

New perspectives on the prevention of myopia

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Abstract

The high prevalence of myopia and its public health and clinical consequences make prevention of myopia a top priority. Traditional approaches to prevention have been based on reducing accommodative load, and have generally been unsuccessful. Only treatment with atropine eye-drops has produced clinically significant effects, which are however of limited duration and suffer from potential side-effects. In addition, based on animal experimentation, it is now clear that atropine blocks eye growth by mechanisms which do not involve accommodation. More generally, experimentation on animal models of myopia has shown that accommodation is not important for the control of eye growth, whereas exposure to hyperopic (growth-promoting) and myopic (growth-inhibiting) defocus is more important. Recent epidemiological evidence has also questioned the importance of near work, although education is clearly important. This suggests a preventive approach based on deliberately increasing the amount of myopic defocus a child is exposed to may be successful. There is also convincing evidence that children who spend more time outside are less likely to become myopic, which also suggests a quite non-invasive approach to prevention. These new directions need to be pursued.

Keywords: Myopia, Prevention, Eye growth, Accommodation, Outdoor activity

In the past few decades, an epidemic of myopia has appeared in China in younger people. In 2002, in Guangzhou, the prevalence of myopia was over 70% in 15 year-olds¹, and similarly high prevalence of myopia have been reported for Chinese children in Shanghai and cities in Xinjiang Province². In contrast, in more rural areas, such as Shunyi³, and more rural areas of Guangdong province, such as

Yangxi⁴, and Xichang⁵, the prevalence was somewhat lower than large cities, but still high by international standards. One of the lowest prevalences of myopia reported in recent studies is that for rural areas of Chongqing⁶. The pattern of high myopia prevalence in children and young adults in urban areas, with lower prevalence in more rural areas, where they exist, is also seen in Taiwan, Hong Kong and Singapore, where the populations are predominantly of Chinese origin, but not, at least to the same extent, in other parts of the world⁷.

The high prevalence of myopia in young people has the immediate implication of both a high demand for optical correction, and the visual impairment associated with under-correction^{1,4,8}. Furthermore, there is potential for increased later development of glaucoma and for those who are highly myopic, the high prevalence will be reflected in the emergence of high levels of myopic chorio-retinal degenerations and pathologies⁹, which will in turn lead to higher levels of visual impairment and legal blindness. These appear much earlier in life than the common age-related potentially blinding conditions¹⁰⁻¹¹, such as cataract, glaucoma and macular degeneration, and therefore impose a more prolonged duration of decreased visual function.

The size of the myopia problem in China has been recognized by a recent resolution of the State Council, which requires schools to adopt strategies to limit the development of myopia. The critical question is then, which of the many preventive approaches to myopia is evidence-based and works in practice.

Are Chinese more susceptible to myopia?

We first need to address a key issue is Chinese more susceptible to myopia, and is myopia in Chi-

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nese inevitable? Because of the high prevalence of myopia amongst Chinese in many different environments, it has often been asserted that people of Chinese origin are genetically myopic, or at least have a genetic propensity to become myopic. The most influential paper in this respect is that of Rasmussen¹⁰, who reported that the prevalence of myopia was over 60% in China 70–80 years ago. However, Rasmussen did not actually measure refractions, or report the prevalence of myopia. Rather, he reported a clinical measure, the percent of spectacle prescriptions which were for myopia, which does not, in any population, equate to the prevalence of myopia in the population. Wu and Edwards¹² documented an increasing prevalence of myopia in China over three generations, but the sample size was small, and the refractions were not cycloplegic. More recently, by analyzing the changing patterns of visual acuity in schools in Guangzhou, we have found that the prevalence of low unaided visual acuity has at least doubled in the last 30 years in Guangzhou (unpublished results), which is most plausibly explained by an increasing prevalence of myopia. The significantly lower prevalence of myopia reported for older people in epidemiological surveys in China^{13–14} is also consistent with the idea that there has been a marked increase in the prevalence of myopia over the past decades, although a genuine longitudinal hyperopic shift with age can also contribute to this.

The idea that people of Chinese origin are inevitably myopic does not fit with the sometimes marked differences recently reported in the prevalence of myopia between urban and rural areas in China^{6,15}. It also does not fit with the lower prevalence of myopia reported in children of Chinese origin growing up in Malaysia¹⁶, and the even lower prevalence reported in children of Chinese origin growing up in Sydney, Australia¹⁷. Moreover, the propensity to develop myopia does not appear to be restricted to people of Chinese origin, but is found in other East countries such as Japan. In Singapore, children of South Asian (Indian) origin, who are closer in genetic origin to Europeans than to Chinese¹⁸ are almost as myopic as their peers of Chinese origin¹⁶, although Indian children in India have a low prevalence of myopia¹⁹. The variability in the

prevalence of myopia, including in people of Chinese ethnicity, across different environments highlights the importance of environmental exposures, which implies that myopia can be reduced if the right environmental conditions can be achieved.

Is the problem excessive accommodation and near-work?

Numerous studies over a long period of time have demonstrated that increased education and increased myopia go hand in hand⁷. Initial approaches to prevention were based on the plausible link between education, nearwork and the high need for accommodation associated with reading and writing. Attempts were therefore made to reduce accommodative demand by using reading glasses, bifocals or most recently, progressive addition lenses. At best, these trials have achieved statistically significant, but clinically insignificant gains, except for the small group of near esophores, where significant gains were achieved^{20–21}.

This line of thinking also led to the use of atropine to block accommodation. Atropine eye-drops do block the progression of myopia, but there are problems associated with the limited period over which they work (approximately one year), and the appearance of a rebound acceleration of progression when the treatment is discontinued^{22–23}. In addition, there is need for considerable caution in the long-term use of atropine, given that the effects of chronic cycloplegia and mydriasis are unclear. Pirenzepine ophthalmic gel has also been trialed, with more limited success²⁴. Nevertheless, the successful use of atropine eye-drops appears to give strong support to the idea that blocking accommodation can prevent myopia or at least myopic progression.

Despite this, in recent years, the importance of excessive accommodation has been questioned. As noted above, attempts to reduce the demand for accommodation using optical techniques have not been particularly successful. Studies on experimental myopia in animals have also questioned the importance of accommodation. In these studies, it has been shown that atropine blocks axial elongation and the development of myopia, even in species such as chickens where accommodation is mediated by nico-

tinic rather than muscarinic receptors, and hence is not blocked by atropine²⁵. Eye growth regulation and the inhibitory effects of atropine have also been demonstrated in animals with little or no accommodative capacity²⁶, and in experimental animals where control of accommodation has been blocked by section of the ciliary nerve or destruction of the Edinger-Westphal nucleus²⁷⁻²⁸. Most strikingly, form-deprivation or exposure to lens-induced defocus of only part of the visual field, leads to similarly localized regional changes in eye growth²⁹, which are difficult to explain in terms of a global process such as accommodation.

Other experimental work now suggests that the site of action of atropine is either directly on the sclera³⁰, or at sites within the retina, where reduced gene expression that correlates with increased rates of eye growth is rapidly reversed by intravitreal injections of atropine³¹. The evidence obtained favours the idea that the receptors involved are M4 muscarinic receptors³²⁻³³, and one hope for the future is that the development of selective M4 antagonists may provide a route to more selective pharmacological block of the development of myopia.

A new explanatory framework-the balance of myopic and hyperopic defocus

Experimental work on animals has replaced the emphasis on excessive accommodation with a different explanatory framework-namely that the retina is able to generate growth control signals in response to image defocus by mechanisms which are currently unclear³⁴. The link between education and myopia would thus not be explained by the excessive need for accommodation, but rather by the hyperopic defocus induced by accommodative lag when large amounts of near work are performed.

Despite uncertainties about the mechanisms, the experimental evidence is strong-fitting negative lenses over eyes leads to hyperopic defocus, and even when the animal can clear the defocus by accommodating, leads to increased axial elongation. This probably reflects a mechanism for clearing neonatal hyperopia. In contrast, fitting a positive lens over eyes leads to myopic defocus, and decreased eye growth. This probably reflects a mechanism for

clearing neonatal myopia. The impact of imposed myopic defocus is much more powerful than that of imposed hyperopic defocus, and quite brief periods of imposed myopic defocus can over-rule much longer exposures to hyperopic defocus³⁵. This may be of critical importance for myopia prevention.

The observation that imposed myopic defocus blocks the development of myopia is, of course, paradoxical, because taken literally, it should lead to myopia being a self-limiting condition, and myopia should be impossible. Two possible resolutions of this paradox are that the strength of the inhibitory growth signal generated by myopic defocus declines in older children, requiring longer or stronger exposures to produce effective inhibition of growth³⁶⁻³⁷. Alternatively, it is possible that the defocus-detecting systems habituate to the slowly changing habitual level of defocus in a developing myope, and thus more defocus is required to inhibit eye growth. More work on these possibilities is required.

Whatever the resolution of these uncertainties, the idea that imposed myopic defocus has the potential to prevent myopia has now become an active area of research. A simple approach based on asking children to wear positive lenses instead of their normal correction for 30 minutes per day has had some success in practice-based interventions (Morgan, unpublished results). There are numerous more complicated variants now being trialed, including spectacles that simultaneously provide a clear image, and a myopically blurred image which can be suppressed perceptually, but which inhibits eye growth³⁸. Spectacles which correct peripheral refractive errors, or which provide myopic defocus in the periphery of the retina but not in the fovea are also being trialed, based on the idea that growth signals generated in the periphery can be more effective than central signals because of the greater area of peripheral retina³⁹. Considerable further work needs to be done to develop the optimal approaches, but many are at a stage where trialing is appropriate and on-going, and some early reports are now available⁴⁰.

This new framework requires some rethinking of older ideas. For example, it has generally been assumed that outdoor environments involve relaxed accommodation, which is true when people are look-

ing into the distance at the horizon. But from the perspective of defocus, if someone is looking at the horizon, then nearer objects will be hyperopically defocused, with a tendency to promote eye growth. Of course, people outside do not spend all their time focusing on the horizon, they look at nearby objects and particularly other people, and often engage in near-work. In this situation, closer objects will be hyperopically defocused, with more distant objects myopically defocused, which might inhibit eye growth. From the point of view of defocus, performing near-work outside might be a very effective myopia preventive. The same principles apply to indoor environments, except that the amount of myopic defocus during near-work is likely to be limited by the smaller range of potential viewing distances.

Or is time spent outdoors the key factor ?

Very recent work has brought forward a powerful factor that prevents the development of myopia-time spent outdoors^{17,41-42}. Children who spend a lot of time outside are much less likely to become myopic than those who do not. The effect is robust, since it has now been reported in children of European and Chinese origin in several different environments, and powerful, since it is able to reduce markedly the impact of high amounts of nearwork and of parental myopia. The original hypothesis was that the protective effect was due to the typically higher light intensities outside during daylight hours, possibly acting via increased release of the retinal transmitter dopamine which is known to be able to inhibit eye growth in some circumstances. This hypothesis has now been confirmed in laboratory studies⁴³.

Is the balance between education and outdoor time the critical issue ?

Results from the Sydney Myopia Study suggest that children who combine high amounts of near-work with little time outdoors are the most at risk of myopia, while those who combine little near-work with lots of time outside are at low risk. However, all children who spent higher amounts of time outside were protected from the development of myopia. In the global analysis, time outdoors appeared to be a strong factor, while there was little overall im-

pact of near-work⁴¹. Recently the idea that near-work is of any importance has been challenged⁴⁴, but there has to be a factor that mediates the impact of education on the biology of the eye, and, in our opinion, near-work, via induced defocus, remains a viable candidate. One possibility, that the effects of education are due to reduction in time spent outdoors seems unlikely, since this would require a clear negative correlation between time outdoors and hours of nearwork, whereas the actual correlation is weak, but positive⁴¹.

Only one side of the balance can really be addressed, since the commitment to education, and the study involved, is part of modern life. However, the epidemiological evidence suggests that the protective effect of time spent outdoors is able to neutralize the effects of even high levels of near-work. What this means is that it should be possible to obtain high standards of education without inducing an epidemic of myopia if the balance is right. There is evidence that this can be done, since, while Shanghai, Singapore and Hong Kong have amongst the highest educational outcomes in the world, and have correspondingly high myopia rates, Australia also ranks in the highest educational outcomes in the world⁴⁵, but has some of the lowest levels of myopia⁴⁶⁻⁴⁷. This demonstrates that these two aims are not incompatible. Importantly, Australia has characteristically high levels of time spent outdoors, and high ambient light levels, and appears to achieve protection from myopia quite naturally. More efforts may be required in other environments.

Some concrete interventions

Based on this analysis, two obvious school-based interventions can be suggested.

The first is to increase the amount of time children spend outside during school hours. This does not necessitate increased time for sport and physical education, although this is one way to achieve increased time outdoors, which would have additional health benefits. Options for classes outside in appropriate areas of the curriculum should also be considered. Part of this intervention might be to increase the level of lighting in classrooms, preferably by increasing natural lighting. This would require more attention to

design of new schools, and of school renovations. These school-based interventions will need to be backed up by family-based initiatives to increase the amount of time spent outside, outside of school hours.

The advantage of this approach is that it is non-invasive and can be applied on a whole-school basis, thus optimising the chances of both preventing myopic progression, the aim of most earlier work, and also of preventing incident myopia. A small longitudinal trial on myopic children has reported that outdoors activities slowed the myopia progression⁴⁸, and a large-scale intervention trial of this approach is now underway in Guangzhou, and we expect that results will become available over the next two to three years.

The other approach is to attempt to impose myopic defocus. A simple way of doing this is to ask children to wear reading glasses for a limited period time, while using distance vision. It needs to be stressed that this approach is very different in principle to that of previous trials with reading glasses, since it is designed to impose myopic defocus rather than reduce the need for accommodation. Experience from animal studies and from practice-based trials suggests that 30 minutes to one hour is sufficient to produce reductions in axial elongation. This is an approach that clinicians dealing with progressing myopia could consider applying, and preliminary planning is under way for a school-based trial in the future. Other approaches to imposed myopic defocus are likely to emerge in the near future.

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