

# EMMETROPIZATION: An Overview

---

■ KRISTIE YACKLE, O.D.  
■ DAVID E. FITZGERALD, O.D.

## Abstract

*Emmetropization is the process by which the eye moves from a state of ametropia to emmetropia. Though emmetropization is not fully understood, the process is of great interest. Many researchers have made contributions and proposed theories that facilitate insights into the process. Structural alterations, genetic disposition, environmental adaptations, biochemical interactions, and the effect of spectacle lenses have been major areas of investigation. This paper will provide an overview of the current literature.*

## Key Words

*Emmetropization, emmetropia, ametropia, refractive error.*

Grosvenor describes emmetropia as the “normal” state of the eye in which accommodation is relaxed and parallel rays of light focus on the retina.<sup>1</sup> However, Zadnik and Mutti introduce the concept of a normal distribution of refractive errors whose ranges revolve around low hyperopia with age.<sup>2</sup> Others consider emmetropia to be between +0.50<sup>3</sup> and +1.50<sup>4</sup> diopters of hyperopia. Ametropia is all that is not emmetropia. Though not all researchers present a precise definition of emmetropia, it is the general consensus that it is a low amount of hyperopia. This is consistent with Zadnik and Mutti, and we will use it as the working definition for this paper.

Emmetropization is the process occurring during the normal growth period by which the eye changes from a state of ametropia to emmetropia. The topic of emmetropization is very complex and at times studies appear to be confusing and contradictory. The multiplicity of factors, which many well qualified researchers have explored, is certainly a contributing element. Considerations must be given to questions, such as:

- > Is emmetropization an active or a passive process?
- > What are the structural changes that occur during the process?
- > What effects does visual deprivation have upon the process?
- > Is there a biochemical aspect to emmetropization?
- > Is the process controlled locally within the eye or at a higher neurological level?
- > Animal models are more easily studied, but how well do these findings translate to the human?

- > How and when does the optometrist apply the results of human studies?

Though there may not be specific answers to these questions, we will attempt to review some of the more major highlights.

Triolo and Wallman<sup>5,6</sup> propose the term “functional emmetropization” as the eye being emmetropic for its most frequently encountered needs. To date it is a phenomenon occurring in animals and is guided by the visual needs of the organism. For example, some birds have their superior retina myopic for viewing the ground while the remaining retina is positioned for distance.

The actual emmetropization mechanism remains unclear, though theories have been suggested. Two oppositional theories suggest emmetropization is achieved by means of an active (visual feedback) or a passive (predetermined growth) mechanism.<sup>5,6</sup> As Saunders, et. al., indicates, it is more likely a combination of both mechanisms.<sup>7</sup> However, it has been established that successful completion of the process is dependent upon appropriate visual stimulation and an uncompromised system.<sup>6,8-10</sup>

## Active Process

The active process mechanism theory proposes that emmetropization is regulated by the retinal image. The eye analyzes the amount of retinal blur, and proportionally elongates or shortens until the image and retina are conjugate. Various observations are used to support the concept that emmetropization is an actively regulated visual process. One is provided by the refractive outcomes of visually deprived human neonates. The development of the refractive state in human

neonates is very sensitive to visual disturbances.<sup>11-16</sup> It has been shown that in this population visual deprivation from corneal opacifications,<sup>17</sup> congenital cataracts,<sup>11</sup> lid aperture,<sup>18-20</sup> vitreal hemorrhage,<sup>21</sup> and retinopathy of prematurity<sup>22-23</sup> cause the eye to elongate and therefore fall farther away from emmetropia. A study of twins has shown one twin with a media opacity to have a 2.0mm longer eye than the contralateral eye or the axial length of the twin brother's eyes.<sup>24</sup> This would equate to about 6.00D difference in refraction between the normal eyes and the visually deprived eye, based on the ratio of 1mm to 3.00 Diopters.<sup>25</sup>

A second observation to suggest that emmetropization has an active component is the association of sustained near vision and myopia.<sup>26-27</sup> It is not uncommon to find the onset or increase in myopia associated with close visual tasks. Though this occurs later in life, college<sup>28</sup> or law students<sup>29</sup> are prime examples. Clinically, one sees this in individuals who spend a significant portion of the working or school day at computers. With the onset of early-in-life computer use, this near element may play a more substantial role.

Other support is found in animal studies, where the alteration of visual input correlates positively to refractive changes. Convex and concave lenses are placed in front of newborn chicks. Initially the convex lens converges light to form an image in front of the retina, and the concave lens image is situated behind the retina. The eye with the convex lens has now effectively been rendered myopic. In order for the animal to regain the plane of focus must move anteriorly. Effectively, the eye becomes shorter, and this is achieved by a reduction in the rate of growth. The eye with the concave lens has effectively been made hyperopic. Here conjugacy is achieved by the anterior-posterior length of the eye growing at a faster rate. The eyes of chicks and monkeys made functionally myopic with convex spectacle lenses or hyperopic with concave spectacle lenses thus alter their axial lengths to partially compensate for the effects of the lenses. This results in functionally hyperopic eyes growing longer and becoming myopic, and functionally myopic eyes growing less and becoming hyperopic.<sup>6,30-31</sup> Similarly, Irving, et al., fitted animals with +10.00

diopter lenses. After two weeks of wear the axial lengths were found to be  $0.15 \pm 0.25$ mm shorter, resulting in hyperopia of  $9.8 \pm 0.3$  diopters. Those eyes wearing -10.00 diopter lenses were found to have, on average,  $0.37 \pm 0.34$ mm longer posterior chambers resulting in myopia of  $9.7 \pm 0.8$  diopters.<sup>32</sup>

In an attempt to induce hyperopia, Troilo and Wallman reared chickens in the dark from birth to 4 weeks of age. The ocular structures were then evaluated. The resulting induced hyperopia was attributed to a flatter cornea and a shorter vitreous chamber as compared to a control group.<sup>5</sup> Recovery from this induced refractive error occurred within one week following removal of visual deterrents.<sup>6</sup> Appropriate timing appears to be critical for restoration of emmetropia.<sup>6,10,31,33-34</sup>

### Passive Process

The passive theory suggests that occurs as a result of physical and genetic determinants of normal eye growth. As the infant physically grows, the degree of initial myopia or hyperopia decreases. This is caused by the appropriate proportional interactive changes of the dioptric components and axial length. Thus, both myopic and hyperopic eyes gravitate towards emmetropia.<sup>3</sup> Sorby, et al., have described the natural alteration of ocular components to include axial lengthening in concert with lens and corneal power reduction.<sup>27</sup> It has been suggested that the development of high ametropia is the result of genetic inheritance of an abnormality in one of the variables, usually axial length.<sup>35,36</sup> This may be reflected in the amount of myopic offspring of myopic parents. If both parents are myopic, there is a 42% chance their child will become myopic. Whereas, there is only a 22.5% chance of the child becoming myopic if one parent is myopic. If neither parent is myopic, the child still has an 8% chance of becoming myopic.<sup>37</sup>

There are several supporters for the passive theory of emmetropization who provide suggestions to a mechanism for the process. Gernet and Olbrich<sup>38</sup> suggest emmetropization occurs primarily as a result of lenticular changes. Mark<sup>39</sup> and Sorby<sup>40</sup> have suggested that emmetropization occurs via changes in the anterior segment with alterations in the cornea, anterior chamber, and the lens. Myopic children have displayed a thinner crystalline

lens than expected which gives credence to a mechanical relationship between eye growth and lens compensation. This provides evidence of emmetropization being a non-visual feedback process.<sup>41</sup>

### Emmetropization and Related Structural Changes

Each structure from the anterior cornea to the posterior sclera may affect the process. The ocular dioptric components with the greatest potential for causing relatively large alterations of refractive error are corneal power, anterior chamber depth, crystalline lens power and vitreous chamber depth. In humans the ocular components with the greatest effect on dioptric power are corneal curvature, lens power, and vitreous chamber depth.<sup>42</sup> Anterior chamber depth has a lesser influence on the overall dioptric power of the human eye.<sup>43</sup> These studies would tend to refute some of the concepts proposed by Mark<sup>39</sup> and Sorby,<sup>40</sup> previously cited. In order to survey the effects of ocular components on the process of emmetropization one must keep in mind the subject used, i.e., specific animal or human.

Corneal changes appear to have a lesser influence and role on spherical emmetropization. In a chick study by Troilo and Wallman, the natural corneal flattening, which occurs by the second or third week of life, was interrupted. This resulted in the 4-week-old chicks having more myopia than would be expected. However, the authors found no statistically significant difference of refractive condition between the experimentally altered corneas than those of a control group. Of note was the vitreous change which preceded those of the anterior segment and continued after emmetropization. The authors concluded that although the corneal curvature is a major contributor of astigmatic emmetropization, it doesn't play a major role in spherical emmetropization.<sup>6</sup>

In chicks, the largest change toward emmetropization, whether from hyperopia or myopia, occurred in the first week under normal seeing conditions regardless of zero point. Troilo and Wallman<sup>6</sup> show that both myopic and hyperopic eyes which were initially larger than normal had vitreous chamber growth stopped in eyes compensating for myopia and continue in eyes compensating for hyperopia, regardless of the size of the eyes. The ces-

sation and the continuation of growth of the eyes occur in an attempt to reach emmetropia. They conclude that the refractive development of the eye is susceptible to alterations in the image plane and there is strong evidence that an active emmetropization mechanism exists and is vision dependent.<sup>6</sup>

Gernet and Olbrich suggest that emmetropization is primarily caused by decreased lenticular power. They suggest that since the larger eyes have a larger equatorial diameter, there is more tension on the zonular fibers. Those fibers are stretched and consequently flatten the lens and reduce the optical power.<sup>38</sup> In animals compensating for hyperopia, the lens has been shown to have a statistically significant increase in thickness (0.27mm)<sup>6</sup> during the emmetropization process. The increase in lens thickness did not account for the increase in anterior chamber depth, so it is suggested that there is also a posterior shift in the position of the lens to increase the anterior chamber depth.

The thickness of the choroidal may change during the emmetropization process resulting in a slight modifications of the vitreous chamber depths.<sup>44</sup> This enables the retina to make subtle modifications for small amounts of blur. In hyperopia, the choroid thins, moving the retina backward; and in myopia, the choroid thickens, pushing the retina forward. Compensation for lack of focus in chicks involves a change in the thickness of the choroid, followed by a change in the length of the eye, during which the choroid tends to revert to its original thickness.<sup>16</sup>

A critical factor in regulating axial elongation is control of the amount, and possibly the specific composition of the extracellular matrix. There is a hypothesis that the image clarity or defocus at the neuroretina leads to cellular and extracellular physiological changes that directly affect the rate of posterior segment growth and axial elongation in the adjacent sclera. In one study, eyes deprived of form vision early in the "juvenile" period became myopic, and had a thinner sclera and a reduced amount of collagen and proteoglycans than in control eyes.<sup>45</sup> Scleral shape change coupled with vitreous chamber lengthening or shorting helps to facilitate the process of emmetropization.

### Biochemical Effects

There is evidence of biochemical communication from the bipolar or amacrine cells in the retina through the retinal pigment epithelium (RPE) and choroid to the sclera by means of neurotransmitters or growth factors.<sup>44</sup> Here, enzyme levels may regulate the synthesis of the scleral extracellular matrix, and have a direct effect upon posterior chamber elongation. It is important to note that these signals may remain local within the eye and not involve the higher nerve centers of the visual system.

The retina may release neurotransmitters or growth factors in response to clarity. These neurotransmitters are thought to be released by the retinal amacrine cells and migrate to the choroid and sclera, where they take effect. Neurotransmitters in the emmetropization process have a major biochemical change effect associated with eye enlargement by increasing the amount of DNA, protein synthesis, and proteoglycan production in the cartilage of the sclera.<sup>46-47</sup>

Dopamine is found in the amacrine cells, and these cells may detect defocused retinal image. Apomorphine, a dopamine agonist, seems to have the effect of reducing the axial growth of the eye without an effect on the equatorial diameter.<sup>44</sup> Apomorphine, along with its metabolite, DOPAC, are found in reduced quantities in form-deprived myopes, allowing the eye to continue to elongate.<sup>48</sup> It appears that the amount of axial elongation is dependent upon the dosage of dopamine and its agonists.

Vasoactive Intestinal Peptide (VIP), a growth peptide, is found in a class of amacrine cells that comprises about 1% of the total amacrine cells.<sup>44</sup> It is felt that VIP immunoreactivity has an effect on the choroidal blood flow, thereby stimulating eye elongation. While dopamine quantities are low in form-deprived myopia, VIP is found in elevated levels.<sup>49</sup>

The sclera has the ability for regional or sector alterations in which a portion of it elongates while the remainder is unaltered. This phenomenon has been demonstrated experimentally in tree shrews and chickens by defocusing a portion of the retina. The sclera grows so that the part of the eyeball with the diffused image becomes myopic, while the part of the eye with a clear image remains emmetropic. This is thought to occur by direct retino-scleral biochemical communication.

Here local cellular activity is regulated by cellular glutamate.<sup>50</sup> In nature this is seen as the previously mentioned functional emmetropization. An example is the pigeon who has a myopic superior retina for looking down at the ground and emmetropic inferior retina to see what is straight ahead.

### Higher Level Control

Brain mediation of emmetropization was explored by Troilo and Wallman.<sup>5,6</sup> Various optic nerve sectioned and visual deprivation experimental paradigms were used. Initially, the optic nerve-severed eyes responded appropriately in moving from the induced refractive errors to emmetropia. However, they eventually overshot emmetropia, resulting in a reversal of the original refractive error.<sup>5</sup> The initially myopic eye become hyperopic compared to the contralateral control eye, and the initially hyperopic eye became myopic. They note that brain feedback cannot be ruled out since the eyes of chicks with severed optic nerves initially responded appropriately to the induced refractive errors. They conclude that emmetropization is more accurate with an intact optic nerve, meaning brain feedback may be essential for regulating emmetropization.

The effect of higher level accommodative control centers on emmetropization has been studied. Here the Edinger-Westphal nucleus, the accommodation functioning center, of chicks were severed. Even though the Edinger-Westphal nucleus was severed, emmetropization still occurred, but more slowly.<sup>5</sup> The authors conclude that accommodation is not a prerequisite for emmetropization, but still may have some role in regulating eye growth.

### Humans and Emmetropization

Studies have been conducted on children in an attempt to determine the process/trends in humans. Infants tend to have a wide range of refractive errors at birth which narrow with age to the smallest range at 6 years. Infants tend to have an average refractive error of +2.00 (+2.75) diopters,<sup>51-53</sup> which gradually approaches the adult emmetropia state (+1.00 diopters).<sup>54</sup> The neonatal group tends to have only 22%<sup>8</sup> emmetropic with the greatest change from ametropia to emmetropia occurring from 12-17 months of age. Overall, the total

emmetropization process occurs mostly during the first 4 to 5 years of life with both initial myopia and hyperopia converging on low hyperopia<sup>55</sup> and by 6 years, 80% of the children are found to be emmetropic.<sup>37</sup>

Woods, et al.,<sup>56</sup> have proposed the following longitudinal change in refractive errors of infants during the first year of life.

- 1) 2-12 weeks: Low myopic errors tend to show a low hyperopic shift similar to those who were hyperopic, and became more hyperopic. The most significant change of the spherical equivalent was the increase from near emmetropia to 2.6 diopters of hyperopia, observed in 75% of the infants in the 2-12 week (+/-2 weeks).
- 2) 12-26 weeks: A "non-significant myopic shift and decrease in the spread of the differences of the spherical equivalent." (p.553)
- 3) 26-36 weeks: "There are a greater number of infants (60%) showing a myopic shift than the infants (24%) showing a hypermetropic shift. This is coupled with a decrease in the spread of differences in the spherical equivalent." (p.553)
- 4) 36-52 weeks: The "shift is the net result of a larger decrease in hypermetropia for infants and the smaller increase in hypermetropia" in others. (p.553-4)

By the time of the last visit at 52 weeks, the distribution pattern of ametropia is similar to that in adults, taking into account the small hyperopic shift.

Most children are born with some hyperopia. Ingram and Barr<sup>57</sup> state that if the child is born with less than +2.50 diopters of hyperopia, the trend is for them to become emmetropic. Whereas, if the child is born with more than 2.50 diopters of hyperopia, the tendency is for them to become more hyperopic by the age of 3.5 years. One sample of nine children with hyperopia greater than 4.00 diopters at 6 months resulted in five who were in the expected range of refractive errors at 12 months.<sup>57</sup>

On average, for each diopter of hyperopia present during the first 6 months of life, the amount decreased by 0.06 diopters per month between the initial refraction and 12-17 months of age.<sup>7</sup> If significant levels of ametropia are maintained beyond the first year, they may signify a failure of the normal

emmetropization process and warrant spectacle correction to prevent amblyopia and reduce the risk of strabismus.<sup>7</sup>

There is a shift towards emmetropia by 6 months of age for children with an initial myopic spherical equivalent. On average this group does not reach the same level of hyperopia as those with an initial hyperopic spherical equivalent. Infants with the most myopia also later retained the most myopia. However, after 5 years of age, the refractive status tends to return to the original level of myopia. Therefore, it might be possible to predict refractive status in older children based on the earliest manifest refraction, with one year being optimal.<sup>4</sup>

At birth, the average amount of astigmatism is predicted to be 2.98 diopters, decreasing to 1.00 diopter by 129-256 weeks (2.5-5 years of age).<sup>58</sup> The initial amount of astigmatism may increase slightly to a peak value at 2-3 months and then begin the emmetropization process. Infants tend to lose 1/3 of their spherical equivalent ametropia and 2/3 of the astigmatism during the first two years of life. The cornea continues to flatten during normal eye growth, and this process is almost complete by 2 years of age. Refractive astigmatism also stabilizes around the age of 2 years, indicating that most of it is from corneal curvature.<sup>3</sup> Significant meridional emmetropization has been shown for both "with" and "against" the rule astigmatism.<sup>4</sup> If the astigmatism increases, there is a 7% chance of a resultant amblyopia, though in one study, 90% of the children had a reduction in astigmatism.<sup>59</sup> However, this has not been shown for all races.<sup>60</sup>

The initial amount and the onset of the astigmatism may help determine whether it is likely to undergo emmetropization. Astigmatism that is  $\geq 2.50$  Diopters has an equal chance of increasing or decreasing over time.<sup>61</sup> Astigmatism present prior to 6 months of age is most likely to disappear by 1 year of age.<sup>57</sup> However, astigmatism present in the second six months of life is more likely to persist with values of 1.50 diopters at 12 months and has been shown to be a risk factor for amblyopia.<sup>57</sup>

The orientation of the astigmatism may also play a role in the magnitude of the spherical equivalent. "With"-the-rule astigmatism tends to be associated with a proportionally greater change toward emmetropia. "Against"-the-rule astigma-

tism tends to be associated with a higher value of ametropia with a lesser shift towards emmetropia. It is also a risk factor for becoming myopic at an earlier age than those having "with"-the-rule astigmatism or no astigmatism.<sup>57</sup>

Abrahamsson and Sjostrand feel that anisometropia during the normal growth period of the eye is common. Low amounts of anisometropia ( $\geq 2.50$  diopters) typically can arise and vanish throughout the normal growth process with substantial amounts ( $> 5.00$  diopters) possibly vanishing during this growth period.<sup>62</sup> They further state that children who display 3.00 diopters or more of anisometropia at one year of age will have a 90% chance of retaining it at the age of 10, and 60% of this group will be at risk to develop amblyopia.<sup>62</sup> Anisometropia of  $> 5.00$  diopters seems to be the limit beyond which the emmetropization cannot occur during early childhood. More than 5.00 diopters may induce too much blur on the retina, causing amblyopia since the emmetropization regulatory components are inefficient.<sup>62</sup> In some instances, the anisometropia of an apparently non-strabismic adult may be the result of a juvenile microtopia in which the anisometropia is the result of a gradual lack of emmetropization.<sup>63</sup>

Some studies<sup>62,65</sup> have shown that only 25%-30% of those who have anisometropia at 1 year, retain it by 4 years of age. This shows that the most pronounced change in anisometropia occurs during the first four years of life. And those infants who do not reduce or emmetropize their astigmatism or anisometropia by 3 years of age are at risk for amblyopia. Anisometropia  $> 3.00$  diopters at 1 year of age leads to a lasting anisometropia in the majority of cases.

The relationships of accommodation, convergent strabismus and emmetropization has been investigated. Ingram, et al., tracked 6-month-olds for a period of three years. They conclude that children who eventually present with an esotropia or a microtopia were less likely to have a spontaneous reduction of hyperopia and were more likely to have accommodative problems. These results are compared to a control group that didn't develop a deviation. Both fixing and non-fixing eyes demonstrated accommodative abnormalities, and the authors question whether the underlying defect was congenital or re-

lated to an acquired form deprivation which preceded the turn.<sup>66</sup>

Children born to families with strabismic risk factors were routinely examined from 3 months to 4 years by Aurell and Norrsell.<sup>67</sup> They note the most marked amount of emmetropization occurred within the first two years of life. Children with 4 diopters of hyperopia at 6 months of life who became strabismic did not emmetropize while those who did were aligned. Abrahamsson, et al.,<sup>68</sup> noted an increase in hyperopia in the deviating eye subsequent to the development of a squint. The increase in anisometropia has been linked to the emmetropization of the fixing eye. This phenomenon didn't occur in exotropes who displayed a more stable equal refraction. Though his sample was of older children, Rutstein, et al., concludes that the use of excessive concave lens prescription to lessen exotropia didn't significantly alter their baseline refraction.<sup>69</sup>

### Corrective Lenses

Studies on children prescribed spectacle lenses shows that emmetropization occurs more rapidly and more completely in those children who do not wear their prescription full time. Hyperopia in very young children appears to be maintained if fully corrected and the glasses worn.<sup>61,70</sup> Therefore, hyperopes may benefit from a partial correction, since a full prescription may reduce the degree of emmetropization.<sup>71,72</sup>

Using less than full correction to promote emmetropization does not imply poor visual acuity for myopes or hyperopes as long as most visual demands are kept between the near- and far-points.<sup>73</sup> And, when making prescribing decisions in infants, the optometrist should determine the rate reduction that is occurring before deciding on a spectacle correction in infants.<sup>4</sup> Thus it is prudent to conduct several time-spaced visits.<sup>59,74</sup> In addition, there should be considerations of age, refractive error, visual acuity, binocularity, and risk factors in determining the need for a prescription.<sup>69</sup>

### Conclusion

Emmetropization appears to have an active and a passive component. The exact nature of the process has been investigated by many well qualified investigators who are making significant progress toward understanding the mechanism. Besides animal studies, there have

been a number of enlightening human longitudinal and cross sectional studies and more of these are needed. Pediatric optometric practitioners need to stay informed of current emmetropization concepts and to translate them into patient care. By doing so we can provide our little patients with the optimal conditions for their visual development.

### References

1. Grosvenor T. Primary Care Optometry, Butterworth-Heinemann. Boston. 1996;17.
2. Zadnik K, Mutti Do. Incidence and distribution of refractive anomalies. In Borish's Clinical Refraction. Benjamin WJ ed. WB Saunders. Philadelphia. 1998;30-46.
3. Ehrlich D, Braddick O, Atkinson J, Anker S, Weeks F, Hartley T, Wade J, Rudenski A. Infant emmetropization: Longitudinal changes in refraction components from nine to twenty months of age. *Opt Vis Sci.* 1997;74:822-843.
4. Ehrlich DL, Atkinson J, Braddick O, Bobier W, Durden K. Reduction of infant myopia: a longitudinal cycloplegic study. *Vision Res.* 1995;35:113-124.
5. Troilo D. Neonatal eye growth and emmetropization—a literature review. *Eye* 1992;6:154-160.
6. Troilo D, Wallman J. The regulation of eye growth and refractive state: an experimental study of emmetropization. *Vision Res.* 1991;31:1237-1250.
7. Saunders, KJ, Woodhouse JM, Westall CA. Emmetropisation in human infancy: rate of change is related to initial refractive error. *Vision Res.* 1995;35:1325-1328.
8. Wiesel TN, Raviola E. Myopia and eye enlargement after neonatal lid fusion in monkeys. *Nature.* 1977;266:66-68.
9. Ingram RM, Gill LE, Goldacre MJ. Emmetropisation and accommodation in hypermetropic children before they show signs of squint: a preliminary analysis. *Bulletin de la Societe Belge d Ophthalmologie* 1994;253:41-56.
10. Norton TT, Siegart JT Jr. Animal models of emmetropization: matching axial length to focal plane. *JAOA.* 1995;66:405-414.
11. Calossi A. Increase of ocular axial length in infantile traumatic cataract. *Optom & Vis Sci.* 1994;7:386-91.
12. Lorenz B, Worle J, Friedl N, Hasenfrantz G. Ocular growth in infant aphakia, *Ophthalmic Pediatrics and Genetics.* 1993;14:177-188.
13. Toulemont PJ, Urvoy M, Coscas G, Lecallonnec A, Cuvilliers AF. Association of congenital microcoria with myopia and glaucoma. *Ophthalmol.* 1995;102:193-197.
14. M, Fabian G, Sjostrand J. Refraction changes in children developing convergent or divergent strabismus. *British J Ophthalmol.* 1992;76:723-727.
15. Evans NM, Fielder AR, Majer DL. Ametropia in congenital cone deficiency – achromatopsia: a defect of emmetropisation. *Cli Vis Sci.* 1989;4:129-136.
16. Daw NJ. Visual Development. Plenum Press. New York. 1995:193-200.
- 17.

18. Hoyt CS, Stone RD, Fromer C, Billson FA. Monocular axial myopia associated with neonatal eyelid closure in human infant. *Am J Ophthalmol.* 1981;91:197-200.
19. O'Leary DJ, Millodot M. Eyelid closure causes myopia in humans. *Experientia.* 1979;35:1478-1479.
20. Robb RM. Refractive errors associated with hemangiomas of the eyelids and orbit in infancy. *Am J Ophthalmol.* 1977;83:52-58.
21. Miller-Meeks MJ, Bennett SR, Keech RV, Blodi CF. Myopia induced by vitreous hemorrhage. *Am J Ophthalmol.* 1990;109:199-203.
22. Lue C-L, Hansen RM, Reisner DS, Findl O, Petersen RA, Fulton AB. The course of myopia in children with mild retinopathy of prematurity. *Vis Res.* 1995;35:1329-1335.
23. Fledelius HC. Pre-term delivery and subsequent ocular development. *Acta Ophthalmol Scand.* 1996;74:301-305.
24. Johnson CA, Post RB, Chalupa LM, Lee TJ. Monocular deprivation in humans: a study of identical twins. *Invest Ophthalmol Vis sci.* 1982;23:135-138.
25. Borish IM. Clinical Refraction. 3<sup>rd</sup> ed. Chicago. Professional Press. 1970:505.
26. Ong E, Ciuffreda KJ. Accommodation Nearwork and Myopia. *Optometric Extension Program.* Santa Ana, CA 1997.
27. Goss DA, Wickham MG. Retinal-image mediated ocular growth as a mechanism for juvenile onset myopia and for emmetropization: A literature review. *Documenta Ophthalmologica.* 1995;90:341-375.
28. Baldwin WR, Adams AJ, Flattau. Young adult myopia. In *Refractive anomalies.* Grosvenor T, Flom MC. Eds. Butterworth-Heinemann. Boston. 1991;104-120.
29. Zadnik KS, Mutti DO. Refractive error changes in law students. *Am J Optom Physiol Opt* 1987.
30. Smith EL. Spectacle lenses and emmetropization: the role of optical defocus in regulating ocular development. *Optom Vis Sci.* 1998;75:388-398.
31. Smith EL, Hung LF, Harwerth RS. Effects of optically induced blur on the refractive status of young monkeys. *Vision Res.* 1994;34:293-301.
32. Irving EL, Callender MG, Sivak JG. Inducing myopia, hyperopia, and astigmatism in chicks. *Optom Vis Sci.* 1991;68:364-368.
33. Napper GA, Brennan NA, Barrington M, Squires MA, Vessey GA, Vingrys AJ. The duration of normal visual exposure necessary to prevent form deprivation myopia in chicks. *Vision Res.* 1995;35:1337-1344.
34. Wallman J, Adams JI. Developmental aspects of experimental myopia in chicks: susceptibility, recovery and relation to emmetropization. *Vision Res.* 1987;27:1139-1163.
35. Sorby A, Leary GA, Richards MJ. Correlation ametropia and component ametropia. *Vision Res.* 1961;2:309-313.
36. Carrol JP. On emmetropization. *J Theor Biol.* 1982;95:135-144.
37. Gwiadzda J, Thorn F, Bauer J, Held R. Emmetropization and the progression of manifest refraction in children followed from infancy to puberty. *Clin Vision Sci* 1993;8:337-344.
38. Gernet H, Oblrich. Excess of the human refraction curve. In Gitter KA, Deeney AH, Sarin LK,

- Meyer D eds. *Ophthalmic Ultrasound*. St. Louis, C.V. Mosby. 1969:42-148.
39. Mark HH. Emmetropisation: physical aspects of a statistical phenomenon. *Ann Ophthalmol* 1972;4:393-401.
  40. Sorby A. Biology of the eye as an optical system. In Duane TD ed. *Clinical Ophthalmology*. Philadelphia. Harper & Row 1979;1-17.
  41. Zadnick K, Mutti DO, Fusaro RE, Adams AJ. Longitudinal evidence of crystalline lens thinning in children. *Invest Ophthalmol Vis Sci*. 1995;36:1581-1587.
  42. Erickson P. Optical components contributing to refractive anomalies. In Grosvenor T, Flom MC eds. *Refractive Anomalies: Research and Clinical Applications*. Boston. Butterworth-Heinemann. 1991:199-218.
  43. Goss DA, Erickson P. Effects of changes in anterior chamber depth on refractive error of the human eye. *Clin Vis Sci*. 1990;197-201.
  44. Daw NW. *Visual Development*, Plenum Press. New York. 1995;193-200.
  45. Kang RN, Norton TT. Alterations of scleral morphology in tree shrews with induced myopia. *Invest Ophthalmol Vis Sci*. 1993;34:1209 (abstract 2482).
  46. Christensen AM, Wallman J. Evidence that increased scleral growth underlies visual deprivation myopia in chicks. *Invest Ophthalmol Vis Sci*. 1991;32:2143-2150.
  47. Rada JA, Thoft RA, Hassell JR. Increased aggrecan (cartilage proteoglycan) production in the sclera of myopic chick. *Dev Biol*, 1991;147:303-312.
  48. Stone RA, Lin T, Laties AM, Iuvone PM. Retinal dopamine and form-deprivation myopia. *Proc Natl Acad Sci USA*. 1989;86:704-706.
  49. Stone RA, Laties AM, Raviola E, Wiesel TN. Increase in retinal vasoactive intestinal peptide after eye lid fusion in primates. *Proc Natl Acad Sci USA*. 1988;85:257-260.
  50. Wallman J. Retinal factors in myopia and emmetropization: Clues from research on chicks. In Grosvenor T, Flom MC. eds. *Refractive Anomalies*. Boston, MA. Butterworth-Heinemann. 1991:270-280.
  51. Hirsch MJ, Weymouth FW. Prevalence of refractive anomalies. In Grosvenor T, Flom MC. eds. *Refractive Anomalies*. Boston, MA. Butterworth-Heinemann. 1991:15-38.
  52. Banks MS. Infant refraction and accommodation. *International Ophthalmology Clinics*. 1980;20:205-232.
  53. Sorby A, Benjamin B, Sheridan M, Leary GA. Refraction and its components during growth of the eye from the age of three. *Medical Research Council Special Report Series No. 301*. London:HMSO. 1961.
  54. Saunders KJ, Woodhouse JM, Westall CA. Emmetropisation in human infancy: rate of change is related to initial refractive error. *Vision Res*. 1995;35:1325-1328.
  55. Lam SR, LaRoche GR, De Becker I, Macpherson H. The range and variability of Ophthalmological parameters in normal children aged 4.5 to 5.5 years. *J Pediatr Ophthalmol Strab*. 1996;33:251-256.
  56. Wood ICJ, Hodi S, Morgon L. Longitudinal change of refractive error in infants during the first year of life. *Eye*. 1995;9:551-557.
  57. Ingram RM, Barr A. Changes in refraction between the ages of 1 and 3.5 years. *Br J Ophthalmol*. 1979;63:339-342.
  58. Mohindra I, Held R. Refraction in humans from birth to five years. *Doc Ophthalmol Proc Series* 1981;28:19-27.
  59. Abrahamsson M, Fabian G, Anderson AK, Sjostrand J. A longitudinal study of a population based sample of astigmatic children I. Refraction and amblyopia. *Acta Ophthalmologica*. 1990;68:428-434.
  60. Maples WC, Herrmann M, Hughes J. Corneal astigmatism in preschool Native Americans. *J Amer Optom Assoc*. 1997;68:87-94.
  61. Ingram RM, Arnold PE, Dally S, Lucas J. Emmetropisation, squint, and reduced visual acuity after treatment. *BR J Ophthalmol*. 1991;75:414-416.
  62. Abrahamsson M, Sjostrand J. Natural history of infantile anisometropia. *Br J Ophthalmol*. 1996;80:860-863.
  63. Almeder L, Peck L, Howland H. Prevalence of anisometropia in volunteer laboratory and school screening population. *Invest Ophthalmol Vis Sci*. 1990;31:2448-2455.
  64. Birch E, Stager D, Everett M. Natural history of infantile anisometropia. *Invest Ophthalmol Vis Sci*. 1995;suppl36:s45.
  65. Abrahamsson M, Fabian G, Sjostrand J. A longitudinal study of a population based sample of astigmatic children. II. The changeability of anisometropia. *Acta Ophthalmol Copenh*. 1990;68:435-440.
  66. Ingram RM, Gill LE, Goldacre MJ. Emmetropisation and accommodation in hypermetropic children before they show signs of squint—a preliminary analysis. *Bulletin de la Societe Belge d' Ophthalmologie*. 1994;253:41-56.
  67. Aurell E, Norrsell K. The longitudinal study of children with a family history of strabismus: factors determining the incidence of strabismus. *Br J Ophthalmol*. 1990;74:589-594.
  68. Abrahamsson M, Fabian G, Sjostrand J. Refraction changes in children developing convergent of divergent strabismus. *Br J Ophthalmol*. 1992;76:487-491.
  69. Rutstein RP, Marsh-Tootle W, London R. Changes in refractive error for exotropes treated with overminus lenses. *Opt Vis Sci*. 1989;66:487-491.
  70. Dobson V, Sebris SL, Carlson MR. Do glasses prevent emmetropisation? *Invest Ophthalmol Vis Sci* 1986;27(ARVO suppl):2.
  71. Jennings JAM. In *Visual problems in childhood*. Buckingham T. (ed). Boston. Butterworth-Heinemann. 1993. 130.
  72. Hung L, Crawford M, Smith EL. Spectical lenses alter eye growth and the refractive status of young monkeys. *Nature Medicine*. 1995;1:761-765.
  73. Medina A, Fariza E. Emmetropization as a first order feedback system. *Vision Res*. 1993;33:21-26.
  74. Ciner EB. Management of refractive error in infants, toddlers, and preschool children. In: *Problems in optometry*. ed: Schmeim M. 1990;2:394-419.

Corresponding author:

Kristie Yackle, O.D.  
5455 East Garick Drive  
Anaheim, CA 92807

Date accepted for publication:  
November 6, 1998