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Environmental Factors and Progressive Myopia: A Global Health Problem

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Abstract

Myopia, or nearsightedness, is a refractive error whose prevalence has increased over the past three decades, leading to a growing concern and interest among both the public and scientific communities. For years, the only explanation and basis for myopia has been genetic factors. However, the genetic model does not explain the dramatic increase in prevalence. Current research suggests that the increase is also due to environmental factors, such as fewer hours of outdoor activities, early educational pressures requiring intense close work, as well as a lack of exposure to sunlight. One study compared the prevalence and risk factors for myopia in 6 and 7-year old children of Chinese ethnicity in Sydney and Singapore. In another study, a diffuser was placed over the eyes of chicks which caused the eyes to grow excessively myopic. This increased myopia was due to the lack of dopamine which originates from cells in the eye when stimulated by sunlight. One additional study suggested that formula milk, unlike breast milk, lacks DHA and can also result in myopia. The results of these studies suggest that progressive myopia is due not only to hereditary factors but also due to environmental factors. Recognition of these factors may be useful in developing future treatments.

Introduction

Nearsightedness, or myopia, as it is medically termed, is a vision condition in which close objects are seen clearly, but objects farther away appear blurred. Myopia generally occurs when the eyeball becomes elongated, or when the cornea, the clear front cover of the eye, has increased curvature. In myopia, light entering the eye does not focus directly on the retina rather in front of the retina, hence distant objects appear blurred. The more elongated the eye, the greater the myopia.

Myopia is a common refractive condition affecting approximately 100 million people in the United States (Vitale, et al., 2009). Its prevalence has increased over the past three decades, leading to a growing concern and interest in both the public and scientific communities. Myopia today is emerging as a global health problem, not only because of the costs associated with correcting refractive errors, but also because of the pathology associated with higher levels of myopia, such as retinal tears, retinal detachments, and macular degeneration. The prevalence of myopia varies in different parts of the world. Generally speaking, myopia is much more prevalent in industrialized countries and cities compared to rural areas (Uzma, et al., 2009). In 2009, a study showed that the prevalence of myopia in the United States, for people between the ages of 12 and 54, surged from 25% in the early 1970's to 42% by 2000. In Taiwan and Singapore, myopia is found in approximately 30% of all children 6 and 7 years old, and increases to 80% in young adults (Saw, et al., 2002). The rapid increase in the prevalence of myopia strongly suggests that environmental factors are having a considerable influence on the development of myopia not explainable by the genetic model. The cause of myopia has been debated for decades, and the exact mechanism responsible for the development of progressive myopia still remains unclear. There is significant evidence that many people inherit nearsightedness, or at least the tendency to develop nearsightedness. If one or both parents are nearsighted, there is an increased likelihood that their children will be nearsighted (Kurtz, et al., 2007). However, heredity alone does not explain why today there is such a dramatic increase in myopia. The dramatic increase in nearsightedness strongly suggests that, on top of the genetic model, environmental factors must be having a considerable influence on the development of myopia. Numerous studies support this hypothesis. This paper will review some of the recent research that supports the theory that environmental factors are contributing to the increase in progressive myopia, and will briefly review some of the solutions that may help slow down this progression.

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Discussion

A study carried out by Rose et al. (2008), showed differences in the prevalence of myopia in 6 and 7-year old children of Chinese ethnicity living in Sydney Australia vs. those living in Singapore. The study discovered that the prevalence of myopia was much greater for children living in Singapore (29.1%) than similarly aged children living in Sydney (3.3%). The range of spherical equivalents was −6.70 to +4.85 diopters for Singapore vs. −2.88 to +3.50 diopters for Sidney. The mean spherical equivalent was −0.16 diopters for the former vs. + 0.86 diopters for the latter. Consistent with these differences in refraction, the axial lengths and anterior chamber depths, two additional markers of myopia, were also significantly greater in Chinese children living in Singapore vs. those living in Sydney (Table 1). (Rose, et al. 2008)

Certainly, one factor that could possibly contribute to these large differences is parental myopia, which when present, has always been associated with a greater likelihood of myopia developing in children (Mutti, et al., 2002). However, in this study, there were no differences in the proportion of children with 0, 1, or 2 myopic parents between the two cities. In the Sydney sample, 32% of children had no parents with myopia, 43% had one myopic parent, and 25% had two myopic parents. This is comparable to the Singapore sample where there were 29% with no myopic parents, 43% with one myopic parent, and 28% with two myopic parents. The genetic differences related to myopia in the two populations is not significant, hence environmental factors must be playing a role.

Lifestyle factors that could possibly be contributing to the differences are outlined in Table 2. The children of Chinese origin living in Sydney actually read slightly more books, spent more time reading, writing, using computers outside of school, and watched less television than did the Chinese children living in Singapore. The cumulative measure of near-work activity was greater in the Sidney children

Table 1. Distribution of Refractive Error and Ocular Biometry Values in the Right Eyes of Children of Chinese Origin Living in Singapore and Sydney

	Sydney		Singapore		
	Children, No. (n=124)	Mean (SD)[a]	Children, No. (n=628)	Mean (SD)[a]	*P* Value
Female sex, %		53.2		50.3	.60
Myopia (spherical equivalent of ≤−0.5 D), %		3.3		29.1	<.001
Age, y	124	6.41 (0.35)	628	7.16 (0.39)	<.001
Spherical equivalent refraction, D	124	0.86 (0.78)	628	−0.16 (1.43)	<.001
Axial length, mm	123	22.60 (0.67)	613	23.13 (0.90)	<.001
Anterior chamber depth, mm	124	3.27 (0.22)	613	3.58 (0.27)	<.001
Corneal radius of curvature, mm	124	7.87 (0.25)	626	7.73 (0.25)	<.001
Axial length to corneal radius ratio	123	2.87 (0.07)	611	2.99 (0.10)	<.001

Abbreviation: D, diopter.
[a] Except where noted otherwise.

Table 2. Myopia Risk Factors in Children of Chinese Origin Living in Singapore and Sydney

	Sydney		Singapore		
Activity Outside School	Children, No. (n=124)	Mean (SD)	Children, No. (n=628)	Mean (SD)	*P* Value
Books read, No./wk	119	4.44 (2.46)	628	2.39 (2.27)	<.001
Reading and writing, h/wk	109	20.81 (13.88)	611	17.76 (8.78)	.03
Computer use, including computer games, h/wk	108	4.65 (6.62)	625	3.55 (4.48)	.10
Total near-work activity, h/wk[a]	106	29.93 (20.09)	608	23.54 (11.84)	.002
Coaching classes, h/wk	118	1.21 (1.75)	622	1.74 (2.02)	.007
Television viewing, h/wk	113	11.32 (6.47)	627	12.65 (7.37)	.07
Outdoor activities and sports, h/wk	102	13.75 (1.02)	586	3.05 (0.12)	<.001

[a] Includes reading, writing, computer use, crafts, and playing musical instruments.

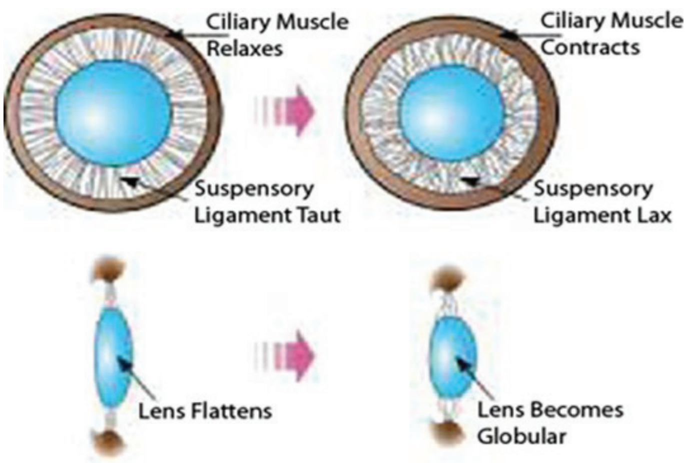
vs. the Singapore children, but the differences were small in magnitude, not statistically significant, and do not account for the increased myopia in the Singapore children. The largest statistically significant difference observed was that Chinese children living in Sydney spent nearly 14 hours per week in outdoor activities compared with just over 3 hours per week in Singapore. (Rose, et al., 2008) The authors offered two theories as to why the greater time spent outdoor by the children from Sydney may have resulted in less myopia. The first theory is that when outdoors, children require less accommodation in their vision, since their focus is not on near objects. Viewing near objects such as reading requires an accommodative response from within the eye. Viewing distant objects does not require a similar response. The second theory is that outdoor activity results in more exposure to brighter sunlight, which stimulates the release of dopamine, a known growth inhibitor within the retina.

Accomodation

The first explanation to account for the differences between the Singapore and Sydney children is related to the different styles of education within the two countries. In Singapore, most students are enrolled in a structured 3-year preschool program, with the aim of ensuring that children read fluently by the time they start school. In Sydney, most children attend a one year part-time preschool program, which is largely concerned with social development. This is followed by enrollment in a full-time kindergarten year before 1st grade, again with an emphasis on social development (Singapore Ministry of Education, 2004). Differences in the educational intensity at such an early stage can certainly have an impact on the early appearance of myopia in Singapore. The higher levels of myopia in Singapore is a result from Singapore's competitive and academically oriented schooling system, where there is an emphasis on educational achievements (Saw, et al., 2007). Continuous close work requires increased accommodation which can start the children in Singapore on a trajectory toward developing myopia from a very early age.

Why does intense education and competitive educational achievement increase the prevalence of myopia in Singapore? When one views distant images, parallel rays of light enter the eye and converge at a focal point on the retina. However, when viewing objects from near, instead of parallel rays entering the eye, the rays are diverging. The diverging rays activate an internal ocular mechanism called accommodation, which stimulates the circular ciliary muscles causing the lenses to change their curvature to a more convex shape (Figure 1). This change in curvature allows the diverging rays to now focus on the retina. The authors postulated that the constant contracting and relaxing of the ciliary muscles will eventually result in an increase in the axial length and a greater depth of the anterior chamber.

Figure 1: Accommodation (Elkington et al., 1999)



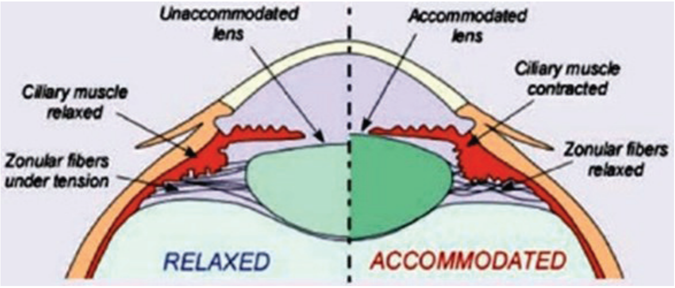
A more in depth understanding of the mechanism of accommodation will show how accommodative stress can result in axial elongation. Since small or near objects are typically focused at a further distance because of their diverging light rays, the eye accommodates by assuming a lens shape that has a shorter focal length. This reduction in focal length will cause more refraction of light and serve to focus the images on the retinal surface.

For near objects, the circular ciliary muscles contracts, allowing the lenses to assume a more convex shape. The increase in the lens curvature corresponds to a shorter focal length. On the other hand, a distant object is typically focused at a closer distance because the light rays entering the eye are parallel rays. The eye accommodates these parallel rays by assuming a lens shape that has a longer focal length. Hence, for distant objects the ciliary muscles relax and the lens returns to a flatter shape. This decrease

in the curvature of the lens corresponds to a longer focal length.

As outlined in Figure 2, the ciliary muscles adjust the shape of the lens since the muscles are attached to the zonules of Zinn, which in turn are attached to the lenses. Contraction of the ciliary muscles slackens the zonules, so that they do not pull as much on the lenses. The lenses become rounder, and the eyes can now focus on near objects. When the ciliary muscles relax, the zonules pull the edges of the lenses so that they become flatter and thinner to accommodate viewing distant objects.

Figure 2: Accommodation Mechanism (Dortonne, 2011)



The intense contraction of the ciliary muscle is believed to be the basis for the abnormal elongation of the myopic eye. The constant focusing on near objects causes a spasm of the ciliary muscle, and traction on the sclera, to which the ciliary muscle is attached on its external side. As the muscle contracts and pulls on the sclera, it compresses and increases the pressure within the vitreous cavity or larger chamber of the eye. Over time, with continuous contraction on the outer sclera, the sclera stretches and elongates, resulting in an enlarged eye. The body produces more aqueous liquid to fill the increased aqueous and vitreous cavity volumes. This increased elongation of the eye results in a progressive myopic state.

This explains why in Singapore the prevalence of myopia is higher. Since there is a greater amount of continuous intense accommodative stress at a younger age, involving reading, continuous computer viewing and other intense close visual work, the Singapore children may be more likely to develop nearsightedness. The assumption is that the continuous and intense accommodative mechanism of contracting and relaxing at a young age when the eye is in its formative years of growth is responsible for axial length elongation. The constant viewing of objects at 16-26 inches causes the focusing system to contract and get stuck at the near reading distance, thus stimulating the ciliary muscle leading to eye elongation and myopia.

Additional evidence supporting this hypothesis comes from Dr. Roger Zylberman, from the department of Ophthalmology at Shaare Zedek Medical Center, Jerusalem, Israel (Zylbermann, et al., 1993). He examined Jewish teenagers attending school in Jerusalem. He took 870 students: 175 males and 224 females from general schools, and 193 males and 278 females from Orthodox schools. The students' ages ranged from 14 to 18 years, as outlined in Table 3 (Zylbermann, et al., 1993) .

The distribution of the degree of myopia among the teenage students in Zylberman's study is outlined in Table 4. The prevalence of myopia was 31.7% in females attending general schools, and 36.2% in females from Orthodox schools. However, it was 27.4% in males from gen-

Table 3. Age Distribution of Subjects

	Female, No. [%]		Male, No. [%]		
Age (Years)	General Schools	Orthodox Schools	General Schools	Orthodox schools	Total
14	40 (17.9)	64 (23.0)	56 (32.0)	43 (22.3)	203 (23.3)
15	61 (27.2)	61 (21.9)	45 (25.7)	37 (19.2)	204 (23.4)
16	42 (18.8)	46 (16.5)	22 (12.6)	37 (19.2)	147 (16.9)
17	39 (17.4)	57 (20.5)	24 (13.7)	30 (15.5)	150 (17.2)
18	42 (18.8)	50 (18.0)	28 (16.0)	46 (23.8)	166 (19.1)
Total	224 (25.7)	278 (32.0)	175 (20.1)	193 (22.2)	870 (100.0)

eral schools, and 81.3% in males attending Orthodox schools. The difference in the prevalence of myopia between Orthodox males and all the other groups was statistically significant Table 4 (Zylbermann, et al., 1993) . release of dopamine from the retina, which is known to act as an eye growth inhibitor (Stone, et al., 1989).

Dopamine is a neurotransmitter that plays a number of important roles in the brains and bodies of animals.

Table 4. Distribution of the Degree of Myopia

Diopters Needed to correct Myopia	% of Females		% of Males	
	General Schools	Orthodox Schools	General Schools	Orthodox Schools
- 0.50 to - 1.75	36.6	36.8	58.3	22.9
- 2.00 to - 3.75	38.0	41.9	31.3	33.8
- 4.00 to - 5.75	18.3	17.1	6.3	22.9
≥ - 6.00	7.0	4.3	4.2	20.4
Total Myopes	31.7	36.2	27.4	81.3

In the brain, dopamine functions as a neurotransmitter, a chemical released by nerve cells to send signals to other cells in the brain. Outside the nervous system, dopamine functions in several parts of the body as a local chemical transmitter. It has a paracrine function, which means it is synthesized locally and it affects cells near the cells that release it. For example, in blood vessels it's a vasodilator. In kidneys, it increases sodium excretion and urine output. In the pancreas it reduces insulin production. In the digestive system it reduces gastrointestinal motility, and in the immune system it reduces lymphocyte activity.

In the eye, dopamine is released by a set of amacrine cells which then activate D1 and D2 dopamine receptors distributed throughout the retina (Rohrer, 1993). Dopamine plays a role in light adaptation. A reduction in retinal dopamine is known to occur in parkinsonian patients, resulting in reduced contrast sensitivity. Dopamine is also essential for eye cell survival, and for controlling normal eye growth (Witkovsky, 2004).

A study from the Australian National University showed that increased dopamine release, resulting from light exposure, stimulates D2 receptors within the eyes of chickens, resulting in suppression of axial elongation, or eye growth (McCarthy, et al., 2007).

The study was conducted as follows. When the eyelids of young chicks were sutured or when diffusers were put on the eyes of the young chickens, there was axi-

The authors explained that the reason the incidence of myopia was much higher in Orthodox Jewish males, was due to differences in their education systems. The curriculum and study methods in the Orthodox schools are distinctly different from secular schools. A moderate amount of accommodative eye use is required of male and female students in general schools, and of female students in Orthodox schools. Males in Orthodox schools, however, differed from all three other groups by their uncommon study habits characterized by sustained near vision, and frequent changes in accommodation due to their habitual swaying while studying. The rocking habit, by its constant defocusing and refocusing action, the variety of print size, and the need for accurate accommodation when reading the very tiny print in the Talmud, all require more intense accommodation. Overall, there is a very heavy accommodative stress in the young Orthodox males. The high degree and increased prevalence of myopia observed in the Orthodox male group is presumed to be due to their heavy accommodative needs, resulting from their unusual study habits. The higher accommodative needs of Singapore youth, could account as well for their increased myopia.

Sunlight Effect

The second explanation for the differences in myopia between Singapore and Sydney children, in regard to time outdoors, is related to sunlight exposure. Brighter light may reduce the development of myopia through the

al elongation of the eyes, resulting in form deprivation myopia. However, if during the day the diffusers were removed for short periods, allowing normal exposure to light, the young chicks did not develop elongation and myopia. The authors concluded that light deprivation resulted in myopia because of a decrease in retinal dopamine. The authors proved that by suturing the eyelids or using diffusers on the young chicks there was impaired contrast sensitivity. This led to decreased dopamine release, decreased D2 dopamine receptor stimulation and finally increased eye growth.

In a second experiment when the diffuser was not removed, injecting dopamine during total darkness also prevented myopia in the young chicks. And finally when the authors injected a dopamine antagonist before removing the eye diffuser, there was again increased myopia, even though the eyes were exposed to light, since the dopamine stimulation of the D2 receptor was now blocked (Boelen, et al., 1994).

To further support his hypothesis, McCarthy citied a similar study that showed that by removing the diffuser for three hours there was an increase in measurable dopamine and less myopia in young chicks (Napper, et al., 1995).

We see from these studies that normal vision and the prevention of myopia are related to the stimulation of dopamine release and activation of D2 dopamine receptors. Since dopamine is necessary to maintain normal eye growth and prevent myopia, we can now explain why the children in Sydney who were exposed to more sunlight had less myopia, since their dopamine levels were higher than the Singapore children who spent most of their time indoors.

Breastfed Children

A third theory as to why Singapore children are more myopic has been advanced. This theory is based on a retrospective study from Singapore, which showed that breastfed children were 50% less likely to be nearsighted (Chong, et al., 2005, Williams, et al., 2001).

They studied 797 children, aged 10 to 12 as part of the Singapore Cohort Study of the Risk Factors of Myopia. There was no significant difference with the participants as regards to sex, age, or race. A total of 418 of the 797 children were breastfed and 379 were not. The degree of myopia was measured using cycloplegic autorefraction. Cycloplegia temporarily paralyzes the accommodative mechanism, allowing for a precise measurement of the degree of myopia. Myopia was defined as any individual with a spherical equivalent of at least a -0.5 diopters. All the study participants were given medical tests and also answered a series of questions including the number of books they read per week.

The results showed that children who were breastfed had a lower prevalence of myopia. Only 259 out of the 418 or 62.0% were myopic. Of the children who were not breastfed, 262 out of the 379 or 69.1% were myopic. The authors concluded that since these differences were statistically significant, breastfeeding is independently associated with a decreased likelihood of myopia.

They believed that docosahexaenoic acid also known as (DHA) is the main element responsible for early visual development in babies. DHA is found at very high concentrations in the cell membranes of the retina, and plays an important role in the regeneration of the visual pigment rhodopsin, and in the visual transduction system that converts light hitting the retina to visual images in the brain (SanGiovanni and Chew, 2005). Since breast milk is the main source of DHA in newborns, Chong et. al. (2005) concluded that reduced DHA in non-breastfed infants can result in an impairment of normal ordered eyeball growth, which can then lead to the development and severity of myopia. They recommended infant breastfeeding as a protective measure to lower the probability of the development of myopia.

In an article regarding the association between breastfeeding and myopia, it was shown that infant feeding did not influence visual development (Rudnicka, et al., 2008). Their findings were contrary to the previous study linking myopia with breastfeeding rather than formula feeding, and they concluded that other environmental factors were important for visual development and myopia in early life, and not breastfeeding.

Environmental Modifications

Based on the three environmental theories leading to myopia, society should consider the use of DHA supplementation in bottled milk especially in preterm infants, insistence on more outdoor or brighter light exposure for young children, and finally, based on the accommodative theory, the use of cycloplegic drugs or reading glasses in myopic children to reduce accommodative stress. These environmental modifications may reduce the risk of progressive myopia in young children (Gross, et al., 2006).

Drug Therapy

The use of a cycloplegic eye drop to reduce accommodation in children has been the most controversial of the proposed modifications. Numerous drug studies, requiring the use of atropine, or atropine-like drugs have concentrated on the role of accommodation in progressive myopia. The most convincing information was documented in the Atropine in the Treatment of Myopia (ATOM) study, which is the largest randomized controlled trial of its kind to date (Chua, et al., 2006). The ATOM study followed 400 eligible children between the ages of six and 12 for two years. After two years, in the placebo-treated eyes not receiving atropine, the mean progression of myopia was -1.20±0.69D with axial elongation of 0.38±0.38mm. In the atropine-treated eyes, myopia progression was only -0.28±0.92D with the axial length essentially unchanged (-0.02±0.35mm).

Despite the efficacy of atropine in reducing childhood myopia progression, atropine therapy is not accepted as a standard treatment. Although no serious adverse events related to atropine were reported in the ATOM study, side effects include increased light sensitivity due to mydriasis of the dilated pupil, which can impair a child's ability to perform well in school and athletics. The cosmetic issues of pupil dilation caused by atropine can also be awkward for children during the critical periods of social development, when they seek the acceptance of their peers.

While atropine therapy may not be appropriate for most children, the ATOM study suggests that pharmaceutical management has potential for reducing myopia, and that other atropine-like drugs, including pirenzepine and cyclopentolate, may be options. These drugs are weaker and not as long acting and have fewer side effects. One study found that 2% pirenzepine gel slowed childhood myopia progression by almost half after a year of treatment; however, 11% of subjects still withdrew from the study because of minor side effects (Tan, et al., 2005, Siatkowski, et al., 2008). Hence, there is no simple answer.

Conclusion

This paper has highlighted the fact that today there is an increased prevalence of myopia not explainable on the basis of the genetic model. Numerous environmental factors have been advanced including intense near activity resulting in accommodative stress, diminished exposure to outdoor light resulting in dopamine expression within the eye, and finally the reduced intake of DHA in non-breastfed babies. Finally, we have suggested that recognizing the significance of these environmental factors may help prevent some of the devastating complications associated with progressive myopia.

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