Thermal Gradients in the Chick Eye: A Contributing Factor in Experimental Myopia

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Domestic chicks were reared for 4 weeks with a plastic dome or a plastic ring glued to the skin surrounding the right eye. The domes, which degraded retinal images by reducing high spatial frequencies and contrast, have been reported to produce enlargement of the ocular globe and large myopic refractive errors. The rings, which do not produce refractive errors, did not affect vision and served as a control for the mechanical effects of having a device glued to the circumorbital skin. At the end of the rearing period, the chicks were anesthetized and a thermoprobe (a thermocouple in a 29 gauge needle) was inserted into the eye along the optic axis. Temperature readings were made at 1 mm intervals to a depth of 12 mm. Temperature readings also were taken of the circumorbital skin and the air inside the dome. The results indicated that the temperature in the dome eyes was elevated from 2.8 to 5.2°C at the cornea and 0.7 to 2.0°C at the axial sclera. Smaller elevations were found in the ring eyes. Two dome chicks that had lost their devices 24-48 hr prior to temperature measurement had thermal gradients that were nearly identical to those from untreated control eyes. Measurement of the air temperature inside the dome revealed a temperature elevation of nearly 4.0°C above that recorded at an equal distance from control eyes. The circumorbital skin of treated eyes was 0.96°C warmer than the comparable tissue of untreated eyes. The results suggest that the domes contribute to the development of this type of experimental myopia by trapping heat radiated from the cornea. The elevated temperatures may encourage scleral growth, which would result in an elongated globe and a myopic refractive error. Invest Ophthalmol Vis Sci 28:1859-1866, 1987

Experimental myopia has been induced in chickens by a variety of techniques such as manipulation of the spectral composition, duration or intensity of the ambient illumination,1,2 eyelid suture3 and restriction of visual fields.4 Recently, Hodos and Kuenzel5 reported that degradation of the retinal image in young chicks by the use of hemispheric plastic "domes" resulted in enlargement of the ocular globe. Hodos, Fitzke, Hayes and Holden,6 who used an electrophysiological refraction technique7,8 based on the Fitzke optometer,9 found that the increase in posterior segment length5,10 produced by these dome devices resulted in an average refractive error of −14.9 D, with the upper 50% of refractive errors ranging from −16.4 D to −27.3 D.

Following a morphological analysis of the eyes that were refracted by Hodos et al.,6 Hayes, Fitzke, Hodos and Holden10 described several signs that appeared to be responses to inflammation. These were an increased thickness of the choroid and a cloudiness of the anterior vitreous that extended from the ciliary body to the region of the pecten. These inflammatory reactions and the swollen appearance of the circumorbital skin suggested that elevated temperature may play a role in the development of this form of experimental myopia. The dome could serve to trap heat radiated not only from the site of inflammation but also from the cornea and lids to produce an elevation of intraocular temperature. A prolonged temperature elevation of the globe could affect the collagen structure of the sclera or perhaps its growth.

To gain further information on this hypothesis, one of two types of device was attached to the circumorbital skin of young chicks. One device was the same type of dome used by Hodos and Kuenzel5 and Hodos et al.6 The second device was a thin plastic ring of the sort used by Hodos et al6 as a control for the mechanical effects of having a device glued to the circumorbital skin. The ring device does not directly affect vision in any way. The second device was a thin plastic ring of the sort used by Hodos et al6 as a control for the mechanical effects of having a device glued to the circumorbital skin. The ring device does not directly affect vision in any way. A third group of chicks served as untreated controls. After a period of 4 weeks, thermal gradients were measured both inside and outside of the eye. The results indicated that both the ring and dome devices produced elevated intraocular temperatures, but the dome effect was greater.
Materials and Methods

Subjects

The subjects were 14 3-day-old broiler chicks. Three chicks were discarded because extreme body temperature variations during the temperature-recording procedure resulted in unstable eye temperatures. Thus data from 11 chicks were included in the results. All animals were treated in accordance with the ARVO Resolution on the Use of Animals in Research.

The chicks were reared in temperature-controlled, stainless steel cages. Ambient illumination of 3551 lux was provided by fluorescent tubes behind diffuser screens. The light-dark cycle was 15L/9D.

Experimental Groups

The 11 chicks were divided into three groups. One group of three chicks served as untreated controls. The chicks in the two remaining groups were fitted with a plastic device that was glued to the circumorbital feathers and skin of the right eye with collodion and cyanoacrylate adhesive while the chicks were restrained gently with masking tape. One of two types of device was used. One type, the dome, which was the same device used by Hodos and Kuenzel and Hodos et al was approximately equivalent to a spherical lens of −6D. This device reduced contrast and high spatial frequencies and introduced some spherical aberration. Five chicks were fitted with domes. The second type, the ring, was a 1 mm thick plastic ring of the same diameter as the dome, but which had no optical effect and served as a control for the presence of a rigid object glued to the circumorbital skin. Three chicks wore ring devices and three chicks served as untreated controls. In all groups, the left eye was untreated and served as a basis of comparison with the right, treated eye.

Apparatus

The apparatus consisted of a Kopf stereotaxic instrument (Kopf Instruments, Tujunga, CA) fitted with a pigeon headholder and ear bars. The instrument was enclosed in a tent of polyethylene sheets to minimize air currents and to stabilize ambient temperature. During the course of the temperature recordings, the mean ambient temperature was 23.3°C ± 0.26. Eye temperatures were measured with a Sensortek Model BAT-12 digital thermometer from a Sensortek Microprobe model MT-29/3 thermocouple mounted in the end of a 29-gauge needle (Sensortek, Inc., Clifton, NJ). The needle was advanced by a Kopf electrode carrier. Core temperature was monitored with a Vitec model 101 digital electrothermia monitor reading from a themistor inserted into the cloaca (Vitec, Inc., Cleveland, OH). The mean core temperature was 40.0°C ± 0.16. Core temperature fluctuations were minimized by the use of a Braintree Scientific Isothermal Pad, model 39DP (Braintree Scientific, Inc., Braintree, MA) that had been stored in a 40°C oven.

Procedure

After 28–31 days of wearing the devices, the chicks were anesthetized with 20% urethane administered intraperitoneally, supplemented as needed with intramuscular Ketamine (33 mg/kg). After being placed in the stereotaxic instrument and the eye lids were retracted with 4-0 sutures and 2% Xylocaine was applied to the cornea. In some cases the sharp tip of the thermoprobe was sufficient to puncture the cornea. In others, the tip of a number 11 scalpel blade was used to make a corneal puncture that was slightly larger than the diameter of the thermoprobe. No difference in temperature was observed as a result of using one or the other method of penetrating the cornea.

The thermoprobe was oriented at 65° from the bird’s midline and 10° below the horizontal to approximate the optic axis and avoid penetration of the pecten.

Two of the five dome cases had lost their devices 24–48 hr prior to the temperature measurement procedure. These were measured in the same manner as the ring and normal groups. The three dome chicks with their domes still attached required a slightly different procedure. For these chicks, a small flap was made in the dome with a gas turbine dental drill. The flap was just large enough to insert the scalpel blade to puncture the cornea after application of Xylocaine. The flap was then replaced and the gaps plugged except for a small opening through which the thermoprobe was inserted.

When the ambient temperature within the tent stabilized, usually after a minute or two, the thermoprobe tip was advanced just into the corneal puncture to measure the intracorneal temperature. Subsequent readings were made at 1.0 mm intervals to a depth of 12 mm. The sharp thermoprobe tip had no difficulty in penetrating the soft lens of the chick eye.

Several readings were repeated as the probe was withdrawn as a check on the stability of the measurements. In several cases, the external thermal gradient was measured from a distance of 10 mm to the cornea in 1 mm steps. This provided some information about the temperature conditions within the dome. In half the cases, the right eye was measured first and in the other half the left eye was measured first. No consistent effects of the order of measurement were observed.
In addition to eye temperature measurements, the thermoprobe also was used to measure the temperature of the circumorbital skin at the site of attachment of the devices. The probe was advanced until the tip of the probe made an indentation in the skin of about 1 mm in depth. Within a minute the temperature reading stabilized and was recorded.

After the temperature measurements were completed, the chicks were deeply anesthetized with intravenous sodium pentobarbital (60 mg/ml). The eyes were excised and all extraocular tissues were removed. The chicks then were sacrificed by decapitation. The eyes were fixed for 30 min in phosphate-buffered, 3% glutaraldehyde and photographed laterally and anterior-posteriorly. The eyes then were partially hemisected and allowed additional fixation overnight at 5°C after which the hemisection was completed and the upper and lower halves of the hemisected eyes were photographed. The photographs were enlarged to X8.5 and measured with a Bitpad (Summagraphics, Fairchild, CT) digitizing tablet interfaced to a Kaypro 10 computer (Nonlinear Systems, Inc., Solana Beach, CA). The digitizing tablet has a resolution of 0.1 mm.

Results

The supraorbital skin in the region of the attachment of the devices had a swollen and somewhat inflamed appearance. The mean right-minus-left difference in surface temperature of skin in this region in the three untreated chicks was −0.13°C ± 0.12. The mean difference for all of the eight treated chicks was 0.96°C ± 0.13. This difference was significant at P < 0.008 by a Mann-Whitney U test. No systematic difference was observed between the two device types. Loss of a device did not eliminate the elevated skin temperature; the skin remained inflamed for several days after removal of the device. The largest temperature difference observed in any of the chicks, 1.4°C, was in one of the dome cases that had lost its device 24 hr before. No signs of infection were observed in any of the animals.

Table 1 presents the results of the eye measurements. The data of the two dome groups have been combined and the data of the ring and normal groups also have been combined.

Because of the puncturing of the anterior chamber, the corneal curvature and anterior chamber depth were greatly distorted; these data are therefore not presented. A number of other measurements such as lens thickness and diameter, retinal thickness, corneal diameter, etc. were taken. None of these showed a consistent pattern and are not reported here. The data in the table represent measurements that were consistent across subjects, within device types and experimental treatments.

### Table 1. Right minus left eye measurements (mm)

<table>
<thead>
<tr>
<th></th>
<th>Domes</th>
<th>Rings + Normals</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Range</td>
</tr>
<tr>
<td>Anterior-posterior length</td>
<td>+0.100</td>
<td>1.03</td>
</tr>
<tr>
<td>Nasal-temporal length</td>
<td>+1.163</td>
<td>2.72</td>
</tr>
<tr>
<td>Dorsal-ventral length</td>
<td>+1.429</td>
<td>2.63</td>
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<tr>
<td>Posterior lens to retina</td>
<td>+0.637</td>
<td>1.56</td>
</tr>
<tr>
<td>Choroid + PE thickness</td>
<td>+0.067</td>
<td>0.20</td>
</tr>
<tr>
<td>Scleral thickness</td>
<td>+0.072</td>
<td>0.26</td>
</tr>
</tbody>
</table>

A multivariate analysis of variance (MANOVA) was attempted on these data using the REGM statistical package on a University of Maryland Sperry UNIVAC mainframe computer (Sperry Corp., Blue Bell, PA). Although the data were consistent with our previous findings, the number of cases in each group was insufficient to achieve statistical significance. In order to effectively increase the number of cases, the data of the two dome groups (domes on and domes off) were combined into a single group. Likewise, since the data of the rings and normal groups were not significantly different, and since our previous research has shown that they do not differ in refractive state, their data too were combined.

Two separate MANOVAs were performed on the combined data; one on the dimensions of the globe (anterior-posterior, nasal-temporal, dorso-ventral and posterior lens to retina) and a second MANOVA on the thicknesses of the sclera and choroid + pigment epithelium. The results of the first MANOVA were F(4,2) = 5.057, P < 0.04, which indicate that some significant differences in the dimensions of the globe exist between the combined dome groups and the rings + normals group. None of the individual F tests, however, were significant, which is an indicator that no single dimension had been affected by the treatments, but rather that a particular combination of measures accounted for the effect. F tests then were made on the various pairwise combinations of measures; the results were F(2,8) = 5.693, P < 0.03, for the combination of anterior-posterior dimension and the posterior lens to retina dimension and F(2,8) = 5.322, P < 0.03, for the dorso-ventral dimension and the posterior lens to retina dimension. None of the other pairwise combinations of measures was significant. The overall F ratio for the sclera and choroid + pigment epithelium PE thickness was not significant.

Although the small number of cases was insufficient to achieve significance given the amount of variance in the data, the results, nevertheless, are consistent with our previous findings and offer...
Figure 1 presents sample thermal profiles for each of the treatment groups. Each data point represents a single temperature measurement at a given location and each profile was obtained from a single animal. The triangles represent temperature measurements from the left (untreated) eye and the diamonds represent the right eye (treated) measurements. The measurement at zero represents the intracorneal temperature. The readings at 1 and 2 are in the anterior chamber, 4 is in the lens, 5–9 are from the vitreous, 10 is approximately in the retina, 11 is in or close to the sclera and 12 is in the orbit.

The preceding values apply to the normal and ring groups. The dome group had a greater axial length than the others and for them 11 mm would be approximately at the retina and 12 would be in the sclera.

The bottom pair of profiles were taken from a chick in the normal group in which both eyes were untreated. The two profiles are virtually identical. Corneal temperature is 32.5°C and rises smoothly to 38.0°C.

The middle pair of profiles was obtained from a chick with the ring device in place. The left, untreated eye shows a profile that is similar in form to that of the eyes of the untreated chick. The right, treated eye profile is shallower than its companion untreated profile and shows a corneal temperature difference of about 3.0°C and subsequent differences of 1–2°C.

The dome example was from a chick with the dome in place. Its control eye profile also resembles that of the other untreated eyes. In contrast, the profile for the treated eye is virtually flat except for the corneal and anterior chamber readings. The posterior segment thermal gradient of the dome eye has a range of only about 1.0°C. The temperature difference between the two eyes at the cornea is 5.2°C and at the sclera is about 2.0°C.

Figure 2 shows the temperature difference between the right and left eyes for each subject in the normal ring groups. The temperature difference gradients for the three normals are flat and generally remain within 0.5°C of zero difference. In contrast, the three ring cases show right eye temperature elevations of 0.8 to 2.8°C, which diminish as the probe passed through the anterior chamber and lens. In the vitreal chamber and beyond, the gradients are essentially flat. Two of the three chicks in this group showed temperature differences that were comparable to those of the normals in the posterior segment. The third, however, maintained a flat, but elevated thermal difference throughout this zone of the globe.

Figure 3 presents the data of the two groups of chicks with domes. The upper pair of curves are from the two chicks that had lost their domes 24–48 hr...
prior to the temperature measurements. The 48-hr-off eye showed a 1.3°C temperature elevation at the cornea, which diminished somewhat in the anterior chamber. The two eyes differed by less than 0.5°C in the posterior segment. The 24-hr-off eye showed a slightly elevated corneal temperature; the temperature of the remainder of the globe did not differ from the untreated eye.

The lower curves were collected from the three chicks that retained their domes. In each case, the corneal temperature of the treated eye was considerably elevated. The temperature differences ranged from 2.8–5.2°C. The elevations decreased as the thermoprobe passed through the anterior chamber and lens; but at the sclera the treated eyes were still warmer by 0.7–2.0°C.

The mean temperature differences at the cornea were: normals = -0.67 ± 0.12; domes off = 1.0 ± 0.30; rings = 1.96 ± 0.56; domes on = 3.87 ± 0.84. The mean temperature differences at 12 mm, which were in the retina or sclera for the smaller eyes and in the orbit for the larger eyes, were: normals = -0.10 ± 0.21; domes off = -0.20 ± 0.10; rings = 0.66 ± 0.20; domes on = 1.17 ± 0.43.

The data in Figures 2 and 3 were subjected to a multivariate analysis of variance (SPSS-X). The degrees of freedom were corrected for sphericity in the data. The results of this analysis were $F(4,28) = 25.85, P < 0.001$, for the multivariate main effects and $F(12,28) = 4.89, P = 0.001$, for the interaction (Table 2). Because the significant interaction indicated that some of the treatment groups did not show a main effect, tests of the simple main effects of the individual treatments were performed. There results were domes-off group: $F(4,28) = 3.07, P < 0.03$; ring group: $F(4,28) = 7.47, P < 0.001$; domes-on group: $F(4,28) = 29.71, P < 0.001$. $F$ was not significant for the normals (Table 2). These findings indicate that only the normal group lacked a systematic temperature difference profile.

In addition, a test for linear trends was performed to determine whether any of the temperature difference profiles had a slope that differed significantly from zero. The results were non-significant for the

![Figure 2](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933131/)

**Fig. 2.** Temperature differences (right eye minus left eye) for each of the chicks in the untreated, normal control group and the ring-treated group.

![Figure 3](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933131/)

**Fig. 3.** Temperature differences (right minus left eye) for each of the chicks in the dome group. The two curves in the upper panel are from chicks that had lost their dome device 24–48 hr prior to measurement. The data in the lower panel are from three chicks with their domes still in place.

### Table 2. Multivariate analysis of variance results for right minus left eye temperature differences

<table>
<thead>
<tr>
<th></th>
<th>$F$</th>
<th>$df$</th>
<th>$P$</th>
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</thead>
<tbody>
<tr>
<td>Multivariate main effects</td>
<td>25.85</td>
<td>4,28</td>
<td>&lt;0.001</td>
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<tr>
<td>Interaction</td>
<td>4.89</td>
<td>12,28</td>
<td>&lt;0.001</td>
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<td>Simple main effects</td>
<td></td>
<td></td>
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<tr>
<td>Dome-on group</td>
<td>29.71</td>
<td>4,28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dome-off group</td>
<td>3.07</td>
<td>4,28</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Ring group</td>
<td>7.47</td>
<td>4,28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Untreated group</td>
<td>0.29</td>
<td>4,28</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table 3. Results of test for linear trends in right minus left temperature differences

<table>
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<th>Group</th>
<th>F</th>
<th>df</th>
<th>P</th>
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<tbody>
<tr>
<td>Dome-on group</td>
<td>45.53</td>
<td>1.7</td>
<td>&lt;0.001</td>
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<tr>
<td>Dome-off group</td>
<td>3.38</td>
<td>1.7</td>
<td>NS</td>
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<tr>
<td>Ring group</td>
<td>8.92</td>
<td>1.7</td>
<td>&lt;0.020</td>
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<tr>
<td>Untreated group</td>
<td>0.04</td>
<td>1.7</td>
<td>NS</td>
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</table>

normal and domes-off groups. For the ring group F(1,7) = 8.91, P < 0.02, and for the domes-on group F(1,7) = 45.53, P < 0.001. Thus only the ring and domes-on groups had temperature difference profiles that had linear slopes greater than zero (Table 3).

Figure 4 depicts external thermal gradients measured in a dome chick and a ring chick. These data were collected as the thermoprobe was approaching the cornea from a distance of 10 mm. The solid lines represent the thermal gradients outside of the treated eye and the broken lines indicate the control eye external gradients. The dome-case data points are diamonds and the ring-case points are squares. The dome-eye data were collected while the dome was still in place and thus provide information about the thermal gradient within the dome.

The temperatures recorded from the two untreated eyes at 10 mm from the cornea was approximately equal to the ambient temperature, as was the 10 mm temperature of the ring eye. The 10 mm temperature reading was taken just as the thermoprobe entered the interior of the dome. The temperature at this point was nearly 2 degrees warmer than at an equivalent distance from a ring eye or an untreated eye.

The corneal temperature readings in Figure 4, unlike those in the previous figures, are external corneal temperatures that were recorded when the tip of the thermoprobe was minimally in contact with the cornea. The external corneal temperature of the ring eye did not differ from those of the two untreated eyes. In contrast, the gradient within the dome was much steeper and rose to an external corneal temperature of 33.9°C, nearly 4 degrees warmer than the ring or untreated corneas.

**Discussion**

The morphological data reported here are consistent with the morphological findings of Hodos and Kuenzel that indicated increases in the axial length, equatorial length, posterior segment length as a result of post-hatching development with retinal image degradation produced by the dome device. Both the dome and ring devices resulted in inflammation and swelling of the skin surrounding the orbit, especially above the eye. Measurement of the surface temperature of this region indicated that the skin was nearly 1 degree warmer than the comparable tissue above the untreated eye. This effect persisted even in the two cases that had lost their domes a day or two prior to measurement.

The temperature measurements recorded from the untreated eyes indicated the presence of a thermal gradient that is maximal in the depths of the orbit and gradually declines to a minimum at the cornea. Bernstein, Duran and Pinsbowl have described the role of the ophthalmic rete, a vascular network caudal to the avian eye, in the regulation of brain temperature and in the exchange of cerebral respiratory gases. If the ophthalmic rete serves as a heat sink for the brain, then the eye in general and the cornea in particular must be radiators to remove the excess heat from the body. The thermal gradients recorded from the untreated eyes very likely represent the flow of heat from the ophthalmic rete to the surface of the eye. In eyes with dome devices attached, such heat as well as heat radiating from the lids and the inflamed circumorbital skin no doubt would be trapped in the domes. The consequence of this trapped heat would be an elevated ambient temperature near the cornea as well as an increased intraocular temperatures.

Elevated ocular temperature has been implicated
in the etiology of myopia in the past, especially as a result of febrile childhood diseases. For example, Hirsch\textsuperscript{12} reported that children who had contracted measles during years 6–8 had a much higher probability of developing myopia in excess of −1.0 D than did other children. Several studies in rabbits have reported myopic refractive errors after a period of elevated body temperature and increased intraocular pressure.\textsuperscript{13–15} Increased temperature could affect the collagen structure of the sclera by weakening the fibers and permitting the sclera to stretch in response to elevated intraocular pressure (Greene and McMahon\textsuperscript{16}).

In his recent review, Curtin\textsuperscript{17} states that scleral weakness as a result of scleral or sclerociliary inflammation was formerly considered a factor in the etiology of myopia, but has been regarded as less plausible in recent years because of the lack of histological data to support it. The scleral measurements of Hayes et al\textsuperscript{10} are consistent with Curtin’s view. Hayes et al did not find the scleral thinning in dome-treated chicks that one might expect as a consequence of scleral stretching produced by weakness or disorganization of the scleral collagen fibers. The scleral measurements reported here not only showed no thinning but suggested an increase in scleral thickness. A possible explanation of these findings is that the chronic elevated temperature in young, rapidly growing animals stimulated the growth of the sclera. The accelerated rate of scleral growth may have increased the dimensions of the posterior segment. A recent report by Finger et al\textsuperscript{18} indicated that 2 hr per day of scleral heating in the range of 39–46°C in rabbits resulted in scleral hyperplasia, fibroblast activity and the formation of new scleral collagen. A possible mechanism for this accelerated scleral growth may have been an increase in choroidal blood flow in response to the elevated temperature.\textsuperscript{19,20}

That increased ocular temperature is not the sole cause of the severe myopia that has been reported in chicks reared with the dome device\textsuperscript{6} is clear from the observation that the chicks reared with the ring device, which also produces elevated ocular temperatures, were emmetropic.\textsuperscript{5} However, the elevated temperatures of the dome chicks, in combination with the retinal image degradation produced by the dome, may have resulted in the ocular enlargement\textsuperscript{5,10} and high myopia\textsuperscript{a} that has been reported in dome chicks.

The mechanism by which the domes and similar image-degrading devices produce myopia is still obscure. Although the combination of scleral weakness and excessive accommodation appears to be a favored theory,\textsuperscript{5,10,21} the lack of scleral thinning has raised some doubts about it. The increased ocular temperature that results from a device glued to the circumorbital skin that traps heat and restricts the convective cooling of the cornea would appear to contribute to the development of myopia. The latter suggestion is supported by results using two similar devices, arches\textsuperscript{6,10} and crescents,\textsuperscript{5} that distort only a portion of the visual field and interfere much less with convective cooling of the cornea. These devices produce smaller myopic refractive errors and less enlargement of the globe than do the domes.

That retinal image degradation results in myopia suggests that the quality of the retinal image may be part of a feedback loop that synchronizes the growth of the posterior segment with the changes in the power of the refractive media that are necessary to achieve emmetropia; i.e., a decrease in the quality of the retinal image may signal a scleral growth to compensate for decreased optical power. Retinal image degradation may affect this feedback mechanism by giving a false signal for growth. The growth process may be affected by changes in choroidal blood flow. Elevated temperature in the ocular environment may further enhance this growth to result in even larger myopic refractive errors.

Key words: chicks, myopia, ocular enlargement, temperature, hyperthermia, inflammation

Acknowledgments

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References

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