Albinism: Its Implications for Refractive Development

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PURPOSE. Albinism involves the mutation of one or more of the genes associated with melanin synthesis and has many ramifications for vision. This study focuses on the refractive implications of albinism in the context of emmetropization.

METHODS. Refractive, biometric, and visual acuity data were collected for a group of 25 albino individuals that included the following: 18 oculocutaneous (13 tyrosine positive, 5 tyrosine negative); 7 ocular (2 autosomal recessive, 5 sex-linked recessive). Their age range was 3 to 51 years. All exhibited horizontal pendular nystagmus.

RESULTS. There were no statistically significant differences relating to albino subtype for any of the measured parameters. All the subjects had reduced visual acuity (mean: 0.90, logMAR) and overall, there was a bias toward hyperopia in their refractive errors (mean: +1.07 D). However the refractive errors of the group covered a broad range (SD: 4.67 D) and included both high myopia and high hyperopia. An axial origin to the refractive errors is implied by the high correlation between refractive errors and axial lengths. Refractive astigmatism averaged 2.37 D and was consistently with-the-rule and highly correlated with corneal astigmatism, which was also with-the-rule. Meridional analysis of the refractive data indicated that the vertical meridian for hyperopic subjects was consistently nearer emmetropia compared to their horizontal meridian. Myopic subjects showed the opposite trend.

CONCLUSIONS. The overall refractive profile of the subjects is consistent with emmetropization being impaired in albinism. However, the refractive errors of hyperopic subjects also can be explained in terms of “meridional emmetropization.” The contrasting refractive profiles of myopic subjects may reflect operational constraints of the emmetropization process. (Invest Ophthalmol Vis Sci. 2000; 41:1–7)

Albinism is relatively rare, affecting approximately 1 in 20,000 people. For humans, this term encompasses a number of different, related conditions involving the mutation of one or more genes associated with the synthesis of melanin. The consequence of such mutations is a reduction or absence of melanin in the hair, skin, and/or eyes. The deficiency in melanin also appears to underlie associated neurologic problems that reflect its key regulatory role in the development of neural tissue.1 Foveal hypoplasia (including abnormal macular retinal vasculature), optic nerve hypoplasia, and strabismus are some of the common ocular features of albinism.1,2 Not surprisingly, visual acuity is typically reduced, and subjects generally also have severe photophobia, a consequence of ocular hypopigmentation. The foveal changes presumably underlie the horizontal pendular nystagmus that is also a feature of this condition, although neural abnormalities within the oculomotor control pathways may be a contributing factor. Furthermore, nystagmus appears to contribute to the reduced acuity in these subjects, as evidenced by the meridional bias to their sensitivity loss, i.e., sensitivity is higher for horizontally orientated stimuli compared to vertically orientated stimuli.3,4

Many forms of albinism have been described.1 However, they can generally be categorized into one of two broad categories, oculocutaneous and ocular albinism, based on the involvement of both the skin and the eyes versus only the eyes, respectively. Oculocutaneous albinism may be further divided into tyrosinase-positive (Ty+) and -negative (Ty−) subtypes on the basis of the functional state of the enzyme, tyrosinase, which is involved in the synthesis of melanin, with a further subtype being sometimes included to cover subjects showing variable tyrosinase activity.5 Ocular albinism includes both autosomal recessive (ARO) and sex-linked recessive (XRO) subtypes. Although poor visual performance has been linked to reduced ocular pigmentation (and thus albino subtype),6–8 ocular pigmentation does not appear to be a reliable predictor of the former.9

Our interest in albinism is in its implications for refractive development. Published refractive profiles for albino populations are generally abnormal, with high refractive errors, including high with-the-rule astigmatism, being frequently encountered.5,10–12 However, there are discrepancies between studies in terms of the overall bias in refractive errors, with both myopia2,10 and hyperopia2,11,12 being reported. One of the questions addressed in the study reported here was whether...
TABLE 1. Classification and Age of Albino Subjects

<table>
<thead>
<tr>
<th>Type of Albinism</th>
<th>Number of Subjects</th>
<th>Age (y)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oculocutaneous</td>
<td>18</td>
<td>17.4 ± 13.5</td>
</tr>
<tr>
<td>Ty+</td>
<td>13</td>
<td>14.2 ± 14.4</td>
</tr>
<tr>
<td>Ty−</td>
<td>5</td>
<td>25.6 ± 5.6</td>
</tr>
<tr>
<td>Ocular</td>
<td>7</td>
<td>21.0 ± 11.6</td>
</tr>
<tr>
<td>ARO</td>
<td>2</td>
<td>30.0 ± 12.7</td>
</tr>
<tr>
<td>XRO</td>
<td>5</td>
<td>15.0 ± 1.9</td>
</tr>
</tbody>
</table>

Ty, tyrosine; ARO, autosomal recessive; XRO, sex-linked recessive.

*Values are means ± SD.

METHODS

Subjects

Twenty-five albino subjects were examined, ranging in age from 3 to 51 years. All exhibited horizontal pendular nystagmus. They were classified according to the type of albinism on the basis of family history information and results of a tyrosinase assay of hair root bulbs. Broad categories of oculocutaneous and ocular albinism were used, and subjects were further classified into Ty+ and Ty− in the case of the “oculocutaneous group,” and ARO and XRO in the case of the “ocular group.” The number of subjects and mean ages of each of the four subgroups so derived are summarized in Table 1.

Ocular Measurements

Refractive error, corneal radius of curvature, axial length, and visual acuity data were collected for both eyes of most subjects, although nystagmus and/or age limitations precluded complete sets of data being obtained for five subjects.

Refractive errors were assessed both subjectively and objectively; in the latter case, a minimum of five readings were made with a Hoya AR530 autorefractometer (Hoya, Japan). Subjects were not cyclopleged. Results for the two principal meridians were averaged to obtain best sphere data and also differenced to obtain astigmatic errors. Astigmatic errors were also classified as either with-the-rule (WTR), against-the-rule (ATR) or oblique (OBL), using standard criteria. A Nikon KOH3 keratometer (Nikon, Japan) was used to obtain corneal curvature data for both principal meridians; average and difference data were subsequently derived as for refractive error data. Axial length was recorded with a Storz Omega-Scan ul-

TABLE 2. Refractive Error and Biometric and Visual Acuity Data Broken Down According to Type, for the Albino Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Eye</th>
<th>Ty+</th>
<th>Ty−</th>
<th>ARO</th>
<th>XRO</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA (logMAR)</td>
<td>R</td>
<td>0.87 ± 0.25</td>
<td>1.00 ± 0.07</td>
<td>0.81 ± 0.27</td>
<td>0.90 ± 0.30</td>
<td>0.90 ± 0.23</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.84 ± 0.25</td>
<td>1.02 ± 0.18</td>
<td>0.90 ± 0.28</td>
<td>0.84 ± 0.22</td>
<td>0.88 ± 0.22</td>
</tr>
<tr>
<td>Refractive error (best sphere; D)*</td>
<td>R</td>
<td>+1.49 ± 0.65</td>
<td>+2.00 ± 5.88</td>
<td>+0.25 ± 5.30</td>
<td>-0.65 ± 6.65</td>
<td>+1.07 ± 4.67</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>+2.05 ± 2.74</td>
<td>+3.03 ± 5.39</td>
<td>-0.88 ± 8.31</td>
<td>-0.77 ± 6.80</td>
<td>+1.45 ± 4.62</td>
</tr>
<tr>
<td>Refractive astigmatism (D)*</td>
<td>R</td>
<td>2.33 ± 1.65</td>
<td>3.40 ± 0.80</td>
<td>2.00 ± 2.83</td>
<td>1.60 ± 1.07</td>
<td>2.37 ± 1.54</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>2.10 ± 1.37</td>
<td>3.15 ± 0.70</td>
<td>1.25 ± 1.77</td>
<td>1.65 ± 1.28</td>
<td>2.15 ± 1.32</td>
</tr>
<tr>
<td>Corneal curvature (average, D)</td>
<td>R</td>
<td>43.48 ± 1.27</td>
<td>43.06 ± 0.92</td>
<td>44.41 ± 1.55</td>
<td>41.63 ± 2.69</td>
<td>43.08 ± 1.72</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>43.50 ± 1.43</td>
<td>43.01 ± 0.88</td>
<td>44.82 ± 0.26</td>
<td>41.08 ± 2.49</td>
<td>43.00 ± 1.85</td>
</tr>
<tr>
<td>Corneal astigmatism (D)</td>
<td>R</td>
<td>2.25 ± 1.54</td>
<td>3.79 ± 1.74</td>
<td>2.94 ± 1.51</td>
<td>1.35 ± 1.46</td>
<td>2.43 ± 1.68</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>2.60 ± 1.28</td>
<td>4.58 ± 1.81</td>
<td>1.25 ± 1.06</td>
<td>1.25 ± 1.21</td>
<td>2.62 ± 1.75</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>R</td>
<td>22.00 ± 1.43</td>
<td>22.10 ± 2.72</td>
<td>22.48 ± 0.06</td>
<td>24.23 ± 3.39</td>
<td>22.55 ± 2.28</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>21.79 ± 1.30</td>
<td>22.10 ± 2.66</td>
<td>23.50 ± 1.45</td>
<td>24.61 ± 3.38</td>
<td>22.58 ± 2.34</td>
</tr>
</tbody>
</table>

Values are means ± SD.

* Subjective refraction data are shown here; data for right and left eyes were highly correlated (P < 0.001 in all cases); the groups do not differ significantly in relation to any of the parameters (ANOVA).
Ultrasound biometer (Storz, St. Louis, MO) fitted with a soft probe; a minimum of 10 readings were averaged for all subjects, with more readings being taken when, because of nystagmus, the manufacturer’s acceptance criterion for a SD of no greater than 0.1 mm for each reading could not be achieved. Corneas were anesthetized with 0.4% benoxinate before this procedure. Visual acuity was measured using a black-on-white Bailey-Lovie chart following standard procedure and recorded in logMAR format.16

Tyrosinase Assay

Tyrosinase assays were carried out on scalp hair bulbs using the protocol of Kugelman and VanScott,17 and the results were used in categorizing subjects. Up to 10 hairs were epilated from the parieto-occipital region of each subject. Scalp hair bulbs from normal subjects also were assayed as a control measure. A positive classification was made on the basis of darkening of one or more of the hair bulbs; hair bulbs from normal (control) subjects always yielded positive results.

Data Analysis

Linear regression analyses were used to examine the relationship between left and right eyes, for the various measured parameters. Regression analyses also were used to examine the interrelationship of various parameters and one-way analyses of variance (ANOVAs) were used to assess the significance of albinism type.

This study was conducted in accordance with guidelines provided by the Declaration of Helsinki.

![Figure 1](image1.png)

**Figure 1.** Frequency distributions of refractive errors (best sphere data) for the whole group (A) and categorized according to magnitude and size into high hyperopia (HH; > +5 D), low hyperopia (LH; 0 to +5 D), low myopia (LM; −0.25 to −5 D), high myopia (HM; > −5D) for the 4 subgroups: oculocutaneous tyrosinase-positive (Ty+) and tyrosinase-negative (Ty−) and ocular autosomal recessive (ARO) and sex-linked recessive (XRO) (B).

![Figure 2](image2.png)

**Figure 2.** (A) Refractive errors (best sphere data). (B) Corneal radius of curvature (averaged across meridians) plotted against axial length; in each case, these parameters were significantly correlated ($r = 0.903$, 0.932, respectively). These relationships imply an axial rather than curvature-based (refractive) origin to the refractive errors.

**Table 3.** Results of Correlation Analyses Based on Data for Right Eyes of Albino Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refraction versus axial length</td>
<td></td>
</tr>
<tr>
<td>Best sphere</td>
<td>0.903***</td>
</tr>
<tr>
<td>180°</td>
<td>0.932***</td>
</tr>
<tr>
<td>90°</td>
<td>0.851***</td>
</tr>
<tr>
<td>Refraction versus corneal curvature</td>
<td></td>
</tr>
<tr>
<td>Best sphere versus average</td>
<td>0.231</td>
</tr>
<tr>
<td>180°</td>
<td>0.067</td>
</tr>
<tr>
<td>90°</td>
<td>0.219</td>
</tr>
<tr>
<td>Corneal curvature versus axial length</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>0.466*</td>
</tr>
<tr>
<td>180°</td>
<td>0.211</td>
</tr>
<tr>
<td>90°</td>
<td>0.566**</td>
</tr>
</tbody>
</table>

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. 
RESULTS

As a group, the albino subjects were rarely emmetropic, and refractive errors included both high myopia and high hyperopia. The subjects were generally also highly astigmatic, the astigmatism being mainly corneal in origin and with-the-rule in nature. The refraction, biometric and visual acuity data for both right and left eyes are described in detail. Also means for the four subgroups used to categorize our subjects.

These data are described in more detail below with the following constraints. Because data for right and left eyes were highly correlated for all measured parameters (P < 0.001 in all cases) and subjective refraction and objective refraction data were likewise highly correlated (r = 0.975, 0.865, spherical errors (best sphere) and astigmatism, respectively; P < 0.001), only right eye subjective refraction data are described in detail. Also because ANOVA analyses did not reveal any significant differences relating to either the broad (oculocutaneous versus ocular) classification or finer classification of albinism for any of the parameters (P > 0.05 in all cases), descriptions are generally limited to pooled data.

The equivalent spherical refractive error data for our albino subjects yielded a mean of +1.07 D, representing low hyperopia. However, the SD describing these data is large, 4.67 D, reflecting the large scatter in the data. Overall, the refractive errors ranged from −10.50 D to +9.13 D (Fig. 1A), with 8 of the 25 subjects having refractive errors in excess of 5 D, of them being myopic and the remaining 5 subjects being hyperopic. As already noted, albino subtype was not a significant determinant of refractive error. However, low hyperopes tended to be dispropionately represented within the Ty+ group (Fig. 1B). High refractive errors were more uniformly distributed across the groups, although to the exclusion of the ARO group, which was also the smallest (n = 2). The observed high interocular correlation is perhaps surprising, given the presence of high refractive errors in the data. That the latter cases provided no exception here also is reflected in the very poor correlation between monocular refractive errors and interocular refractive differences (right eye best sphere versus interocular difference, absolute values compared: r = 0.153; P = 0.46). The overall mean interocular difference was −0.38 ± 1.59 D (±SD).

Regression analyses provide some insight into the optical origin of the refractive errors just described. The results of these analyses are summarized in Table 3. Refractive errors, expressed as best spheres, correlated highly with axial length (Fig. 2A). High correlations also were observed when the refractive errors representing the two principal meridians were examined separately. Finally, axial length correlated highly with both average corneal curvature (Fig. 2B) and that for vertical meridian, implying that larger eyes had flatter corneas.

Refractive and corneal astigmatism were also characteristic of the albino subjects. Refractive astigmatism was observed in all but one subject, was always with-the-rule, and was frequently high (up to 6.5 D); the average for the group overall was 2.37 D, with high astigmatism (>4 D) being equally distributed among the hyperopic and myopic subjects. The combination of spherical and astigmatic errors for hyperopic eyes renders the vertical meridian more nearly emmetropic than the horizontal meridian while the opposite pattern is seen in myopic subjects. The mean refractive errors for the horizontal and vertical meridians were, respectively, +4.71 and +2.52 D for the hyperopes and −2.97 and −5.72 D for the myopes. Refractive astigmatism correlated highly with corneal astigmatism, although the latter generally exceeded the former (r = 0.831, P < 0.001; slope of regression line = 0.641, y-intercept = 0.640 D; Fig. 3). Only one subject showed no corneal astigmatism, and the mean for the group was 2.43 D. With-the-rule corneal astigmatism was observed in all but two of the

\[ y = 0.64x + 0.64 \]

Figure 3. Refractive astigmatism plotted against corneal astigmatism; refractive astigmatism was generally less than but highly correlated with corneal astigmatism (r = 0.831).

<table>
<thead>
<tr>
<th>Study</th>
<th>Refractive Error (best sphere in D)</th>
<th>Distribution of Refractive Errors &gt;5 D</th>
<th>Astigmatism (D)*</th>
<th>% WTR of Astigmatism†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current (n = 25)</td>
<td>+1.07 ± 4.67</td>
<td>Hyperopes &gt; myopes</td>
<td>2.37 ± 1.54</td>
<td>100</td>
</tr>
<tr>
<td>Edmunds16 (n = 16)</td>
<td>+0.46 ± 7.30</td>
<td>Hyperopes = myopes</td>
<td>2.02 ± 1.60</td>
<td>8/11</td>
</tr>
<tr>
<td>Jacobson et al.17 (n = 2)</td>
<td>+1.63 ± 0.88</td>
<td>Nil</td>
<td>2.5 ± 1.41</td>
<td>100</td>
</tr>
<tr>
<td>Loshin and Browning12 (n = 8)</td>
<td>+2.81 ± 1.78</td>
<td>Hyperopes &gt; myopes</td>
<td>1.60 ± 6.39</td>
<td>100</td>
</tr>
<tr>
<td>Nathan et al.17,25 (n = 70)†</td>
<td>+0.94 ± 5.32</td>
<td>Hyperopes &gt; myopes</td>
<td>2.58 ± 1.62</td>
<td>79</td>
</tr>
<tr>
<td>Pascal25 (n = 32)</td>
<td>−0.04 ± 3.95</td>
<td>−</td>
<td>2.49 ± 1.41</td>
<td>86</td>
</tr>
<tr>
<td>Perez-Carpinell et al.21 (n = 7)</td>
<td>−3.50 ± 6.16</td>
<td>Myopes &gt; hyperopes</td>
<td>1.07 ± 1.17</td>
<td>50</td>
</tr>
</tbody>
</table>

* Values are means ± SD.
† Percentage based on those with astigmatism; small numbers of subjects in some studies had no astigmatism.
‡ Data pooled across both eyes of individual subjects; data for only one eye of each subject generally considered in other studies.
astigmatic subjects who showed relatively low (<1.3 D) against-the-rule astigmatism.

All subjects showed reduced acuity; the mean visual acuity of the group was 0.90 compared to the standard for normal visual acuity of 0 logMAR units. Here too, there was significant spread in the data (SD, ±0.23), eyes with higher refractive errors tending to have poorer visual acuity. The latter trend is reflected in the high correlation between average refractive error (best spheres expressed as in absolute terms), and visual acuity ($r = 0.684$, $P < 0.001$). On the other hand, refractive astigmatism and visual acuity were not well correlated ($r = 0.283$, $P = 0.17$).

DISCUSSION

This study examined the refractive and biometric profiles of a group of albino subjects that included both oculocutaneous and ocular subtypes. We found no significant differences between the individual groups for the parameters examined. As a group, these albino subjects exhibited a bias toward hyperopia in their refractive errors, although there was significant variability among them, with high myopia as well as high hyperopia being encountered. These subjects also exhibited abnormally high levels of refractive astigmatism that was consistently with-the-rule. The following questions arising from these data are taken up in the following: 1. How representative are these data of albino populations? 2. What is the significance of these results in the context of emmetropization and ocular growth regulation?

How do these data compare with previous studies of albinos? Although it is typically reported that albinos are myopic, the opposite trend was seen in the present study, with hyperopia being more common than myopia. A similar trend is evident in a related study by Dickerson and Abadi10; although no mean data are provided, analysis of data shown graphically revealed 15 of their 25 subjects to be hyperopic, with 3 cases having mean refractive errors greater than 5 D. Hyperopic biases also appear to predominate overall (see Table 4). Nonetheless, high myopia is generally represented among refractive errors greater than 5 D, contributing to the typically large SDs reported in studies of albino subjects. In relation to the effect of albino subtype on refractive status, Kasmann and Ruprecht25 describe a loose, albeit not statistical significant, association between myopia and Ty− albinism, and hyperopia and Ty+ albinism; this trend is not borne out by our data, which include a disproportionate number of high hyperopes to high myopes in the Ty− group (3:1); also, in our study, refractive error differences between the various groups were not statistically significant. Reported means for refractive astigmatism range from 1.07 D22 to 2.58 D12 with the prevalence of with-the-rule astigmatism ranging from 50%22 to 100%.3,19

These data are comparable with our findings of 2.37 D for mean refractive astigmatism and 100% for the prevalence of with-the-rule refractive astigmatism.

The present study included a biometric investigation of the components contributing to observed refractive errors. The observed high correlation between “best sphere” refractive errors and axial lengths implies an axial origin to the refractive errors. Although this conclusion is at odds with that drawn by Harris and Heyman24 based on more limited data, it is also indirectly supported by our corneal data. Specifically, it was found that the corneal radius of curvature increased in parallel with eye size; this trend is opposite to that required for a corneal contribution to refractive errors.25

What do refractive data indicate in terms of emmetropization and ocular growth regulation in albino subjects? As already noted, high with-the-rule astigmatism was characteristic of this group, and as infantile astigmatism tends to show an against-the-rule bias (see review by Lyle15), this argues against it being a product of arrested emmetropization. That visual acuity had no bearing on the magnitude of astigmatism ($r = 0.01$, $P > 0.05$) also supports this conclusion. However, that with-the-rule astigmatism is also characteristic of idiopathic nystagmus10,20 raises the alternative possibility of an etiologic link with nystagmus. The suggestion by Grosvenor26 among others that corneal molding by the lids might give rise to astigmatism offers a potential explanation here, if the effect of the accompanying nystagmus is to lower corneal rigidity, thereby rendering it more moldable. The predominantly corneal origin10 of the refractive astigmatism in these cases is consistent with this interpretation. Other indirect support for this interpretation is contained in studies showing acute lid-induced changes in astigmatism: Gray and Yap27 report an increase in with-the-rule refractive astigmatism with narrowing of the palpebral aperture, whereas Masci28 and Wilson et al.29 report that lifting the lid decreases with-the-rule astigmatism. Although demonstration of a reduction in astigmatism with lid retraction in nystagmus subjects would provide direct proof of the above hypothesis, their astigmatism is likely to be less reversible because of the chronic nature of the condition.30

What do the spherical refractive errors indicate about emmetropization in albinos? If the congenital nature of albinism were to preclude any emmetropization, i.e., arrest development, one might predict a refractive error distribution not unlike those reported for neonates (e.g., Cook and Glasscock31). This prediction is at least partly borne out by our refractive data, which have a broad distribution and include both high hyperopia and high myopia. Indeed, 32% of subjects had refractive errors greater than 5 D, which may have been present neonatally. Also overall, our subjects displayed a hyperopic bias as characteristic of normal infants. This bias also is consistent with the more general association made by Nathan et al.12 between hyperopia and visual impairments developing within the first 3 years of life.

In the absence of longitudinal data, it is impossible to exclude the possibility that emmetropization was disrupted rather than arrested. Indeed, visual acuity is reported to be near normal in albino infants over the first 12 months of life,19 and thus some emmetropization might be expected. This situation can be expected to change as visual acuity subsequently declines. Furthermore, that higher refractive errors were associated with greater visual impairment (poorer visual acuity) is consistent with greater disruption of emmetropization in these cases. Although there is ongoing debate over to what extent the reduced visual acuity reflects the underlying pathology versus nystagmus and/or amblyopia13,32–34; nonetheless, the lower than normal cone density in the foveae of albino eyes35 alone is likely to increase the eye’s depth of focus and so impair emmetropization. The generalized nature of the ocular hypopigmentation problem in albinism and the further observation that rods are more affected than cones46 implies that the peripheral retina is also abnormal, although the influence of latter on emmetropization for humans is currently not well
understood. In this context, the significance of the apparent disparity between albinism, where hyperopia predominates, and other conditions encompassing either peripheral or peripheral plus central anomalies, where myopia predominates, is unclear, although it adds weight to the case for arrested development in albinism.

The preceding discussion and conclusion that emmetropization is either arrested or impaired in albinism is based on considerations of best sphere (average) refractive error data. However, a closer inspection of these refractive data in terms of their meridional components raises the possibility of “meridional emmetropization” for our hyperopic subjects. Specifically for this group, the mean refractive error for the vertical meridian, while still hyperopic, was closer to emmetropia than was that for the horizontal meridian. Refractive data from a related study of albino subjects by Dickerson and Abadi show a similar trend. To evaluate the plausibility of this hypothesis and understand why myopic subjects do not follow the same trend, one needs to consider first, the effect of nystagmus on vision and second, the growth processes underlying emmetropization.

Consider first, the effect of nystagmus on vision. Although not the primary limiting factor of visual acuity in albinos, reductions in visual acuity and contrast sensitivity attributable to nystagmus have been documented. It is the meridional differences in the influence of nystagmus, as implied by meridional performance differences that is of greatest relevance to the issue at hand. Specifically, if as to be expected, horizontal details (e.g., vertically elongated objects) are degraded (smearred), whereas vertical details are relatively well preserved, then one might also predict emmetropization to be preserved for the vertical meridian. Hyperopic albinos appear to follow this prediction. Inherent in this interpretation are two necessary assumptions: (1) that the observed refractive astigmatism is not in itself a product of emmetropization (a point taken up again later) and (2) that emmetropization dominates over any influence of image degradation on the other meridian. Thus, in this model, the refractive error of the orthogonal (horizontal) meridian is not directly regulated but will be “dragged along” with the other meridian, with a superimposed influence of corneal molding. As a proviso here, it should be noted that only evidence of active emmetropization in the form of longitudinal refractive data can make the distinction between the model described here and the alternative possibility that the observed refractive pattern is an artifact of the combination of hyperopia and with-the-rule astigmatism.

Neither the myopic subjects described in the study by Dickerson and Abadi nor those from the present study showed the “meridional emmetropization” ascribed to hyperopic subjects. Although one cannot rule out the possibility that the myopic subjects represent a separate subgroup in which there are other, unidentified factors at work, their profiles also can be explained in terms of the mechanisms underlying emmetropization. The potentially significant difference between hyperopic and myopic eyes in relation to emmetropization is that the former must increase eye growth, whereas the latter must slow their growth. Consequently, the capacity to emmetropize is limited for hyperopic eyes only by the capacity of eyes to grow, but is limited for myopic eyes by the capacity of corneas to flatten after eye growth has ceased. If the high with-the-rule corneal astigmatism encountered in albino eyes implies that the amount of developmental flattening is restricted specifically in the vertical meridian, then this would have the effect for myopic subjects of precluding “meridional emmetropization.”

As an aside to the preceding discussion, an underlying assumption throughout has been that the observed with-the-rule astigmatism occurs independently of, and is neither correctable by, or a product of, emmetropization. Direct tests of this assumption through animal studies involving imposed astigmatic errors are generally supportive.

Finally, in the context of emmetropization, the significance of the high interocular correlations that were observed for various ocular parameters warrants some consideration. These relationships imply that whatever the influences on eye growth in these albino subjects, the two eyes of individual subjects are similarly affected. The high correlation between the two eyes in terms of visual acuity suggests that the severity of the underlying pathology, which is presumably genetically determined, is a significant contributing factor. However, if the properties of the emmetropization mechanism, e.g., its gain, are also genetically determined, then as observed, similar refractive outcomes for the two eyes can be expected where there is high symmetry in the “perturbing” pathology.

In conclusion, the refractive profile of albino subjects, which is typified by high refractive errors with an overall bias toward hyperopia, as well as high with-the-rule astigmatism, suggests that normal emmetropization is impaired. However, the data for hyperopic eyes open the further possibility that some capacity for emmetropization is retained in the vertical meridian, where visual function is likely to be less affected by the accompanying nystagmus. That myopic eyes do not follow the same pattern may simply reflect differences in operating physical constraints.

References


**ERRATUM**


The sequence of the PCR primers for rMuc5ac reported in Table 1 on page 1946 is incorrect. The correct sequence for these primers is as follows:

(Primer 1) 5’-TATGAGTTGGAGCTTTTGT-3’ (726–745)
(Primer 2) 5’-CAGTGCGTGGTGAAGTTGTTG-3’ (1195–1176)
(Primer CRS) 5’-CAGTGCGTGGTGAAGTTGTTG-3’
(Primer CRS = primer 2 followed by base pairs 1073–1056)