Correction of myopia is the most common reason that patients visit an eye doctor. The incidence of myopia in the United States increased from 20% in the 1970s to 40% over the next four decades. In Asia, the incidence of myopia is more than 80%. It is expected to affect 50% of the earth’s population by 2050. The magnitude is also increasing, resulting in greater loss of vision from myopia associated with retinal detachment, macular degeneration, and glaucoma. Thus, understanding the etiology/mechanism of myopia is important in trying to control this vision-threatening disease.

Myopia is associated with increased duration and intensity of near-work, education, living in urban areas, lack of outdoor time, increased accommodative lag, esophoria, and introverted behavior. It also has been shown to have strong genetic origins. Tkatchenko et al. identified a low frequency risk allele of the APLP2 gene (amyloid precursor-like protein), which is found in both mice and humans, whose effect is related to the individual’s intensity of reading and results in myopic progression. They demonstrated that myopia arises from an interplay between environmental and genetic factors impacting the normal growth mechanisms of the eye.

In the early 1960s, Hubel and Weisel first studied the effect of the environment on visual development by using visual stimuli to alter cortical visual development. In a subsequent study, Raviola and Weisel sutured one eye of young stumptail macaques. This abnormal visual experience resulted in an enhancement of the normal process of postnatal eye growth, producing axial myopia in the sutured eye. It is important to note that this did not happen if the eye was totally occluded: a visual stimulus was necessary. In this experiment, atropine also prevented myopic development.

Shaef er et al. placed lenses in front of chickens’ eyes during early visual development. The animals’ eyes altered their length to accommodate for the lenses, adapting the eye’s length to keep the visual input in focus on the retina. The changes were almost linear and this occurred for both plus and minus lenses. Cutting the optic nerve had no effect on this process, demonstrating that directional intraocular blur controlled axial length, and brain feedback was not necessary. Interestingly, an intravitreal injection of atropine stopped the process. These studies have been repeated across species from chickens to monkeys to humans.

Smith et al. performed a series of studies that added to our understanding of emmetropization (adaptation of ocular components to prevent refractive error) and myopia development. First, they interposed either a translucent lens or ophthalmic lenses in front of only half of the retina, then they refracted the animal’s eyes, measured axial length, and performed magnetic resonance imaging. All three measures verified that, when minus lenses were interposed on half of the eye, half of the eye elongated (Figure 1). They then asked the most pertinent question: What happens if the eye is exposed to a multifocal lens (center plus, peripheral portion minus, or vice versa)? As occurred in their other experiments, the focused light controlled the growth of the eye, but it was not the central portion of the lens that determined axial length. It was the peripheral portion of the lens,
which focused on the peripheral retina, that controlled the direction and the amount of axial change. Smith et al. suggested that the peripheral lens covered more area of the retina than the center of the lens; thus, the peripheral lens controlled growth.

We know that the myopic eye is an elongated eye and thus not spherical. Correcting the myopic eye with traditional glasses and contact lenses leaves the peripheral retina relatively hyperopic. This peripheral hyperopic blur from traditional correcting lenses for myopia becomes the stimulus for an increase in axial elongation and this cycle is repeated with each correction.

Around the same time that these animal studies were being performed, several orthokeratology (ortho-K) studies serendipitously reported that ortho-K lenses worn at night slowed the progression of myopia. Ortho-K lenses flatten the central cornea by forcing the epithelial cells to move peripherally, resulting in steepening of the peripheral cornea. Thus, a patient fit with a -3.00 diopter ortho-K lens will flatten centrally by 3.00 diopters and steepen peripherally by 3.00 diopters, resulting in a 6.00-diopter shift. This change in corneal shape lasts for 2 to 3 days, with renewal each night. During this time, the steeper corneal periphery overcorrects the relative peripheral hyperopic defocus, which is the stimulus for axial elongation, thereby ameliorating the progression of myopia. This corneal configuration seems to be the optimal one for slowing myopia. Daily wear NaturalVue soft lenses (Visioneering Technologies, Inc., Alpharetta, GA) replicate the optics of ortho-K.

Another way to slow axial length increase is to biochemically block the signal for eye elongation created by peripheral hyperopic blur. This can be done with atropine. Historically, atropine 1% was used and was 80% effective. Currently, there is interest in low concentrations of atropine. The ATOM 2 studies suggest that lower dosages of atropine (even 0.01%) are effective in slowing the progression of myopia. I believe that the pendulum has shifted too far and studies will find that atropine’s effect is dose dependent to a significant degree.

The future of myopia control is great. Ortho-K has led to soft multifocal lenses to slow the progression. We will find the right concentration of atropine or some other pharmaceutical agent to slow myopia progression, or more likely we will combine them to create a more effective modality.

TO LEARN MORE


SEMINAL ARTICLE

CLINICAL CORRELATE
Chia A, Lu QS, Tan D. Five-year clinical trial on atropine for the treatment of myopia 2; myopia control with atropine 0.01% eyedrops. Ophthalmology. 2016;123:391-399.