42 years (Fig. 1B).

The changes in corneal radius and axial ocular component dimensions for all initially emmetropic eyes in the longitudinal study are shown in Figures 2A, 2B, 2C, and 2D. To more easily determine the structural correlate of the observed refractive changes, ocular components have been plotted on both linear metric scales (millimeters) and dioptric equivalent scales (using values from van Alphen[37]) to assess the refractive contribution of any structural change. The major structural correlate to the observed refractive error change was an increase in vitreous chamber depth. There was a significant difference in vitreous chamber elongation during the 2-year period between the three groups who were initially emmetropic (analysis of variance $F = 8.3$, $P < 0.001$). Adult-onset myopic eyes underwent significantly greater vitreous chamber elongation than did emmetropic stable eyes (0.28 ± 0.05 mm versus 0.05 ± 0.02 mm, $P < 0.01$). Emmetropic eyes showing a myopic change but not yet myopic also underwent significantly greater vitreous chamber elongation than did emmetropic stable eyes (0.23 ± 0.05 mm versus 0.05 ± 0.02 mm, $P < 0.02$). There was no significant difference in vitreous chamber elongation between adult-onset myopic eyes and emmetropic eyes undergoing a myopic shift but not reaching clinical myopia. Initial vitreous chamber depth was not significantly different between the eyes of the three groups of emmetropes at the start of the study ($F = 2.2$, $P = 0.11$).

No significant changes were observed in mean corneal curvature between the three initially emmetropic groups throughout the study duration ($P \geq 0.22$). There also was no significant difference in initial corneal curvature at the start of the study ($P = 0.49$) among the three groups. There was no significant difference in anterior chamber depth ($P = 0.10$) or lens thickness ($P = 0.56$) at the start of the study between any of the initially emmetropic groups. Changes in anterior chamber depth and lens thickness were not significantly different at any subsequent visit among the three groups. However, there was a significant reduction in lens thickness in the adult-onset myopic eyes by visit 3 (15 months) and visit 4 (24 months) when compared to the initial lens thickness ($P < 0.05$), which would offset slightly the myopia caused by vitreous chamber elongation (Fig. 2C). Analysis of lens power, as determined from video ophthalmophakometry at visits 3 and 4, showed no significant differences in absolute power ($P = 0.32$) among the three initially emmetropic groups, despite the lens thinning noted in the adult-onset myopic eyes. Using the method of Bennett[38] of calculating crystalline lens power and using the biometric data (keratometry, axial dimensions, and refractive error) collected at all intervals of the longitudinal study also showed no significant changes in lens power among all five groups ($P = 0.30$) during the 2-year study period.

Refractive and Biometric Changes in Subjects Initially Myopic

For eyes that were already myopic at the start of the study and that underwent further myopic change of ≥ 0.37 D, the mean change was -0.77 ± 0.04 D ($n = 108$ eyes; $P < 0.001$) during the 2-year period (Fig. 3A). Eyes myopic at the start of the study that did not undergo a refractive

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change of ≥0.37 D during the study period had a mean change of −0.01 ± 0.02 D (n = 115; P = 0.49). Analysis of astigmatism changes using vectorial methods found no significant change in the J_0 and J_{45} components for either myopic group. The refractive error at the initial visit between the two groups of initially myopic eyes (progressive versus stable) was not significantly different (mean ± standard deviation, −2.36 ± 1.63 D versus −2.07 ± 1.49 D, P = 0.40).

Although both groups of subjects were myopic at the start of the longitudinal study, it was found that, despite being refractively stable during the 2-year study period, 49% of the myopic stable group (n = 23 of 47 subjects; for 4 myopic stable subjects, it was not possible to accurately confirm the age of myopia-onset) actually reported onset into myopia after 20 years of age (i.e., adult-onset myopia). Also, it was found that 51% of the myopic progressor group (n = 32 of 63 subjects) reported onset into myopia after 20 years of age. Of the remaining 49% of those from the myopic progressor group who had onset into myopia before entering their occupation (youth-onset myopes), it was found from analysis of their previous refractive history (based on records from their own optometrist or ophthalmologist) that 61% of these subjects had no change in their spectacle correction for the 5 years before entering their profession (Fig. 3B). However, it could not be confirmed in every case that the criterion used by the subject's optometrist to decide if a change was required was the same as that used in the present study. The average (median) age of the myopic progressor group was significantly lower than the myopic stable group (29.3 years versus 34.4 years, $P < 0.05$).

Figures 4A, 4B, 4C, and 4D show the measured changes in corneal radius of curvature and axial ocular component dimensions for all eyes that were myopic at the start of the study. Once again, vitreous chamber elongation was the major structural correlate to the refractive change in eyes progressing further into myopia. There was a significant elongation of the vitreous chamber in eyes progressing further into myopia (0.24 ± 0.03 mm, $P < 0.01$) during the 2-year period. The change in vitreous chamber depth in stable myo-

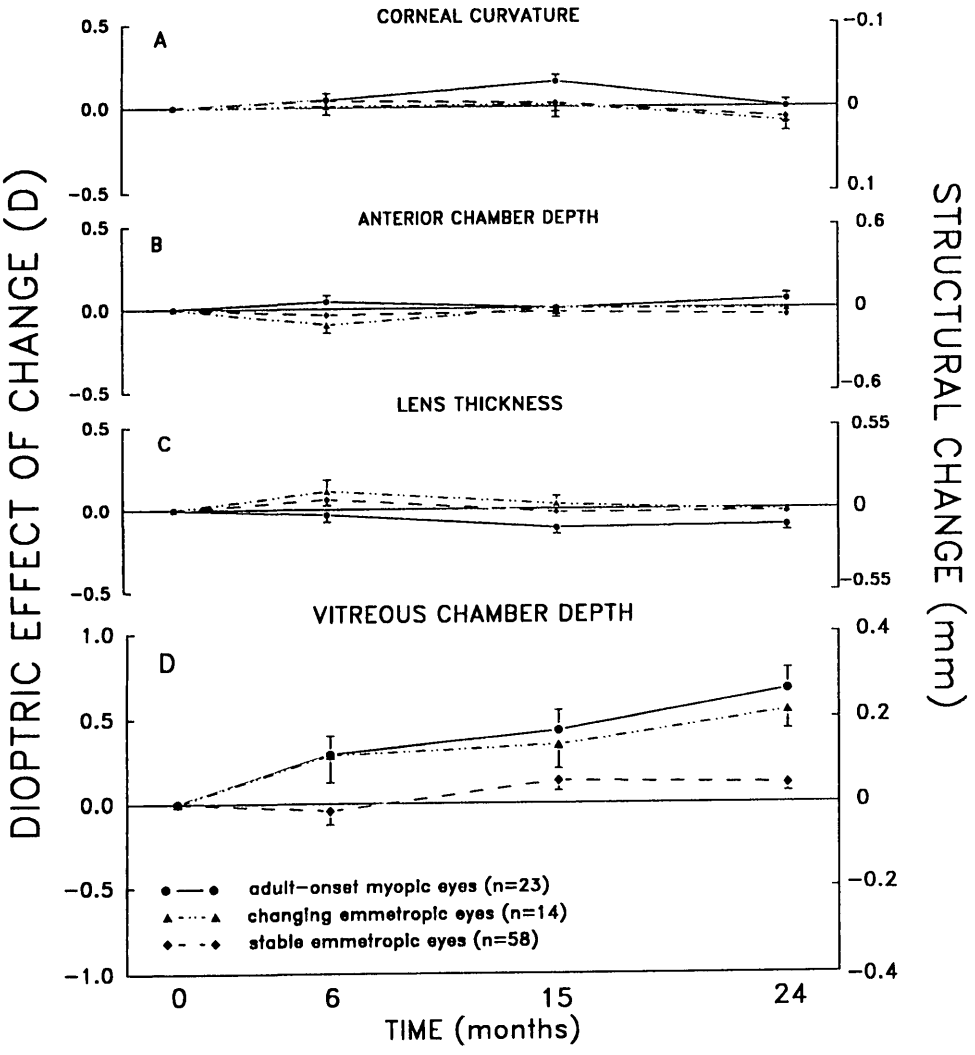

FIGURE 2. Changes in (**A**) corneal radius, (**B**) anterior chamber depth (corneal thickness + anterior chamber depth), (**C**) lens thickness, and (**D**) vitreous chamber depth for all initially emmetropic eyes in the longitudinal study. Data are plotted for both the structural change on a linear metric scale (millimeters) on the right hand ordinate axis and for dioptric effect of structural change (diopters), based on schematic modeling, on the left-hand ordinate. Positive values of dioptric change signify an increase in the power of the eye (myopia), and negative values signify a decrease (hyperopic change). The only structural correlate to the observed change in ocular refraction was vitreous chamber elongation. Error bars = 1 SEM.

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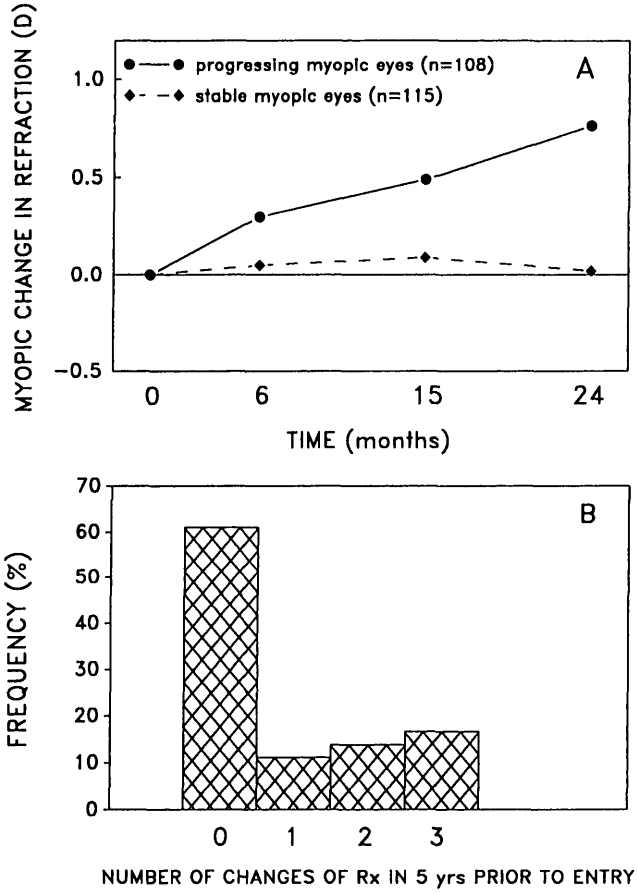

FIGURE 3. (A) Change in noncycloplegic ocular refraction in eyes initially myopic at the start of the longitudinal study. Time 0 is when the first measurements were collected, and subsequent measures were taken at 6, 15, and 24 months after this. "Progressing myopic" eyes underwent a significant increase in myopia ($P < 0.01$) after only 6 months and continued to increase during the 2 years. Error bars = 1 standard error of the mean. (**B**) Number of changes in prescription requiring a change in spectacles for the 5 years before entry into occupation for those subjects who progressed further into myopia during the study and who wore a myopic correction before entry into their occupation (49% of myopic progressor subjects). Sixty-one percent of these myopic progressor subjects had a stable prescription for the 5 years before entry.

pic eyes after 2 years was 0.03 ± 0.03 mm ($P = 0.49$). Vitreous chamber depth at the start of the study was not significantly different between the two groups of initially myopic eyes, although it was slightly longer in the myopic progressing eyes (mean ± standard deviation; 17.39 ± 0.91 mm versus 17.08 ± 1.01 mm, $P = 0.07$), which also were slightly more myopic. There was no significant difference in either initial corneal curvature ($P = 0.1$) or change in corneal curvature at any subsequent measurement session ($P \geq 0.56$) between the two initially myopic groups. It was found that eyes that progressed further into myopia during the study period had significantly deeper anterior chambers (3.86 mm versus 3.74 mm, $P < 0.05$) and thinner lenses (3.74 mm versus 3.86 mm, $P < 0.02$) at the start of the study than did eyes whose myopia remained stable. However, there was no significant difference between the two groups with respect to changes in anterior chamber depth ($P \geq 0.3$) or lens thickness ($P \geq 0.2$) at the subsequent measurement sessions. Lens thickness showed a small reduction in both stable myopic eyes and progressing myopic eyes during the 2-year study period ($P < 0.05$).

Refractive and Biometric Changes in Initially Hyperopic Subjects

There were only 14 eyes that were hyperopic at the start of the study (> +0.75 D) and observed throughout the study period. The average equivalent sphere of these subjects was +2.0 ± 0.4 D with a mean vitreous chamber depth of 16.01 ± 0.36 mm. During the 2-year period, the mean change in equivalent sphere was −0.25 ± 0.13 D, with no significant change in astigmatism ($P \geq 0.40$). The corresponding mean change in vitreous chamber depth was 0.1 ± 0.1 mm. There was no significant change in anterior chamber depth or lens thickness.

Comparison of Ocular Components in Youth-Onset and Adult-Onset Myopia

In an attempt to assess whether the structural causes of adult-onset myopia and youth-onset myopia are the same, a matched-pair analysis was conducted. Subjects were paired for degree of myopia (±0.25 D), age (±6 months) and gender, resulting in 12 pairs of matched subjects. A matched-pair *t*-test analysis showed no significant differences in any of the ocular component dimensions between the two groups of myopes ($P \geq 0.47$).

Refractive Change Related to Initial Refractive Error

Figure 5A compares the mean change in refractive error with respect to the refractive error at the start of the study for all eyes. The greater the degree of myopia at the start of the study, the more likely an eye was to undergo a myopic change during the study period ($P < 0.03$). If only eyes that underwent a refractive change of ≥0.37 D during the 2-year study period were considered, it was found that the degree of change (approximately equal to −0.7 D) was just significantly ($P = 0.05$) greater in myopic eyes compared to emmetropic eyes (Fig. 5B).

Ratio of Axial Length to Corneal Radius of Curvature

It has been proposed previously that the ratio between axial length and corneal radius of curvature (AL/CR) is an indicator of future myopic change, a higher ratio indicating myopia is more likely to develop in an eye.[39] Therefore, it was pertinent to assess the present bio-

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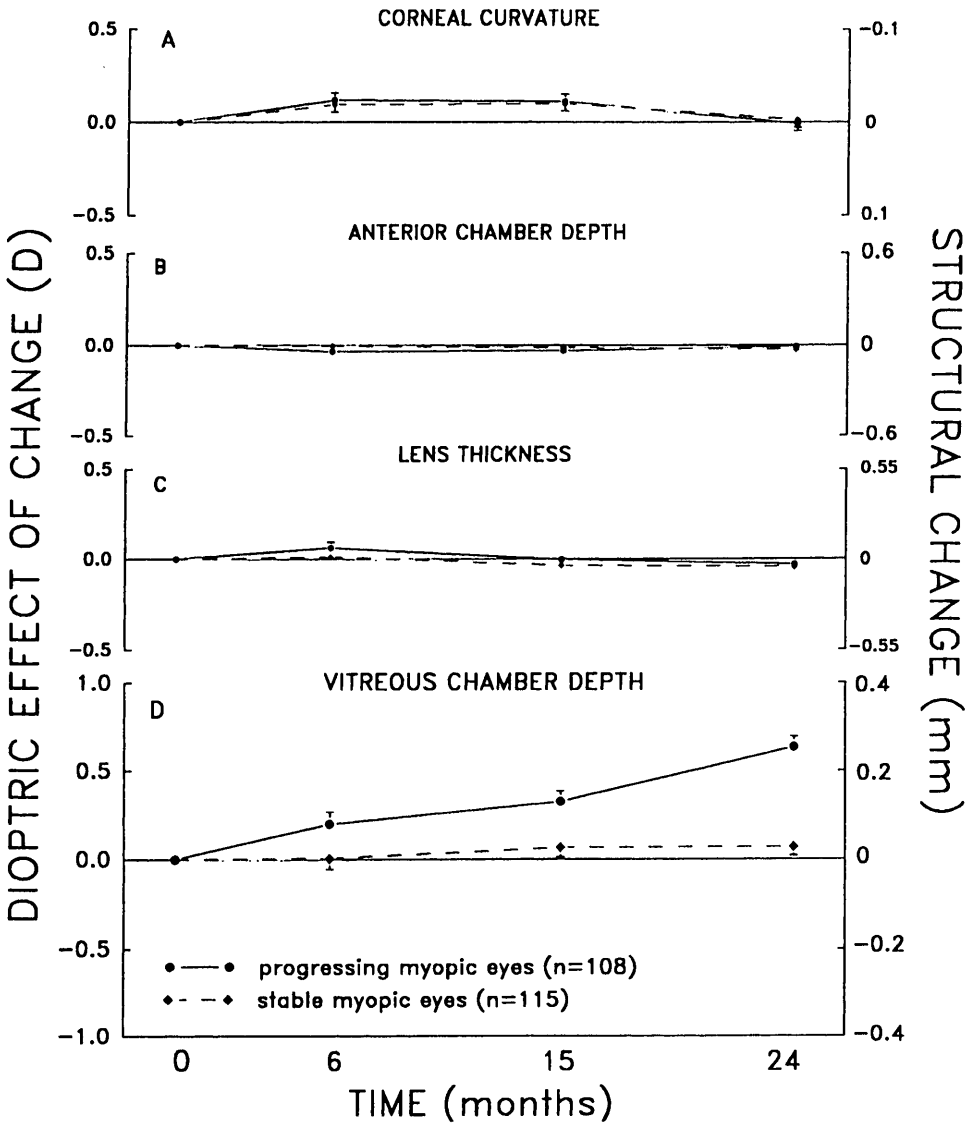

FIGURE 4. Changes in (**A**) corneal radius, (**B**) anterior chamber depth (corneal thickness + anterior chamber depth), (**C**) lens thickness, and (**D**) vitreous chamber depth for all eyes already myopic at the start of the longitudinal study. Data are plotted for both the structural change on a linear metric scale (millimeters) on the right-hand ordinate axis and for dioptric effect of structural change (D), based on schematic modeling, on the left-hand ordinate. Positive values of dioptric change signify an increase in the power of the eye (myopia), and negative values signify a decrease (hyperopic change). The only structural correlate to the observed change in ocular refraction was vitreous chamber elongation. Error bars = 1 SEM.

metric data to determine if this ratio was indeed an indicator for future myopic change. For eyes initially emmetropic at the start of the study, the AL/CR ratios were not significantly different between adult-onset myopic eyes, emmetropic changing, and emmetropic stable eyes (3.02 ± 0.01, 3.00 ± 0.02, 3.01 ± 0.01, $P = 0.50$) at the initial measurement and therefore were not indicative of future myopic change. As might be expected, it was found that eyes already myopic at the start of the study had significantly higher AL/CR ratios than did initial emmetropic eyes (3.16 ± 0.01 versus 3.01 ± 0.01, $P < 0.01$), because existing myopes also had significantly longer vitreous chamber depths than did initial emmetropes. Eyes myopic at the start of the study that progressed further into myopia did not have a significantly higher AL/CR ratio than did myopic stable eyes (3.17 ± 0.01 versus 3.15 ± 0.01, $P = 0.18$).

DISCUSSION

A primary finding from this longitudinal study is that the ultimate structural cause of adult-onset of myopia (i.e., onset after 20 years of age) was the elongation of the vitreous chamber. Schematic modeling of refractive and structural changes supports the above conclusion. Although suggested previously as a cause of adult myopia,[12] the present study found no evidence for changes in corneal curvature contributing to adult myopia development. Also, no evidence was found to support the idea that adult-onset myopia is the result of lenticular changes.[11] Any changes in lens thickness were in the direction of thinner lenses, and no measured or calculated changes in crystalline lens power between groups were observed.

In addition, the current longitudinal findings not only show that the ultimate structural cause of adult-onset myopia is axial in nature but also that there are no significant differences in ocular dimensions among emmetropic eyes before the onset of adult myopia. No evidence was found to suggest that the vitreous chamber elongation associated with myopia is preceded by a corneal steepening. In a study of youth-onset myopia, it has been reported recently that chil-

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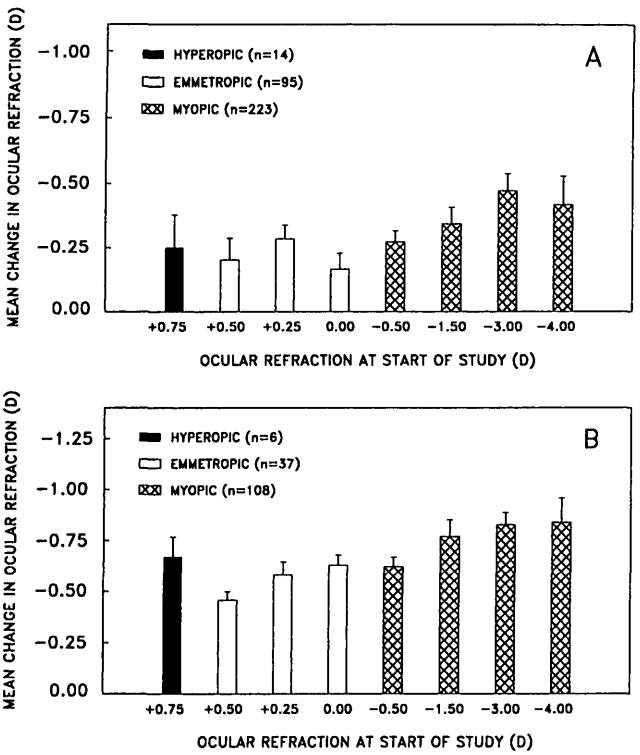

FIGURE 5. (**A**) Mean change in refractive error during the 2-year period compared to the refractive error at the start of the study for all 332 eyes in the longitudinal study. The ranges of entering mean sphere refraction are ≥ +0.76, +0.62 to +0.37, +0.25 to +0.12, +0.00 to −0.25, −0.37 to −0.99, −1.00 to −2.00, −2.00 to −4.00, > −4.0. Error bars = 1 standard error of the mean; N = 332 eyes. (**B**) Mean change in refractive error during the 2-year period compared to refractive error at start of study for only those eyes that underwent a significant myopic change (−0.37 D) during the 2-year period. Error bars = 1 SEM; N = 151 eyes.

dren with emmetropia who have two parents with myopia have significantly longer eyes than do children with emmetropia who have no parents with myopia, with the suggestion that children in whom myopia develops have longer eyes even as emmetropes.[40] The present biometric data do not support a similar possibility for adult-onset myopia development. Adult-onset myopic eyes did not have longer vitreous chambers before axial myopia developed than did initially emmetropic eyes that remained refractively stable.

A previous longitudinal biometric study of late-onset myopia (i.e., onset after 16 years of age) in a university student-based population sample[15] and several cross-sectional studies[13,14,41] have reported that late-onset myopia also is caused by vitreous chamber elongation. Although the current study purposely avoided this late-onset age range, because of suggestions of continued axial elongation in emmetropic eyes up to 18 years of age,[16,17] it would appear that the structural cause of the myopia is identical to the present older adult-onset myopic group.

The biometric findings on adult progression of an existing myopia reported in the present study argue that the structural cause of virtually all adult myopia development is essentially axial in nature, irrespective of age of onset. This, of course, does not mean that the initial stimulus triggering the development of myopia is the same between juvenile-onset and adult-onset or adult-progression of myopia.

It was found that of the initial myopes who progressed further into myopia during the study and in whom myopia developed in youth, approximately 60% were reported to have no change in correction for the 5 years before entering their occupation. This finding supports the suggestion that some form of environmental influence in the occupational task triggers this renewed myopia development. Because the average age of entry into the occupation is 21 to 22 years, 5 years before entry is 16 to 17 years, which is approximately the average age of cessation of juvenile-onset myopia.[5] For subjects already wearing a myopic correction who progressed further into myopia, on average 2 years elapsed after starting in the occupation before renewed progression of myopia required a change in correction.[25] This would argue against simply a continued progression of juvenile-onset myopia.

If eyes were myopic initially at the start of the study, they were found to have an increased chance of having more myopia develop compared to emmetropic and hyperopic eyes, in proportion with the degree of their myopia (Fig. 5A). Thus, as found in a previous retrospective study in military cadets,[42] hyperopia or emmetropia offers some protection against adult myopia development or progression. Analysis of only those eyes in which a significant myopic change developed in adulthood showed that the degree of change (approximately equal 0.7 D) was more similar between refractive groups. This suggests that, for those subjects susceptible to occupational myopia development, the initial refractive state may not be much of an added protection to the degree of change. Also, approximately 50% of all the initial myopes in this occupational group (approximately equal 70% of population sample) had their myopia develop in adulthood, predominantly after entry in their chosen occupation. This translates to a prevalence of adult-onset myopia in this occupational sample of >40%, substantially higher than found in the general population.

The thinning of the crystalline lens found in the adult-onset myopic group would appear to support a previous cross-sectional study on late-onset myopia[13] and also a recent report of longitudinal findings in juvenile-onset myopia[43] in showing thinner lenses in myopes. Although the mechanism of this thinning of the crystalline lens in not known, it is consistent with some attempt at emmetropization in these longer eyes. It has been suggested that this might be caused

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by stretching of the lens due to axial and equatorial growth in both the myopic eye and in the juvenile emmetropic growing eye,[43] with the proposal of a simple mechanical feedback model connecting globe axis, equator, and crystalline lens.[44]

Initial suggestions that adult-onset and adult-progression of myopia might be lenticular or corneal in origin were proposed, in part because it has been reported that normal emmetropic axial length is reached by 13 to 15 years of age.[9,10] It was thought unlikely that the eye could elongate in the third and fourth decades of life. The results of the present study clearly show that with a median age of adult-onset myopia development of 26.3 years, the vitreous chamber of the eye can elongate by significant amounts well into adulthood. The question arises as to the mechanism of vitreous chamber elongation in these older eyes. Because normal eye growth in emmetropes is complete by early adolescence, it has been suggested that this continued axial elongation may be because of mechanical factors that cause a stretching of the sclera and consequent vitreous chamber elongation.[45] It has been postulated that sustained, chronic accommodation can lead to vitreous chamber elongation and myopia due to scleral stretching.[46] Recent findings based on animal models of myopia argue against just a passive stretching of the sclera in axial myopia. Studies in a mammalian model of axial myopia show that the thinning of the sclera at the posterior pole of myopic eyes is associated with a loss of scleral tissue, not just a redistribution, as would be the case if the sclera simply had been stretched to cover the enlarged globe.[47] Also, in both mammalian and avian models of axial myopia, changes in synthesis of scleral proteoglycans have been detected,[48,49] and an increase in levels of a collagen-degrading enzyme (matrix metalloproteinase 2) has been found in mammalian sclera.[50] These findings indicate that active scleral tissue remodeling occurs in axial myopia and also may occur in relatively mature human eyes.

In conclusion, the data from this biometric study clearly show that occupational myopia developing in adulthood is axial in origin, with no other ocular component contributing significantly to the myopic change. The results also show that the structural cause of progression, in adulthood, of an existing juvenile myopia also is vitreous chamber elongation. Youth-onset myopia that has stabilized can once again begin to progress because of environmental influences present in certain occupations. The fact that myopia developed in only approximately 50% of the subjects in this population of clinical microscopists or that it progressed into myopia during adulthood suggests two possibilities. First, some aspect of the occupational workload or how the eyes respond to the various tasks differentiates subjects in whom adult-onset or adult-progression of myopia develops from subjects in whom an occupational myopia does not develop. Second, there is no difference in the occupational workload or measured ocular response to tasks, but certain subjects have a genetic susceptibility to whatever environmental factors present in the occupational task are responsible for the increased incidence of adult myopia. We presently are analyzing data on proposed occupational and accommodative risk factors from this population that hopefully will further elucidate possible mechanisms for the development of myopia in adulthood.

Key Words

adult-onset myopia, emmetropia, occupational myopia, refractive error, vitreous chamber depth

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References

1. Sperduto RD, Seigel D, Roberts J, Rowland M. Prevalence of myopia in the United States. *Arch Ophthalmol.* 1983;101:405–407.
2. Fledelius HC. Is myopia getting more frequent? A cross-sectional study of 1416 Danes aged 16 years +. *Acta Ophthalmol.* 1983;61:545–559.
3. Lin LLK, Shih YF, Tsai CB, et al. Epidemiological study of ocular refractions among school-children (aged 6 through 18) in Taiwan. ARVO Abstract. *Invest Ophthalmol Vis Sci.* 1996;37:S4600.
4. Grosvenor T. A review and a suggested classification system for myopia on the basis of age-related prevalence and age of onset. *Am J Optom Physiol Opt.* 1987; 64:545–554.
5. Goss DA, Winkler RL. Progression of myopia in youth: Age of cessation. *Am J Optom Physiol Opt.* 1983;60:651–658.
6. Curtin BJ. *The Myopias.* Philadelphia: Harper & Row; 1985:52–54.
7. Goldschmidt E. The importance of heredity and environment in the etiology of low myopia. *Acta Ophthalmol.* 1981;59:759–762.
8. Stenstrom S. Investigation of the variation and the correlation of the optical elements of human eyes. *Am J Optom Arch Am Acad Optom.* 1948;58:1–71.
9. Sorsby A, Leary GA, Richards MJ, Chaston J. Ultrasonographic measurement of the components of ocular refraction in life 2. Clinical procedures. *Vision Res.* 1992;3:499–505.
10. Larsen JS. The sagittal growth of the eye IV. Ultrasonic measurement of the axial length of the eye from birth to puberty. *Acta Ophthalmol.* 1971;49:873–886.
11. Goldschmidt E. On the etiology of myopia. *Acta Ophthalmol.* 1968;98:4–172.
12. Goss DA, Erickson P. Meridional corneal components

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of myopia progression in young adults and children. *Am J Optom Physiol Opt.* 1987;64:475–481.
13. McBrien NA, Millodot M. A biometric investigation of late onset myopic eyes. *Acta Ophthalmol.* 1987;65:461–468.
14. Grosvenor T, Scott R. Comparison of refractive components in youth-onset and early adult-onset myopia. *Optom Vis Sci.* 1991;68:204–209.
15. Grosvenor T, Scott R. Three-year changes in refraction and its components in youth-onset and early adult onset myopia. *Optom Vis Sci.* 1993;70:677–683.
16. Fledelius HC. The growth of the eye from the age of 10 to 18 years: A longitudinal study including ultrasound oculometry. *Doc Ophthalmol Proc Series.* 1981; 29:211–215.
17. Garner LF, Meng CK, Grosvenor TP, Mohidin N. Ocular dimensions and refractive power in Malay and Melanesian children. *Ophthalmic Physiol Opt.* 1990;10:234–238.
18. Goss DA, Cox VD, Herrin-Lawson GA, Nielson Ed, Dolton WA. Refractive error, axial length, and height as a function of age in young myopes. *Optom Vis Sci.* 1990;67:332–338.
19. Young FA. The nature and control of myopia. *J Am Optom Assoc.* 1977;48:451–457.
20. Richler A, Bear JC. Refraction, nearwork and education. A population study in Newfoundland. *Acta Ophthalmol.* 1980;58:468–478.
21. Simensen B, Thorud, O. Adult-onset myopia and occupation. *Acta Ophthalmol.* 1994;72:469–471.
22. Miles FA, Wallman J. Local ocular compensation for imposed local refractive error. *Vision Res.* 1990; 30:339–349.
23. Young FA. Primate Myopia. *Am J Optom Physiol Opt.* 1981;58:560–566.
24. Rose L, Yinon U, Belkin M. Myopia induced in cats deprived of distance vision during development. *Vision Res.* 1974;14:1029–1032.
25. Adams DA, McBrien NA. Prevalence of myopia and myopic progression in a population of clinical microscopists. *Optom Vis Sci.* 1992;69:467–473.
26. Dunphy EB, Stoll MR, King SH. Myopia among American male graduate students. *Am J Ophthalmol.* 1968; 65:518–521.
27. Zadnik K, Mutti DO. Refractive error changes in law students. *Am J Optom Physiol Opt.* 1987;64:558–561.
28. Midelfart A, Aamo B, Sjohaug KA, Dysthe BE. Myopia among medical students in Norway. *Acta Ophthalmol.* 1992;70:317–322.
29. Berman M, Nelson P, Caden B. Objective refraction: Comparison of retinoscopy and automated techniques. *Am J Optom Physiol Opt.* 1984;61:204–209.
30. McBrien NA, Millodot M. Clinical evaluation of the Canon Autoref R-1. *Am J Optom Physiol Opt.* 1985; 62:786–792.
31. McBrien NA, Millodot M. The relationship between tonic accommodation and refractive error. *Invest Ophthalmol Vis Sci.* 1987;28:997–1004.
32. Thibos LN, Wheeler W, Horner D. A vector method for the analysis of astigmatic refractive errors. *Vision Science and Its Applications* (Optical Society of America, Washington, DC). 1994;2:14–17.
33. Storey JK, Rabie EP. Ultrasound—A research tool in the study of accommodation. *Ophthalmic Physiol Opt.* 1983;3:315–320.
34. Mutti DO, Zadnik K, Adams AJ. A video technique for phakometry of the human crystalline lens. *Invest Ophthalmol Vis Sci.* 1992;33:1771–1782.
35. Ray WA, O'Day DM. Statistical analysis of multi-eye data in ophthalmic research. *Invest Ophthalmol Vis Sci.* 1985;26:1186–1188.
36. Drasdo N, Haggerty CM. A comparison of the British number plate and Snellen vision tests for car drivers. *Ophthalmic Physiol Opt.* 1981;1:39–54.
37. Van Alphen GWHM. On emmetropia and ametropia. *Ophthalmologica.* 1961;142:S1–S92.
38. Bennett AG. A method of determining the equivalent powers of the eye and its crystalline lens without resort to phakometry. *Ophthalmic Physiol Opt.* 1988;8:53–59.
39. Grosvenor T. High axial length/corneal radius ratio as a risk factor in the development of myopia. *Am J Optom Physiol Opt.* 1988;65:689–696.
40. Zadnik K, Satariano WA, Mutti DO, Sholtz RI, Adams AJ. The effect of parental history of myopia on children's eye size. *JAMA.* 1994;271:1323–1327.
41. Fledelius HC. Adult onset myopia—oculometric findings. *Acta Ophthalmol Scand.* 1995;73:397–401.
42. O'Neal MR, Connon TR. Refractive error change at the United States air force academy-class of 1985. *Am J Optom Physiol Opt.* 1987;64:344–354.
43. Zadnik K, Mutti DO, Fusaro RE, Adams AJ. Longitudinal evidence of crystalline lens thinning in children. *Invest Ophthalmol Vis Sci.* 1995;36:1581–1587.
44. Sorsby A, Benjamin B, Sheridan M. Refraction and its components during the growth of the eye from the age of three. London: Her Majesty's Stationary Office; 1961.
45. Bell GR. A review of the sclera and its role in myopia. *J Am Optom Assoc.* 1978;49:1399–1403.
46. Young FA. The development and control of myopia in human and subhuman primates. *Contacto.* 1975; 19:16–31.
47. Reeder AP, McBrien NA. Biochemical changes in the sclera of tree shrews with high degrees of experimental myopia. *Ophthalmic Physiol Opt.* 1993;13(abstract): 105.
48. Rada JA, Thoft RA, Hassell JR. Increased aggrecan (cartilage proteoglycan) production in the sclera of myopic chicks. *Dev Biol.* 1991;147:303–312.
49. McBrien NA, Lawlor P. Increased proteoglycan synthesis in the sclera of tree shrew eyes recovering from form deprivation myopia. ARVO Abstracts. *Invest Ophthalmol Vis Sci.* 1995;36:S3514.
50. Guggenheim JA, McBrien NA. Form-deprivation myopia induces activation of scleral matrix metalloproteinase-2 in tree shrew. *Invest Ophthalmol Vis Sci.* 1996; 37:1380–1395.

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