Incidence of Myopia in High School Students with and without Red-Green Color Vision Deficiency

Yi-Shan Qian,1,2 Ren-Yuan Chu,1,2 Ji C. He,3 Xing-Huai Sun,1,2 Xing-Tao Zhou,1,2 Nai-Qing Zhao,4 Dan-Ning Hu,5 Matthew R. Hoffman,6 Jin-Hui Dai,1,2 Xiao-Mei Qu,1,2 and Kristina E. Yi-Hwa Pao7

PURPOSE. To investigate the influence of color vision on myopia development by testing refraction error and axial length of the eye for high school students with and without color vision deficiency (CVD).

METHODS. A school-based cross-sectional, cluster sample study was conducted to test the color vision and refractive error of 16,559 high school students. Students were screened for CVD using a pseudoisochromatic plate. CVD was confirmed in students failing the test using a Farnsworth-Munsell 100-Hue Test which also served to classify the subtype (protan or deutan). Three classmates of each CVD subject, matched in five myopia risk factors, were chosen to form the normal color vision (CN) control group. Ophthalmic examinations were performed to determine refractive status and axial length.

RESULTS. Of the students, 309 were found to have red-green CVD and 927 were selected as the CN control group. The prevalence of myopia in the CVD group (45.6%) was significantly lower than that of the CN group (65.8%; P < 0.001). The CVD group was also less myopic in refraction (P < 0.001) than CN, and protan subjects had shorter axial lengths than those in the control group (P = 0.007).

CONCLUSIONS. Color vision deficiencies appear to influence the development of myopia. The observed lower incidence of myopia in people with CVD may be linked to the reduced functionality of the L/M chromatic mechanism. (Invest Ophthalmol Vis Sci. 2009;50:1598–1605) DOI:10.1167/iovs.07-1362

During eye development, early visual experience plays a critical role in controlling eye growth, with a predictable change in axial length to match the position of the image focal plane with the retinal plane.1,2 Placing a positive or negative lens before the eye, thus shifting the image focal plane to a position in front of or behind the retina, leads to a shorter or longer axial length and consequently a hyperopic or myopic eye.3–5 The process by which the eye grows to match its retina with the image focal plane is called emmetropization, a term originally used to describe the elimination of refractive errors in neonates during early eye development. The active emmetropization is functionally analogous to accommodation, by which the focal plane of a near visual target is brought to the retinal plane through a change in the refractive power of the lens.

The optical system is not free of chromatic aberration. Longitudinal chromatic aberration (LCA), caused by the dispersion of the ocular media, causes a single object to form multiple chromatic images within the eye, located at different distances from the retina for different color images. For example, a distant object could produce a red (long-wavelength [L]) image behind the retina, a blue (short-wavelength [S]) image in front of the retina, and green and yellow (middle-wavelength [M]) images near or at the retina. In the human eye, the long-wavelength (700 nm) and short-wavelength (450 nm) images are separated by approximately 1.7 to 2.0 D, with very small individual variations.6–7 Given that multichromatic images simultaneously stimulate the retina with different amounts of defocus, the question of how the mechanisms controlling eye growth respond is of particular interest in the study of emmetropization and myopia development.

Processing of visual information under photopic conditions is initiated by three types of photoreceptors—S-, M-, and L-sensitive cones—and subsequently mediated by a luminance and two opponent chromatic mechanisms, the red/green (or L/M) and yellow/blue (or L-M/S) channels. Each cone type is sensitive to a broad range of wavelengths, but has its own peak sensitivity (e.g., 440, 543, and 566 nm for the S-, M-, and L-cones, respectively).8 Signals of the M- and L-cones are additively fed into the luminance channel and compared in the L/M chromatic opponent channel. The (L+M)/S chromatic opponent channel compares the responses from the S-cone and the summed responses from the L- and M-cones.9–11 Animal studies with chicken and fish demonstrated that when illumination consisted of only a single or narrowband wavelength, the eye grew after the monochromatic image focal plane, determined by LCA.12–15 From these findings, Kroger and Wagner14 inferred that all chromatic mechanisms contribute to the emmetropization process. However, the luminance channel response to LCA alone, without participation of chromatic mechanisms, could also predict the dependency of eye growth on illuminant wavelength. Moreover, emmetropization in humans may be different from that in animals. Therefore, direct study of the human eye is needed to determine the role of chromatic mechanisms in emmetropization and myopia development.

In a series of studies which controlled the effects of LCA and changes in luminance contrast,16–21 chromatic mechanisms were proven to play an important role in controlling
accommodation in the human eye. Given the involvement of chromatic mechanisms in accommodation, it is reasonable to speculate that they contribute to emmetropization and myopia development as well. In a recent study, Rucker and Kruger report a significant correlation between accommodative gain and L-cone luminance sensitivity or contrast.

Rucker and Kruger also found that L-cone responses correlate with refractive error, where a higher level of myopia is associated with higher L-cone sensitivity. Eyes with higher luminance sensitivity in the L-cone, relative to the M-cone, would be more strongly stimulated by images behind the retina, due to LCA, and respond with greater accommodation and an axial elongation to maximize L-cone contrast.

Color vision is mediated by three types of cones and two chromatic opponent mechanisms. Absence or alteration of any cone type is believed to cause color vision deficiency (CVD) and lead to dichromatic or anomalous trichromatic color vision. The most common CVD is X-chromosome-linked and lead to dichromatic or anomalous trichromatic color vision. Absence or alteration of any cone type is believed to cause color vision deficiency (CVD) and lead to dichromatic or anomalous trichromatic color vision. The most common CVD is X-chromosome-linked and characterized by defective M-cones with a shift in peak sensitivity toward that of M-cones. The deutan subtype can be subdivided into deuteranopia, characterized by missing M-cones, and deuteranomaly, characterized by defective M-cones with a shift in peak sensitivity toward that of M-cones. The luminance response for protan subjects is further subdivided into protanopia, characterized by missing L-cones, and protanomaly, characterized by defective L-cones with a shift in peak sensitivity toward that of M-cones. The deutan subtype can be subdivided into deuteranopia, characterized by missing M-cones, and deuteranomaly, characterized by defective M-cones with a shift in peak sensitivity toward that of M-cones. The luminance response for protan subjects is dominated by normal M-cones, whereas L-cones dominate the response for deutan subjects. Thus, relative to normal color vision (CN), with which luminance sensitivity is determined by a combination of both normal L- and M-cones, protan subjects are more sensitive to shorter wavelengths, whereas deutan subjects are more sensitive to longer wavelengths. If luminance sensitivity and cone contrast are important factors controlling emmetropization and myopia development, as suggested by Rucker and Kruger, refraction measurements for eyes with CVD and eyes with CN should be different. In this study, we measured refraction and axial length in 309 school children with CVD and 927 school children with CN, as the control.

METHODS

Study Population and Sampling

A school-based cross-sectional randomized stratified cluster-sampling study was conducted in the Xuhui district, Shanghai, and three cities (Urnumqi, Turfan Basin, and Hettan) of the Xinjiang Province. In China, students graduating from junior high school are placed in different school tracks based on final year grades. If the child performs well in final examinations, he or she may enter into a key senior high school, as well as reading distance). Answers to the questionnaire were used to select matched controls for the CVD cases. Three classmates with normal color vision were chosen as control subjects for each CVD student. The matching factors included: identical sex, similar age (± 1 year), similar parental history (the same number of parents with myopia less than or higher than −5 D), closest diopter-hour (a weighted measure that takes into account viewing distance and the duration of various activities, ±2 diopter-hours), and the amount of time spent outdoors (±1 hour). If more than three matched the condition, a random-number table was used to select three classmates whose student identification numbers were close to that of the CVD student. Analysis of the questionnaire and selection of the controls were performed by a separate specialized technical staff.

Ophthalmic Examination

The following factors were analyzed: visual acuity, with the logMAR chart without refractive error correction; cycloplegic autorefraction (KR-8100; Topcon, Tokyo, Japan) and subjective validation based on the autorefraction results to obtain the best corrected visual acuity (BCVA); noncontact tonometry (CT-60; Topcon); slit-lamp biomicroscopy (model BQ900; Haag-Streit, Bern, Switzerland); axial length of the globe (ultrasound biomicroscopy; Compuscan; Storz Ophthalmic, Inc., St. Louis, MO). Cyclopia was achieved with 1 drop of combined

### Table 1. Sex-Specific Prevalence of Red-Green CVD

<table>
<thead>
<tr>
<th></th>
<th>Participants (n)</th>
<th>n (%)</th>
<th></th>
<th>Participants (n)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td></td>
<td></td>
<td>Females</td>
<td></td>
</tr>
<tr>
<td>SH</td>
<td>5207</td>
<td>186 (3.57)</td>
<td>5297</td>
<td>6 (0.11)</td>
<td></td>
</tr>
<tr>
<td>XJH</td>
<td>1597</td>
<td>59 (3.69)</td>
<td>2161</td>
<td>15 (0.69)</td>
<td></td>
</tr>
<tr>
<td>XJH</td>
<td>981</td>
<td>42 (4.28)</td>
<td>1074</td>
<td>1 (0.09)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7785</td>
<td>287 (3.69)</td>
<td>8537</td>
<td>22 (0.26)</td>
<td></td>
</tr>
</tbody>
</table>

Downloaded From: http://jov.arvojournals.org/ on 10/15/2017
The relative risk of having myopia or hyperopia for the CVD groups in comparison to the corresponding CN groups. A random-effects GLS regression test was performed to assess the effect of CVD on refractive error and axial length (Stata, version 7.0; Stata Corporation, College Station, TX). Graphs were made with another program (SPSS, version 11.5; SPSS Sciences, Chicago, IL).

### Results

There were 309 CVD subjects in the final statistics, including 287 males (3.69% of males tested) and 22 females (0.26% of females tested). Table 1 summarizes the prevalence of CVD in different regional and ethnic groups. The prevalence of CVD in the Han Chinese (from both Shanghai and Xinjiang) was 3.68% in the males and 0.11% in the females. For the Uygur Chinese, the prevalences were 3.69% and 0.69%, respectively. There was no significant difference between the Han and Uygur nationalities in the prevalence of CVD in males ($\chi^2 = 21.35, P < 0.001$). Among the 309 students with CVD confirmed by FM100, 142 (45.95%) were protan subjects (SH: 89, XJU: 31, and XJH: 22) and 167 (54.05%) were deutan subjects (SH: 103, XJU: 43, and XJH: 21). The mean $\sqrt{\text{TES}}$ for CN, protan, and deutan subjects were 4.59, 10.31, and 10.71, respectively (Fig. 1). Of the 927 students selected to be control subjects (CVD: CN at 1:3, Table 2), 426 were matched for protan subjects (CN-P) and 501 were matched for deutan subjects (CN-D).

The median uncorrected logMAR visual acuity was 0.3 (range, −0.1 to +0.8) in the CN group and 0.1 (range, −0.1 to +0.8) in the CVD group. The median BCVA was 0 (range, −0.3 to +0.1) for both the CN and CVD groups. Mean intraocular pressure (IOP) was 16.20 ± 2.93 mm Hg (range, 8–24) in the CN group and 16.53 ± 3.15 mm Hg in the CVD group (range, 9–24). All students with an IOP higher than 20 mm Hg received a second IOP measurement with the Goldmann applanation tonometer, and all measurements fell within the normal range. No significant difference was found in IOP between CVD and CN (random-effects GLS regression test: $P = 0.079$).

The mean refraction and axial length were −1.80 ± 2.47 D (range, −10.0 to +5.5) and 24.44 ± 1.54 mm (range, 20.5–28.0) in the right eye and −1.66 ± 2.50 D (range, −13.5 to +6.0) and 24.35 ± 1.35 mm (range, 20.6–29.9) in the left eye of all students. The correlation coefficients of refraction and axial length between the right and left eyes were 0.93 (Spearman’s correlation: $P < 0.001$) and 0.91 (Pearson correlation: $P < 0.001$), respectively. To standardize statistical analyses, only refraction and axial length of the right eye were used.

#### Analysis of Refractive Error Prevalence by Color Vision Groups

Myopia was present in 45.6% of the CVD subjects and 65.8% of the CN subjects. This difference in myopia...
prevalence was significant (random-effects logistic test: \( P < 0.001 \)). There was also a significant difference in the prevalence of hyperopia, which was found in 14.2% of the CVD subjects and 10.1% of the CN subjects (random-effects logistic test: \( P = 0.03 \)).

Prevalence of refractive error was analyzed separately for each CVD subtype and their corresponding CN groups (Fig. 2). Also shown in Figure 2 are the comparisons between the CVD subtypes and CN groups separated by region and ethnicity (SH, XJU, and XJH). Results from a random-effects logistic test on the difference in prevalence of refractive error between the CVD and CN groups are summarized in Table 3 with the ORs and 95% CIs indicating the relative risk of having myopia or hyperopia in the CVD groups compared with the CN groups. As shown in Figure 2, both the protan (Fig. 2a) and deutan (Fig. 2b) groups had a significantly lower rate of myopia (43.7% for the protan group and 47.3% for the deutan group) than their corresponding CN groups (63.6% for CN-P and 67.7% for CN-D). The CVD subtype groups had higher rates of hyperopia—14.1% for the protan group (Fig. 2c) and 14.4% for the deutan group (Fig. 2d)—in comparison with the corresponding CN groups (9.4% for CN-P subjects and 10.8% for CN-D subjects), but the differences were not significant.

For further analysis by regional and ethnic groups, it can be seen from Figure 2 that the protan subjects had a significantly lower rate of myopia than did the CN-P subjects in both the SH and the XJH groups (Fig. 2a). The prevalence of myopia in deutan subjects was significantly lower than in the CN-D subjects in all three groups (Fig. 2b). The difference in the prevalence of hyperopia, however, was significant only between the deutan and CN-D subjects of the SH group (Figs. 2c, 2d). The difference in prevalence of refractive error between protan and deutan groups was also analyzed; no significant difference was observed for any group.

**Analysis of Refractive Error by Color Vision Groups.**

Mean refractive error for the CVD group was \(-1.31 \pm 2.31 \) D, which was significantly less myopic than the refractive error level of \(-1.97 \pm 2.50 \) D for the CN group (random-effects GLS regression test: \( P < 0.001 \)).

Figure 3 and Table 4 show the mean refractive error for the two CVD subtypes and their corresponding CN groups, analyzed as a whole and also by region and ethnicity. The mean refractive errors for both the protan (Fig. 3a) and the deutan (Fig. 3b) groups were significantly less myopic than for the corresponding CN groups (random-effects GLS regression test: \( P < 0.001 \) for the protan group; \( P < 0.001 \) for the deutan group).

When the random-effects GLS regression test was performed according to region and ethnicity, the difference in mean refractive error was significant for some groups but not for all (Fig. 3). In SH, the mean refractive error of the CN-P subjects was significantly more myopic than that for the protan subjects (\( P = 0.002 \)) and the mean refractive error of the CN-D subjects was significantly more myopic than that for the deutan subjects (\( P = 0.007 \)). No significant difference in mean refractive error was found either between the protan and CN-P subjects or between the deutan and CN-D subjects for XJU (\( P = 0.507 \) for protan subjects; \( P = 0.074 \) for deutan subjects). For XJH, the differences in mean refractive error between both types of CVD and the corresponding CN groups were not significant, but the probability approached the significance level for the protan group (\( P = 0.054 \) for protan subjects; \( P = 0.110 \) for deutan subjects).

Figure 4 shows the regression curves of the mean refractive errors for each CVD subtype and its corresponding CN group, with the estimated marginal means (\( y \)-axis) plotted against the color vision groups (\( x \)-axis). The estimated marginal mean took into account each mean in proportion to its sample size. An interaction analysis in a univariate general linear model indicated that no significant difference in the regression coefficients existed between these two slopes (\( F = 0.018, P = 0.892 \)).

**Analysis of Axial Length by Color Vision Group.**

Mean axial length was significantly shorter for the CVD group (\( 24.30 \pm 1.33 \) mm) than the CN group (\( 24.49 \pm 1.34 \) mm; random-effects GLS regression test: \( P = 0.007 \)).

When CVD subjects were analyzed according to subtype, a significant difference in axial length was found between the
protan (24.25 ± 1.26 mm) and CN-P (24.48 ± 1.32 mm; random-effects GLS regression test: \( P = 0.023 \)) subjects, but not between the deutan (24.36 ± 1.40 mm) and CN-D (24.50 ± 1.35 mm; random-effects GLS regression test: \( P = 0.117 \)) subjects. Figure 5 and Table 4 show the mean axial length for the two CVD subtypes and their corresponding CN groups, analyzed as a whole and also by region and ethnicity.

As shown in Figure 5, no significant difference in axial length was found between the protan and CN-P subjects or the deutan and CN-D subjects for the SH (random-effects GLS regression test: \( P = 0.210 \) for protan subjects; \( P = 0.258 \) for deutan subjects) and XJU (\( P = 0.481 \) for protan subjects; \( P = 0.606 \) for deutan subjects) groups. In the XJH group, the axial length of the CN-P group was significantly longer than that in the protan group (random-effects GLS regression test: \( P = 0.016 \) for protan subjects; \( P = 0.293 \) for deutan subjects).

Figure 6 shows regression curves of the mean axial length for each CVD subtype and its corresponding CN group. No significant difference in the regression coefficients between the two slopes was found (\( P = 0.236, P = 0.628 \)).

**DISCUSSION**

Color vision, refractive error, and axial length were evaluated for 309 high school students with red-green CVD and 927 students with CN. A lower prevalence of myopia was found for the CVD group than the CN group. The CVD group also had less myopic refraction (~0.66 D) and shorter axial length (~0.19 mm) than the CN group had. Matching each CVD subject with three CN controls ensured any difference found could not be attributed to behavioral or genetic risk factors. The findings suggest that color vision influences the refractive development of the human eye with the tendency of red-green color-defective eyes to be less myopic.

In comparison to CN subjects, protan subjects had a lower prevalence and milder degree of myopia as well as a shorter axial length. This difference could be explained by responses of the luminance channel under the influence of LCA. The luminance channel for protan eyes is dominated by M-cones and is thus more sensitive to light of shorter wavelength, whereas the luminance channel of eyes with normal color vision is dominated by both L- and M-cones. Therefore, protan eyes are more sensitive to images focused at a position in front of that of CN eyes, since the focal plane of a shorter wavelength is located in front of that of a longer wavelength due to the LCA. This could result in a shorter axial length and lower degree of myopia for the protan eyes.

In comparison to CN subjects, deutan subjects also showed a lower prevalence of myopia and less myopic refractive error. However, the axial length of the deutan subjects showed no difference to that of CN eyes. The shorter axial length for protan eyes, but not for deutan eyes, when compared to CN eyes, suggests that the eye may be able to detect a difference in the plane of maximum luminance contrast between the two
CVD groups. However, the similarity of the refractive data for the two CVD groups seems to challenge the above conclusion. Regardless of this disparity, the less myopic refractions for both of the CVD groups cannot be explained by a simple model that only detects the plane of maximum luminance contrast. Our observations, therefore, could suggest an involvement of the chromatic opponent mechanisms in the development of myopia. For the eye with either protan or deutan CVD, the L/M chromatic opponent mechanism has lost or reduced function in the middle- to long-wavelength range, but the (L+M)/S chromatic opponent mechanism, functioning in the short- to middle-wavelength range, is not significantly affected.

Although we found that CVD subjects were less susceptible to myopia than CN subjects, they can still be affected by it. A high prevalence of myopia among Chinese students (namely, the Han students in this study) has been reported recently, including one study that found myopia in 81% of 15-years-olds and 84% of children between 16 and 18. Intensive near work and a lack of outdoor activities are believed to be the major risk factors for myopia development. For our subjects, the mean amount of near work hours exceeded 80 dipter-hours. Furthermore, more than 30% of the students reported having taken extra classes (either private or school) on the weekends. Students also reported spending little time on outdoor activities. These behavioral factors may explain the high prevalence of myopia, even in students with CVD.

Myopia is also associated with ethnicity and the intensity of the educational system. Shanghai is a highly urbanized city, and its educational system is much more intensive than that in Xinjiang. This difference may explain why Han students of Shanghai had a higher rate of myopia than did Han students from Xinjiang (Fig. 2). Of note, The Uygur students had a much lower rate of myopia and a higher rate of hyperopia than their Han classmates had. This result may have an ethnic explanation, because Uygur people have both yellow and Caucasoid race lineages as well as unique habits and customs. However, the prevalence of CVD in the Uygur students was close to that of the Han students.

Myopia is a complex trait influenced by as yet unidentified genetic factors. Previous studies have reported the impact of family history on the development of myopia. CVD is unquestionably a genetic disease. It could be interesting to study the association between genetic factors for both CVD and myopia in future research.

### Table 4. Mean Refractive Error and Axial Length

<table>
<thead>
<tr>
<th></th>
<th>Protan</th>
<th>CN-P</th>
<th>Deutan</th>
<th>CN-D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Refractive Error (D)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>-1.27 ± 2.24*</td>
<td>-1.96 ± 2.52</td>
<td>-1.84 ± 2.37**</td>
<td>-1.98 ± 2.48</td>
</tr>
<tr>
<td>SH</td>
<td>-2.04 ± 2.29*</td>
<td>-2.84 ± 2.46</td>
<td>-2.26 ± 2.29**</td>
<td>-2.93 ± 2.30</td>
</tr>
<tr>
<td>XJU</td>
<td>0.56 ± 0.71</td>
<td>0.37 ± 1.11</td>
<td>0.71 ± 0.74</td>
<td>0.15 ± 1.68</td>
</tr>
<tr>
<td>XJH</td>
<td>-0.75 ± 1.83</td>
<td>-1.65 ± 2.03</td>
<td>-1.06 ± 2.27</td>
<td>-1.73 ± 1.90</td>
</tr>
<tr>
<td><strong>Axial Length (mm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>24.25 ± 1.26</td>
<td>24.48 ± 1.32</td>
<td>24.36 ± 1.40</td>
<td>24.50 ± 1.35</td>
</tr>
<tr>
<td>SH</td>
<td>24.76 ± 1.10</td>
<td>24.92 ± 1.25</td>
<td>24.92 ± 1.30</td>
<td>25.06 ± 1.15</td>
</tr>
<tr>
<td>XJU</td>
<td>23.11 ± 0.82</td>
<td>23.24 ± 0.91</td>
<td>23.10 ± 0.78</td>
<td>23.18 ± 0.93</td>
</tr>
<tr>
<td>XJH</td>
<td>23.77 ± 1.15*</td>
<td>24.41 ± 1.05</td>
<td>24.17 ± 1.12</td>
<td>24.45 ± 1.07</td>
</tr>
</tbody>
</table>

Data are expressed as mean millimeters ± SD.

* P < 0.05.

FIGURE 4. Regression curves for the mean refractive errors for the protan and deutan groups with their corresponding CN groups. The estimated marginal mean considered each mean in proportion to its sample size. An interaction analysis indicated that no significant difference in the regression coefficients existed between these two slopes.

FIGURE 5. The mean axial length for the (a) protan and (b) deutan groups and their corresponding CN groups analyzed as a whole and also by region and ethnicity. Overall, a significant difference in axial length was found between the protan and CN-P subjects, but not between the deutan and CN-D subjects. As for the three regional and ethnic groups, the only significant difference was between the protan and CN-P subjects in XJH (random-effects GLS regression, *P < 0.05). Error bar, ±SE.
The prevalence of color vision deficiency is relatively low in our group (~2%) compared with the Caucasian population. The low prevalence of CVD in Asian populations has been reported before, with an incidence of approximately 2.98% for Chinese. In this study, the presence of CVD was determined in a pseudoisochromatic plate color vision test and then was confirmed with an FM-100 test, but not by anomaloscopy. Thus, some anomalous color vision defects may have been undetected.

In this study, we investigated the association between color vision deficiency and refractive state in human eyes. Students with abnormal color vision presented with a significantly lower prevalence and milder degree of myopia than did those with normal color vision. The results suggest that color vision may influence the development of myopia.

**Acknowledgments**

The authors thank the Adiya Ophthalmology Hospital in Xinjiang for staff support and Jack Jiang for technical assistance.

**References**


30. Hamasaki I, Hasebe S, Kimura S. Cycloplegic effect of 0.5% tropicamide and 0.5% phenylephrine mixed eye drops: objective as-

Incidence of Myopia with and without CVD