Saudi Journal of Ophthalmology (2012) 26, 293—297

Pediatric Ophthalmology Update

Juvenile myopia progression, risk factors and interventions

Elliott H. Myrowitz, OD, MPH *

Abstract

The development and progression of early onset myopia is actively being investigated. While myopia is often considered a benign condition it should be considered a public health problem for its visual, quality of life, and economic consequences. Nearly half of the visually impaired population in the world has uncorrected refractive errors, with myopia a high percent of that group. Uncorrected visual acuity should be screened for and treated in order to improve academic performance, career opportunities and socio-economic status.

Genetic and environmental factors contribute to the onset and progression of myopia. Twin studies have supported genetic factors and research continues to identify myopia genetic loci. While multiple myopia genetic loci have been identified establishing myopia as a common complex disorder, there is not yet a genetic model explaining myopia progression in populations.

Environmental factors include near work, education levels, urban compared to rural location, and time spent outdoors. In this field of study where there continues to be etiology controversies, there is recent agreement that children who spend more time outdoors are less likely to become myopic.

Worldwide population studies, some completed and some in progress, with a common protocol are gathering both genetic and environmental cohort data of great value. There have been rapid population changes in prevalence rates supporting an environmental influence.

Interventions to prevent juvenile myopia progression include pharmacologic agents, glasses and contact lenses. Pharmacological interventions over 1–2 year trials have shown benefits. Peripheral vision defocus has been found to affect the emmetropization process and may be affected by wearing glasses or contacts. Accommodation accuracy also has been implicated in myopia progression.

Further research will aim to assess both the role and interaction of environmental influences and genetic factors.

Keywords: Myopia, Refractive error, Emmetropization, Review

http://dx.doi.org/10.1016/j.sjopt.2011.03.002

Introduction

The prevalence rate for myopia, an extremely common eye disorder worldwide, rose over the past three decades in the United States from 25% to 41%[50] and has risen to 70–90% in some Asian countries.[22,43] Higher myopia, over six diopters, is also increasing[50] and is associated with an increased lifelong risk of rhegmatogenous retinal detachment, glaucoma, and myopic degeneration.[27] The cost each year in the United States for optometric examinations, optical and surgical refractive corrections is several billion dollars.[17] Worldwide there are 153 million visually impaired persons due to uncorrected refractive errors accounting for 49% of all visually impaired persons.[40] Uncorrected visual acuity should be screened for and treated in order to improve academic performance, career opportunities and

Received 3 January 2011; received in revised form 29 January 2011; accepted 8 March 2011; available online 15 March 2011

The Wilmer Eye Institute, The Johns Hopkins University, Baltimore, MD, USA

* Tel.: +1 410 583 2800; fax: +1 410 583 2842.
e-mail address: emyrowitz@jhmi.edu

Peer review under responsibility of Saudi Ophthalmological Society, King Saud University

Production and hosting by Elsevier

Access this article online:
www.saudiophthaljournal.com
www.sciencedirect.com

socio-economic status.[38] Understanding the risk factors and interventions for the most common form of myopia, juvenile myopia is the aim of this review.

Juvenile myopia

Most studies classify over 60% of myopia as early onset also called juvenile or school myopia, occurring between 9 and 11 years of age with progression throughout the early teenage years.[11] There is agreement that both genetic and environmental factors contribute to the onset and progression of myopia. One variable predicting the future onset of myopia is a cycloplegic auto refraction of 0.75 diopter or less of hyperopia at a mean age of 8.6 years which has been shown to have a sensitivity of 87% and specificity of 73% in predicting future myopia.[57]

While prevalence studies may look at the same age group, their protocols can differ making comparisons difficult. Starting with a year 2000 report,[26] many population studies around the world are using a common protocol. The Sydney Myopia Study[34] uses a protocol common with six studies starting with the Refractive Error Study in Children (RESC) in 2000. However, there are also 13 myopia prevalence studies in similar age groups that have different protocols for determining prevalence of myopia.[34]

The prevalence of myopia reported for 6 year old children varies from 0.6% in Oman[23] to 29% in Singapore.[44] The prevalence in Oman for 6 year old children was 0.6%, but the definition of myopia was more than −1.0 diopter when most studies use −0.5 diopter. The prevalence of myopia among pre-school children at King Abdulaziz Medical City, Riyadh, Saudi Arabia is 2.5%.[1]

The visual system has an active process of emmetropization that involves defocus detection and a coordinated growth of the refractive components toward emmetropia with active structural changes.[54,39] It is amazing how well emmetropization works and understanding what occurs when this process fails is the target of the research.[30] In the first three years of life the cornea and lens change to counterbalance an approximately 20 diopter increase in axial length of the growing eye.[47] Between ages 3 and 13 the lens and or cornea need to adjust about 3 diopters to maintain emmetropia.

As the human eye grows the lens adds layers of tissue yet thins by stretching in the equatorial plane so that it flattens, thins and loses power to compensate for the increasing axial length and maintains emmetropia.[32,25] When the lens fails to stretch and thin the eye becomes myopic and the eyeball shape becomes more prolate or less oblate. The source of this interruption of equatorial expansion is unknown with one hypothesis being the thickening of the ciliary muscle which is found in myopic children and adults.[35,2]

When myopia develops the eye is longer than it is wider (greater anteroposterior length than lateral transverse dimensions). This prolate shape of the eyeball will create a relative hyperopic defocus in the peripheral vision, along the lateral dimensions away from the macula. This peripheral vision refraction is another hypothesis as a potential impact or trigger on the active emmetropization process.[33] Peripheral refraction in the myopic eye becomes relatively more hyperopic (Fig. 1). Local retinal regions can control local eye growth and myopia.[52] The peripheral refractive state of the eye can affect eye development especially the progression of myopia.[46] An interesting study found 77% of young entering emmetropic pilots with relative hyperopic defocus in their peripheral refraction developed myopia during their training.[13] Hyperopic eyes are usually myopic in the periphery adding to the hypothesis that the periphery focus could be a trigger in eye growth. Also being investigated is the increase in the lag of accommodation during near work and the increase in myopia.[4,29]

A 2010 search in PubMed yields over 14,000 citations with many research disciplines working to identify risk factors and potential interventions to help control myopia. Understanding, controlling and treating myopia are also a goal of the World Health Organization, Vision 2020 project.[53]

Genetic factors

High heritability in myopia suggests that there is a significant genetic component to explain the variance in the population. A high heritability index is found in twin studies varying from 75% to 94%. A recent large sample study of monozygotic and dizygotic twins estimates a heritability index of 77%.[24] However, this high index does not preclude an environmental precursor, and has some contestable assumptions (Morgan and Rose). Other genetic evidence pointed to is the prevalence of myopia in children increased with the number of myopic parents from 7.6, 14.9, to 43.6 percent for no, one or two myopic parents.[15] However, it is an interesting observation of low heritability values in parent-offspring correlations when there has been rapid environmental change between generations.[28] The Genes in Myopia (GEM) family study calculated the heritability index between 27% and 55%.[5] In a non twin study heritable factors accounted for 80% of juvenile myopia.[31]

Multiple myopia genetic loci have been identified establishing myopia as a common complex disorder.[14] A recent review of data from the past decade in searching for myopia genes points to axial length and refraction sharing common genes and states that the majority of myopia cases are not likely caused by defects in structural proteins, but in defects involving the control of structural proteins.[16] They conclude in discussing genes and their effects on myopia, ''it is hard to show anything but a modest effect on their etiologies. Thus we are still left with the impression that the influence of environment exerts a greater effect than does the concerted action of several genes''.[16]

Environmental factors

While we wait for more evidence for genetic determination of refractive error there does exist evidence pointing to environmental risk factors. The increasing prevalence of myopia and high myopia which at times has rapidly changed in Taiwan, Singapore, Hong Kong, Scandinavia, and the United States has been pointed out as likely being environmental.[34,50] In can be difficult to compare prevalence studies if the protocol for sampling, refraction and use of cycloplegia is not standardized. Starting with a year 2000 study there have been population studies in Chile, China, Nepal, Urban India, Rural India, South Africa, and Australia using a common or comparable protocol.[34] This common protocol was further advanced in The Sydney Myopia Study which had a stratified

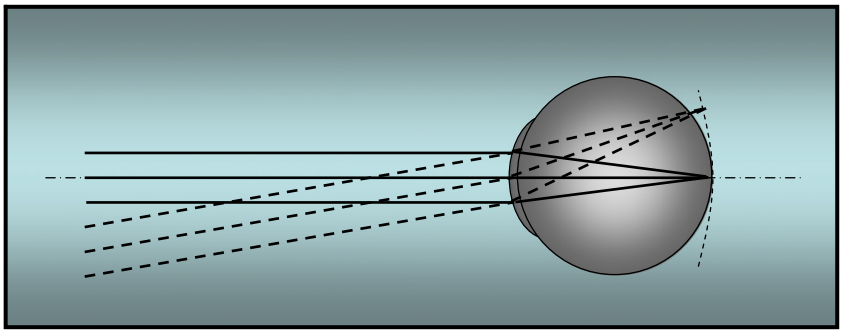

Figure 1. Emmetropic eye with relative hyperopic defocus in pheriphery.

random cluster sample a group of children aged 6 and a group aged 12, with a three year interval for reexamination. Data on eye structure and changes over time in this study include using Cyclopentolate use with auto refraction, noncontact biometry including optical coherence tomography. By also gathering data from the parents of the study population the study aimed to assess interactions between genetic and environmental risk factors.[34]

Urbanization and educational attainment also has some contribution toward myopia development but only explains a small proportion of the variance seen.[28] Near work has been identified as a risk factor but with a weak association and difficult to quantify.[56]

Recently data have shown a protective effect of the time spent outdoors in 6–7 year old children.[31,36,41,18,20] This outdoor protective effect was also reported in 12 year old Sydney children.(Rose et al., 2008b) The time outdoor protective effect has been reported in the United States,[31,18] in Turkey,[36] and in Jordan.(Khader et al., 2006) The Orinda longitudinal study found this protective difference precedes the onset of myopia.[18] The reduction in the probability of developing myopia by eighth grade if a child had two myopic parents went from 0.60 if the outdoor time in the third grade was low (0–5 h per week) to 0.20 if the outdoor time is high (>14 h per week).[18] Statisticians have modeled risk factors that include age, gender, ethnicity, school, IQ level, number of books read per week, height, parental myopia and adding time spent outdoors significantly improves the fit of the model.[9]

To help measure the relative roles of the environment and genes it is valuable to examine the prevalence of similar ethnicity in a population that migrates to a different environment. This was done in comparing the prevalence and risk factors in 6 and 7 year old children of Chinese ethnicity in Sydney and Singapore. The prevalence of myopia in the Chinese children was 3.3% in Sydney and 29.1% in Singapore yet the children in Sydney read significantly more books and had more total time in near activities. The most significant factor between the two sites was much more time on outdoor activities in Sydney.[42] Measuring the prevalence rates in Caucasian and Chinese students in local and international schools in Hong Kong found both an effect of the different genetic background and an effect of the Hong Kong environment.[21] Indians show a very low prevalence of myopia in India, however, the prevalence of myopia in Indians in Singapore is high.[55] Park and Congdon[37] argue that many of the prevalence studies in the literature have ''significant shortcomings'' chiefly due to lack of longitudinal data. Morgan and Rose[28] feel there is enough environmental evidence that in high pressure environments with intensive mass-education systems in highly urbanized environments, almost everyone could become myopic.

Interventions

Interventions to control juvenile myopia progression have included pharmaceutical agents, bifocal and Progressive lens glasses, and rigid gas permeable contact lenses. In a review of myopia trials to retard myopia progression in 2002 it was felt there was insufficient evidence to support any interventions.[44]

Animal studies show myopic defocus produced by positive lenses reduce axial length increase.[58] Yet, a two year controlled prospective study on myopic children aged 9–14 who were under corrected by approximately +0.75 diopter showed an enhanced rather than an inhibited myopia development in axial length and thus more myopia.[8]

In a randomized masked 2 year trial giving myopic children atropine in one eye the treated eye progressed 0.38 diopters and the untreated eye progressed 1.20 diopters.[7] This difference in myopia progression of −0.92 D was also accompanied by a reduced axial elongation of 0.40 mm. No serious adverse events related to atropine were reported. However, this difference narrowed one year after the atropine was stopped.[49] This atropine study group also reports embarking on a new randomized clinical trial using three different atropine concentrations with bilateral treatment for more than two years with a post treatment monitoring to evaluate long term comparative myopia control effects of the treatment.[7] There have been two studies using Pirenzepine gel, in the United States,[45] and, in Asia,[48] showing a nearly 50% reduction in progression when used twice a day.

Rigid contact lenses have been reported to slow myopia progression but had not been studied in a controlled randomized trial until 2003. Rigid gas permeable contact lenses were found to have only a mild nonsignificant protective effect.[19] A more recent two year study of forty, 8–11 year old children given corneal reshaping contact lenses during sleep reported slowed eye growth compared to the matched soft contact wearing children.[51]

Two randomized trials of Progressive addition lens showed a very small protective effect of wearing the progressive glasses.[10,12] However, recently in a two year study, three randomized groups of children wearing single vision glasses, bifocals, or bifocals with base in prism progressed after two years 1.55 D, 0.96 D, and 0.70 D, respectively.[6]

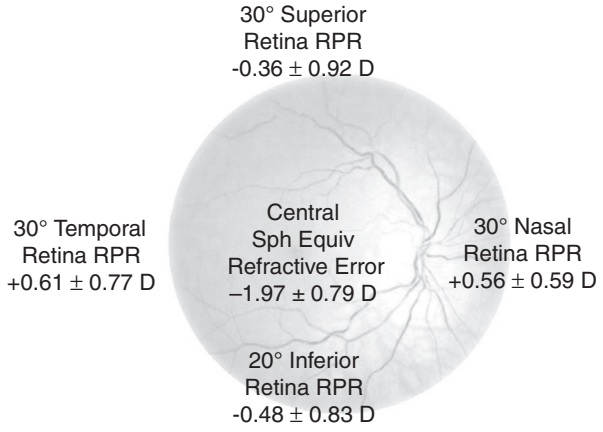

Figure 2. Mean (SD) and relative peripheral refractions in the Study of Theories about Myopia Progression (STAMP) baseline data.

Baseline data for the Study of Theories about Myopia Progression (STAMP) have recently been reported.[3] This 2-year, double-masked, randomized trial will look at Progressive addition lenses compared to single vision glasses and myopia progression and also look at peripheral refraction, accommodative response and convergence, crystalline lens radii of curvature, axial dimensions, intraocular pressure, corneal curvature and thickness, as well as near work and outdoor activity assessment. The STAMP study will gather complete biometric data at 6 month intervals. The STAMP baseline data found that indeed the myopic children did have a peripheral hyperopic defocus similar to other reports along the lateral meridian of the eye and a new finding was a myopic defocus along the vertical peripheral meridian of the eye.(Fig. 2)

Conclusion

Genetic studies are actively continuing, but to date have not yet identified a genetic pathway for familial risk of myopia. The emmetropization process continues to be investigated looking for risk factors, such as peripheral vision defocus and accommodative lag, contributing to juvenile myopia progression. Pharmacologic treatments have reduced myopia progression but more studies including longer follow up are needed. Recent epidemiological studies have identified the time spent outdoors to be protective of the development of myopia. Much progress has been made in the past decade both in epidemiological studies as well as in clinical trials leading to new questions requiring more research.

References

1. Al-Rowaily MA. Prevalence of refractive errors among pre-school children at King Abdulaziz Medical City, Riyadh, Saudi Arabia. *Saudi J Ophthalmol* 2010;**24**:45–8.
2. Bailey MD, Sinnott LT, Mutti DO. Ciliary body thickness and refractive error in children. *Invest Ophthamol Vis Sci* 2008;**49**:4353–60.
3. Berntsen D, Mutti DO, Zadnik K. Study of theories about myopia progression (STAMP) design and baseline data. *Optom Vis Sci* 2010;**87**:823–32.
4. Charman WN. Near vision, lags of accommodation and myopia. *Ophthalmic Physiol Opt* 1999;**19**:126–33.
5. Chen CY, Scurrah KJ, Stankovich J, Garoufalis P, Dirani M, Pertile KK, Richardson AJ, Mitchell P, Baird PN. Heritability and shared environment estimates for myopia and associated ocular biometric traits: the genes in myopia (GEM) family study. *Hum Genet* 2007;**121**:511–20.
6. Cheng D, Schmid KL, Woo GC, Drobe B. Randomized trial of effect of bifocal and prismatic bifocal spectacles on myopic progression: two-year results. *Arch Ophthalmol* 2010;**128**:12–9.
7. Chua W-H, Balakrishnan V, Chan Y-H, Tong L, Ling Y, Quah B-L, Tan D. Atrophine for the treatment of childhood myopia. *Ophthalmology* 2006;**113**:2285–91.
8. Chung K, Mohidin N, O'Leary DJ. Under correction of myopia enhances rather than inhibits myopia progression. *Vision Res* 2002;**42**:2555–9.
9. Dirani M, Tong L, Gazzard G, Zhang X, Chia A, Young TL, Rose KA, Mitchell P, Saw S-M. Outdoor activity and myopia in Singapore teenage children. *Br J Ophthalmol* 2009;**93**:997–1000.
10. Edwards MH, Li RW, Lam CS, Lew JK, Yu BS. The Hong Kong progressive lens myopia study: study design and main findings. *Invest Ophthalmol Vis Sci* 2002;**43**:2852–8.
11. Gilmartin B. Myopia: precedents for research in the twenty-first century. *Clin Exp Ophthalmol* 2004;**32**:305–24.
12. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci* 2003;**44**:1492–500.
13. Hoogerheide J, Rempt F, Hoogenboom WP. Acquired myopia in young pilots. *Opthalmologica* 1971;**163**:209–15.
14. Hornbeak DM, Young TL. Myopia genetics: a review of current research and emerging trends. *Curr Opin Opthalmol* 2009;**20**:356–62.
15. Ip JM, Huynh SC, Robaei D, Rose KA, Morgan IG, Smith W, Kifley A, Mitchell P. Ethnic differences in the impact of parental myopia: findings from a population-based study of 12-year-old Australian children. *Invest Ophthalmol Vis Sci* 2007;**48**(6):2520–8.
16. Jacobi FK, Pusch CM. A decade of search of myopia genes. *Front Biosci* 2010;**15**:359–72.
17. Javitt JC, Chiang YP. The socioeconomic factors of laser refractive surgery. *Arch Opthalmol* 1994;**112**:1526–30.
18. Jones LA, Sinnott LT, Mutti DO, et al. Parental history of myopia, sports and outdoor activities and future myopia. *Invest Opthalmol Vis Sci* 2007;**48**:3524–32.
19. Katz J, Schein OD, Levy B, et al. A randomized trial of rigid gas permeable contact lenses to reduce progression of children's myopia. *Am J Ophthalmol* 2003;**136**:82–90.
20. Khader YS, Batayha WQ, Abdul-Aziz SM, et al. Prevalence and risk indicators of myopia among school children in Amman, Jordan. *East Mediterr Health J* 2006;**12**:434–9.
21. Lam CS, Goldschmidt E, Edwards MH. Prevalence of myopia in local and international schools in Hong Kong. *Optom Vis Sci* 2004;**81**:317–22.
22. Lin LL, Shih YF, Tsai CB, Chen CJ, Lee LA, Hung PT, et al. Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1995. *Optom Vis Sci* 1999;**76**:275–81.
23. Lithander J. Prevalence of myopia in school children in the Sultanate of Oman: a nation-wide study of 6292 randomly selected children. *Acta Opthamol Scand* 1999;**77**:306–9.
24. Lopes MC, Andrew T, Carbonaro F, Spector TD, Hammond CJ. Estimating heritability and shared environmental effects for refractive error in twin and family studies. *Invest Opthalmol Vis Sci* 2009;**50**:126–31.
25. Manns F, Parel JM, Denham D, Billotte C, Ziebarth N, Borja D, Fernandez V, Aly M, Arrieta E, Ho A, Holden B. Optomechanical response of human and monkey lenses in a lens stretcher. *Invest Opthalmol Vis Sci* 2007;**48**:3260–8.
26. Maul E, Barroso S, Munoz, et al. Refractive error study in children: results from LaFlorida, Chile. *Am J Ophthalmol* 2000;**129**:445–54.
27. Mitchell P, Hourihan F, Sandbach J, et al. The relationship between Glaucoma and myopia: the Blue Mountains Eye Study. *Opthamology* 1999;**106**:2010–5.
28. Morgan I, Rose K. How genetic is school myopia? *Prog Retin Eye Res* 2005;**24**:1–38.
29. Mutti DO. Hereditary and environmental contributions to emmetropization and myopia. *Optom Vis Sci* 2010;**87**(4):255–9.
30. Mutti DO, Zadnik K, Adams AJ. Myopia: the nature versus nurture debate goes on. *Invest Opthamol Vis Sci* 1996;**37**:952–7.
31. Mutti DO, Mitchell GL, Moeschberger ML, Jones LA, Zadnik K. Parental myopia, near work, school, achievement, and children's refractive error. *Invest Opthalmol Vis Sci* 2002;**43**:3633–40.

32. Mutti DO, Mitchell GL, Jones LA, Friedman NE, Frane SL, Lin WK, Moeschberger ML, Zadnik K. Axial growth and changes in lenticular and corneal power during emmetropization in infants. *Invest Opthamol Vis Sci* 2005;**46**:3074–780.
33. Norton TT, Siegwart JT, Amedo AO. Effectiveness of hyperopic defocus, minimal defocus, or myopic defocus in competition with a myopiagenic stimulus in tree shrew eyes. *Invest Opthalmol Vis Sci* 2006;**47**:4687–99.
34. Ojaimi E, Rose KA, Smith W, Morgan IG, Martin FJ, Mitchell P. Methods for a population-based study of myopia and other eye conditions in school children: the Sydney Myopia Study. *Opthalmic Epidemiol* 2005;**12**:59–69.
35. Oliveira C, Tello C, Leibmann JM, Ritch R. Ciliary body thickness increases with increasing axial myopia. *Am J Opthalmol* 2005;**140**:324–5.
36. Onal S, Toker E, Akingol Z, et al. Refractive errors of medical students in Turkey: one year follow-up of refraction and biometry. *Optom Vis Sci* 2007;**84**:175–80.
37. Park DJ, Congdon NG. Evidence for an ''epidemic'' of myopia. *Ann Acad Med Singapore* 2004;**33**:21–6.
38. Powell, C., Wedner, S., Hatt, S.R., 2006. Vision screening for correctable visual acuity deficits in school-age children and adolscents. Cochrane Database of Systematic Reviews (2). Art. No.:CD005023. doi: 1002/14651858. CD 005023. pub2.
39. Rabin J, Van Sluyters RC, Malach R. Emmetropisation: a vision-dependent phenomenon. *Invest Opthamol Vis Sci* 1981;**20**:661–4.
40. Resnikoff S, Pascolini D, Mariotti SP, Pokharel GP. Global magnitude of visual impairment caused by uncorrected refractive errors in 2004. *Bull World Health Organ* 2008;**86**:63–70.
41. Rose KA, Morgan IG, Ip J, Kifley A, Hunyh S, Smith W, Mitchell P. Outdoor activity reduces the prevalence of myopia in children. *Opthalmology* 2008;**115**:1279–85.
42. Rose KA, Morgan IG, Smith W, et al. Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney. *Arch Opthalmol* 2008;**126**:527–30.
43. Saw SM, Katz J, Schein OD, Chew SJ, Chan TK. Epidemiology of myopia. *Epidemiol Rev* 1996;**18**:175–87.
44. Saw SM, Carkeet A, Chia KS, Stone RA, Tan DT. Component dependent risk factors for ocular parameters in Singapore Chinese children. *Opthalmology* 2002;**109**:2065–71.
45. Siatkowski, R.M., Cotter, S.A., Miller, J.M., et al. 2004. Pirenzepine 2% ophthalmic gel retards myopic progression in 8–12 year old children over two years. Invest Opthalmol Vis Sci 45: E-Abstract 2733.
46. Smith III EL, Hung LF. The role of optical defocus in regulating refractive development in infant monkeys. *Vision Res* 1999;**39**:1415–35.
47. Sorsby, A., Leary, G.A., 1970. A longitudinal study of refraction and its components during growth. Medical Research Council Special Report Series 309. London: HMSO.
48. Tan, D.T., Lam, D., Chua, W.H., Crockett, R.S., Group APS, 2003. Pirenzephine ophthalmic gel (PIR): safety and efficacy for pediatric myopia in a one-year study in Asia. Invest Opthalmol Vis Sci 44: E-Abstract 801.
49. Tong L, Huang XL, Koh ALT, Zhang X, Tan DT, Chua W-H. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. *Ophthalmology* 2009;**116**:572–9.
50. Vitale S, Sperduto RD, Ferris FL. Increased prevalence of myopia in the United States between 1971–1972 and 1999–2004. *Arch Ophthalmol* 2009;**127**(12):1632–9.
51. Walline JJ, Jones LA, Sinnott LT. Corneal reshaping and myopia progression. *Br J Ophthalmol* 2009;**93**:1181–5.
52. Wallman J, Gottlieb MD, Rajaram V, Fugate-Wentzek LA. Local retinal regions control local eye growth and myopia. *Science* 1987;**237**:73–7.
53. World Health Organization, 2000. Elimination of avoidable visual disability due to refractive errors (WHO/PBL/0079). Geneva: World Health Organization, Vision 2020: http://www.v2020.org/html/sight.html.
54. Wiesel TN, Raviola E. Myopia and eye enlargement after neonatal lid fusion in monkeys. *Nature (London)* 1977;**266**:66–8.
55. Wu HM, Seet B, Yap EP, Saw SM, Lim TH, Chia KS. Does education explain ethnic differences in myopia prevalence? A population based study of young adult males in Singapore. *Optom Vis Sci* 2001;**78**:234–9.
56. Zadnik K, Mutti DO. Prevalence of myopia. In: Rosenfield M, Gilmartin B, editors. *Myopia and Near Work*. Oxford: Butterworth/Heinemann; 1998. p. 13–30.
57. Zadnik K, Mutti DO, Friedmann NE, et al. Ocular predictors of the onset of juvenile myopia. *Invest Opthamol Vis Sci* 1999;**40**:1936–43.
58. Zhu X, Winawer J, Wallman J. Potency of myopic defocus in spectacle lens compensation. *Invest Opthalmol Vis Sci* 2003;**44**:2818–27.