Myopia (short-sightedness) is not only commoner in the Asia-Pacific region than elsewhere in the world, but the presence of myopia in many of the countries in this area is increasing at a rate that is almost epidemic.

In the recent past, myopia was considered to be entirely due to inheritance and there is no doubt that a family history of myopia in parents is a risk factor for myopia in children. The increasing prevalence of myopia, however, has affected populations with no previous history of the condition, such as the Inuit where previously a hypermetropic (long-sighted) population now demonstrates a significant prevalence of myopia.

In a study carried out in Singapore and Xiamen in China, findings are highly suggestive of the role of environmental factors in the genesis of myopia. A great deal of evidence supports the view that some feature of close work is involved, but obvious features such as accommodation (close focus) of the eye seem not to be involved.

The finding that visual deprivation in young animals (and humans) causes myopia is a clear indication that visual input is important in the control of normal eye growth (emmetropisation). Making animal eyes artificially long-sighted with negative contact lenses causes the eyes to elongate and become myopic to an extent that neutralizes the effect of the lenses. Visual deprivation is accompanied by biochemical changes within the eye, retinal dopamine levels being reduced while levels of vasoactive intestinal peptide are increased.

There is evidence that the retina itself can recognize an out-of-focus image and direct ocular growth to try to bring the image into focus. Certain cells in the retina (amacrine cells) appear to be involved in the process but currently the exact nature of the retina signaling that controls ocular growth is not known. It appears that biochemical signals from the retina reach cells in the fibrous outer coat of the eye (sclera) causing overgrowth of this layer and elongating the eye.

Much research in myopia has concentrated on the details of scleral overgrowth including the molecular genetics involved, as discussed by Prof. Roger Beuerman in this issue. In this regard, new techniques such as DNA array are proving useful. This and other techniques of cell and molecular biology hold promises of eventually understanding the complex processes involved in eye growth, and in the long-term, by manipulation of the environment or by suitable medication, to prevent or ameliorate myopia, which currently carries significant economic and other penalties and, in some cases, a risk of sight-threatening complications.
In a normal eye the focus of light is very precise, the length of the eyeball being crucial in this respect. A small change of a fraction of a millimeter in ocular length is sufficient to render images no longer sharp and in focus. The retina at the back of the eye is a specialized light sensitive outgrowth of the brain with many of the characteristics of brain tissue. In the outer layer of the retina are the light sensitive photoreceptors that respond to light rays reaching them and initiate an electrical response that is transmitted through the other cells of the retina to form a message that is transmitted to the back of the brain for interpretation.

In Singapore the majority have to wear glasses or contact lenses for the correction of myopia (short-sightedness or near-sightedness). An increasing number of persons with myopia are undergoing refractive surgery, as described by Dr. Chan Wíng Kwong elsewhere in this issue. Epidemiological studies in Singapore, China, and Hong Kong, referred to in two articles in this issue, have shown that myopia is increasing in prevalence in these countries in an almost epidemic fashion. Genetic inheritance and environmental factors including close work play a dual role in the genesis of myopia.

One of the characteristics of myopia is an overgrowth of the sclera and there is evidence that the scleral cells are directly involved. An understanding of the cellular events associated with scleral overgrowth may lead the way towards targeted drug therapy aimed at specifically modifying the activity of these scleral cells.

Figure 1: In a normal eye rays of light from a distant object are focussed in the photoreceptor layer of the retina. In a myopic eye the length of the eyeball is increased so that light rays are now focussed in front of the retina. The increased length of the globe is related to an overgrowth in the tough connective tissue sclera that forms the wall of the eye.
In the normal eye, rays of light from a distant object are precisely focused in the photoreceptor layer of the retina (Figure 1). The length of the myopic eye is increased compared with normal so that the focal point of distant rays lies in front of the retina and the retinal image is correspondingly blurred. An increase in the length of the eye by one millimeter creates an optical error of three dioptres (300° in Singapore). The outer wall of the eye is the sclera, a biological polymer largely composed of collagen and other structural molecules together with the scleral cells that manufacture the extracellular components of this tissue and control the growth of the eye.

In myopia, one of the characteristics is an overgrowth of the sclera and there is evidence that the scleral cells are directly involved. An understanding of the cellular events associated with scleral overgrowth may lead the way towards targeted drug therapy aimed at specifically modifying the activity of these scleral cells.

Some drugs have a widespread action on the eye and have been shown to decrease the progress of myopia. One such drug is atropine that can decrease myopia in animal models and in affected humans. Atropine is not normally found in the body but has been used to block the action of a common neuro-transmitter acetylcholine (agonist in Figure 2). Scleral cells in animals have been shown to have acetylcholine receptors and more recently we have demonstrated the presence of these receptors in human scleral cells.

Using atropine as a probe, we are investigating how this substance functions to diminish myopia. Uncovering the biochemical actions within the cell will provide information needed to develop therapeutic drugs. There are biochemical pathways from the cell membrane covering the surface of the cell to the nucleus where activation of genes occurs when receptors in the cell membrane are activated (Figure 2).

In SERI we have found that a very potent growth factor, fibroblast factor 2 is regulated by atropine. This growth factor is decreased in myopic sclera. When atropine is used in the eyes of animals made myopic (by modification of the visual input), this growth factor increases to match the level seen in normal eyes coincidentally with a decrease in myopia. The story does not end here as other proteins acting as enzymes (metalloproteinases) modifying the structure of the sclera are also involved.

Although abnormal growth of the sclera appears to be the final abnormality resulting in myopia, this abnormal growth appears to result from biochemical signals generated in the retina in response to an inappropriate retinal image.

Investigation of retinal cell signaling and how these signals are transmitted from retina to sclera are among areas of research identified for further study in SERI. Atropine is a muscarinic antagonist blocking the action of all classes of muscarinic receptors. There is evidence that only one class of muscarinic receptor may be involved in myopia and one aim of SERI’s research is to identify more specific drugs that can be useful in the control of myopia.

Currently in extensive clinical trials in Singaporean schoolchildren, the effects of atropine on the rate of progress of myopia is being compared with pirenzepine, a more specific antagonist of the receptor thought to be implicated in the genesis of myopia.
Paradigm Shifts
in Ophthalmic Surgery

Singapore National Eye Centre 5th International Meeting
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Epidemiology of Myopia

Seang-Mei Saw
Department of Community, Occupational & Family Medicine, National University of Singapore and Epidemiology Unit, Singapore Eye Research Institute

Myopia is a common eye disorder and high myopia (at least –6.0 Diopters) is associated with potentially blinding complications such as glaucoma, cataract and retinal degeneration. The prevalence rates of myopia are highest in Asian countries and lower in predominantly white populations such as the US and Europe. It has been noted that the prevalence rates of myopia decrease with age and perhaps there is a cohort effect, the rates of myopia being higher in younger than in older generations.

The prevalence rates of myopia are highest in certain Asian cities such as Singapore. Several epidemiological studies of myopia, including studies in school children, have been launched to investigate possible risk factors for myopia. Reading and parental myopia appear independently to predict myopia in Singaporean children. In addition, parental myopia modified the effect of reading on myopia, suggesting that a possible gene-environment interaction may exist.

The prevalence rates of myopia are highest in Asian countries and lower in predominantly white populations such as the US and Europe.

Several epidemiological studies of myopia, including studies in school children, have been launched in Singapore to investigate possible risk factors for myopia. A large concurrent cohort study was initiated in November 1999 (SCORM—Singapore Cohort Study of the Risk factors for Myopia). Approximately 2000 children from three schools in the northern, eastern and western parts of Singapore aged seven to nine years have been recruited. Detailed information on near work, night-lights and other factors has been obtained.

Yearly ocular examinations using logMAR visual acuity, cycloplegic autorefraction and biometric ultrasound measurements have been made. The children will be followed up till they are in primary six (12 year old). The multivariate adjusted odds ratio of early onset myopia (at least –3.0 Diopters) for children who read more than two books per week is 3.05 (95 percent CI 1.80 to 5.18). Parental history of myopia was positively related to myopia. Books per week interacted with parental myopia for early
onset myopia (at least –3.0 Diopters). There was no association between night light exposure before age two years and myopia.

In summary, reading and parental myopia appear independently to predict myopia in Singaporean children and in addition, parental myopia modified the effect of reading on myopia, suggesting that a possible gene-environment interaction may exist. The on-going SCORM study complements existing nation-wide myopia prevention programs in Singapore such as the Singapore Myopia Registry and the National Myopia Prevention Program, Ministry of Health.

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As already noted, myopia is not only common in the Asia-Pacific area but is becoming an increasing problem in East Asian countries including Singapore, Japan, and China. Myopia is also a very common eye problem in Hong Kong. It has been found that over 90 percent of students in the Chinese University of Hong Kong were myopic.

Though myopia is a common condition, the exact underlying causative mechanism remains unclear. Both nature and nurture appear to play important roles in the development of this common ocular disorder. Genetic factors have been emphasized in various studies.

Goss et al. reviewed a number of studies, some of which proposed an autosomal dominant mode of inheritance, others autosomal recessive, and still others, an X-linked pattern of inheritance for myopia. Environmental factors such as near work, on the other hand, have also been shown to be associated with the development of myopia in different studies.

In Hong Kong we undertook a study in primary schoolchildren to assess the prevalence of the condition in this age group and to identify risk factors for myopia in primary school children.

The study was conducted from 1998—2000 in nineteen primary schools randomly selected throughout Hong Kong. With parental consent school based ophthalmic examinations were carried out on more than 7000 children aged 5—16 years. The eye examinations included:

1. Visual acuity testing
2. Cover test (to detect ocular muscle imbalance or latent squint)
3. Assessment ocular movements
4. Cycloplegic refraction (determination of the optical strength of the eyes with the focussing power of the eyes temporarily paralyzed by eye-drops) and
5. Ocular biometry (measurement of the length of the eye and its various compartments by the use of ultrasound echography).

Preliminary data analysis showed that more than 36 percent of the study subjects were myopic. Both a parental history of myopia and visual tasks appeared to be significant risk factors for the development of myopia in these children. Among the myopic children more than 3 percent had high myopia of more than six dioptres. A more detailed analysis of the results is currently being undertaken.

In summary, Hong Kong has a high prevalence of myopia in primary schoolchildren. This implies a higher future risk of their developing myopia-associated eye diseases such as glaucoma, retinal tear formation, retinal detachment, macular haemorrhage degenerative chorio-retinal disease and cataract. The social cost will also be very high! Both nature and nurture are implicated in the development of myopia. Further research to delineate more exactly the causation is needed before effective preventive measures can be implemented.

Myopia is becoming an increasing problem in East Asian countries. It is a very common eye problem in Hong Kong, with over 90 percent of students in the Chinese University of Hong Kong being myopic.

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In the Riau province of Sumatra, we found a high rate, over 60 percent, of low myopia in the youngest age range but a very low rate, under one percent, of the more severe high myopia that is more associated with visual loss. Myopia rates decreased with age and increased with socio-economic status in our study, as has been elsewhere.

Myopia in urban Asia is an increasing public health problem of epidemic proportions with extensive economic and health repercussions. Ocular complications of high myopia in particular, such as retinal detachment, are responsible for significant visual disability. Evidence suggests that environmental changes associated with increasing urbanization and acting on susceptible populations may be responsible for the increasing rates. Current theories of aetiology implicate the effects of near-work, and perhaps intensive schooling, as a likely influence. To help clarify the interplay of gene/environment interactions, it is useful to know the relative frequency of myopia and other refractive errors in populations of similar genetic background but differing environmental influences.

The population of rural Sumatra is of similar genetic origin to the Malay population of Singapore but is exposed to differing environmental influences with more recently introduced and less intensive schooling. We thus recently conducted a population-based prevalence survey of refractive errors in the Riau province of South Sumatra. Over a thousand adults in six villages were assessed using a hand-held “auto-refractor” that automatically measures refractive error without the need for an

The prevalence (%) of all myopia (worse than –0.5 Dioptries) in rural Indonesians age 21-29 compared to Singaporeans (male army recruits mean age 19 years).
optometrist. We found a high rate, over 60 percent, of low myopia in the youngest age range (worse than −0.5 Dioptres) but a very low rate, under one percent, of the more severe high myopia that is more associated with visual loss (worse than −6.0 Dioptres). This compares to Singaporean male army recruits who had rates of high myopia of five percent (Malays) to 14.8 percent (Chinese). Myopia rates decreased with age and increased with socio-economic status in our study, as has been seen elsewhere. Myopia rates decreased with age and increased with socio-economic status in our study, as has been seen elsewhere. This supports a hypothesis that suggests myopia is an increasing health problem in the young throughout Asia, including rural Indonesia. This may reflect changes in access to schooling and hence the influence of near-work activities.

REFERENCES


Refractive Surgery for the Correction of Myopia

The refractive surgery technique most widely used today is laser in-situ keratomileusis (LASIK). A thin corneal flap is cut and the laser beam is applied to the underlying corneal tissue. The laser is controlled by a computer and the precise number of shots is delivered in a pattern necessary to reshape the cornea to correct the degree of myopia and astigmatism present.

Most of the refracting power of the eye resides at the air/tissue interface presented by the front surface of the cornea. In myopia the refracting power of the cornea is too great for the axial length of the eye, so that the image of distant objects is formed in front of rather than in the plane of the retina. In addition to the resulting lack of optical focus, the increased length of the globe is associated with potentially blinding complications.

Chan Wing Kwong
Singapore National Eye Center
such as retinal hemorrhage, retinal detachment and macular degeneration. The optical defocus can be corrected by the use of spectacles or contact lenses or more permanently by the use of refractive surgery. However, none of these techniques for the optical correction of the myopic eye reduces the risk of sight threatening complications.

Refractive surgery is the branch of ophthalmology that specializes in the surgical correction of myopia, so as to eliminate the need for spectacles or contact lenses (for vocational, cosmetic, or reasons of convenience). The history of surgical correction of myopia dates back to the 1950s, when ophthalmologists used fine diamond blades to make cuts in the cornea to reduce the focusing power of the eye in a procedure called radial keratotomy (RK). RK was very popular in the US in the 1970s to 1980s as it could correct lower degrees of myopia and astigmatism satisfactorily. RK was also performed in Singapore in the 1980s. It never became popular worldwide, as it was difficult surgery to perform and was not as accurate or as stable as ophthalmologists would wish. In the late 1980s, the excimer laser was invented and it revolutionized refractive surgery.

The excimer laser generates a laser beam from two rare gases, argon and fluorine. The light generated by this laser is in the ultraviolet wavelength of 193nm and is invisible to the human eye. The excimer laser emission is very energetic and with extremely short duration pulse times in the picosecond range achieves a high energy density at the point of focus that can disrupt molecular bonds in the cornea without generating heat or producing collateral damage to surrounding areas. It is a precise and very accurate laser that can remove small (fractions of a micron) amounts of corneal tissue per pulse of laser. By using a computer to control the number and pattern of laser pulses applied to the cornea, the cornea can be reshaped to correct myopia and astigmatism.

The refractive surgery technique most widely used today is laser in-situ keratomileusis (LASIK). The suitable person for LASIK must have a degree of myopia and astigmatism that is within the correction range of the technique. They must understand the benefits and risks of undergoing LASIK and must not have pre-existing eye problems such as cataract, glaucoma or diabetic eye disease.

Unlike earlier techniques using the excimer laser in which the laser beam was applied to the surface of the cornea, in LASIK a thin corneal flap measuring 0.16mm thick and 8mm in diameter (the cornea is 0.5mm thick and 11mm in diameter) is cut with a microkeratome, an instrument capable of cutting the corneal flap with the required degree of accuracy, and the laser beam is applied to the underlying corneal tissue after the corneal flap has been temporarily folded back.

The laser is controlled by a computer that has been programmed by the ophthalmologist, according to the patient’s degree of myopia and astigmatism and the precise number of shots is delivered in a pattern necessary to reshape the cornea to correct the degree of myopia and astigmatism present. After the laser application, the corneal flap is folded back to its original position without the need for stitches and the surgery is complete. Visual recovery is rapid, many patients achieving good functional vision in 24–48 hours with minimal discomfort during the recovery period. The corneal flap bonds spontaneously with the underlying cornea within a week so that normal activities can be resumed thereafter.

More than 10,000 LASIK procedures have been performed at the Singapore National Eye Center. In general, 90 percent of eyes that undergo LASIK achieve an unaided vision (no spectacles or contact lenses) of 6/12 or better (good enough to drive a car by LTA standards) and 50 percent have vision of 6/6 or better (perfect vision). The specific success rate of each individual patient depends on the exact degree of myopia and astigmatism that is to be corrected. LASIK has proven to be a very effective, predictable, stable and safe option for those who are unwilling or unable to use spectacles or contact lenses to correct their myopia. However, like any other surgical procedure, complications and side effects do occur. The more common problems are undercorrection (not enough laser effect so the eye is still...
myopic) and overcorrection (too much laser effect so the eye becomes hyperopic or longsighted). Other side effects include dry eyes and seeing glare, haloes and starbursts around lights at night. These side effects are usually temporary. Serious sight threatening complications such as infection of the cornea is extremely rare. Nevertheless when a person is considering whether or not to undergo refractive surgery, risks and costs have to be weighed against needs and benefits.

An improvement in LASIK methodology is now being developed. This is wavefront guided LASIK (also known as customized LASIK). The fine optical aberrations present in every person’s eye are measured (with an aberrometer) and the laser pattern is customized to correct not only the degree of myopia and astigmatism, but also these optical aberrations. It is anticipated that if these fine aberrations are also corrected, the results of refractive surgery will be even better than with the present technique with an even greater number of patients achieving perfect vision.

The Singapore National Eye Center is one of the sites around the world participating in a multi-center research trial to evaluate this new technique. If it proves to be superior to the current LASIK technique, it will be offered as a treatment option for patients who wish to have refractive surgery in the future.

A new solid state refractive laser may bring refractive correction to many more Asian people.

Q-Vis Ltd., based in Herdsman, Perth, Western Australia, has developed and received international marketing approval for a novel solid state ultraviolet laser which can do the same job as an excimer laser for the treatment of myopia. The solid state laser technology was spun out of the Lion’s Eye Institute in Perth, currently the largest eye research facility in the Southern Hemisphere.

The excimer laser runs on gas and produces a far ultraviolet wavelength that is difficult to pass through the atmosphere and necessary optical devices. The cost of excimer lasers and the frequent maintenance required are also very expensive resulting in a costly surgical procedure which is available only to very few people suffering from myopia worldwide. It is estimated about two percent of the myopic population in developed countries have been treated, while in many Asian cities such as Singapore and Hong Kong up to sixty percent of the population have myopia.

The Q-Vis solid state quantum lasers is smaller than an excimer and requires much less maintenance. It can also be produced for less capital cost than the current excimer lasers. It produces a 213-nm wavelength, which passes more readily through water vapor, air impurities and optical devices.

In the next stage of development the laser will be placed at the prestigious Singapore National Eye Center in the Singapore Eye Research Institute for further research studies and early clinical trials on Asian patients with myopia. Meanwhile, Phase III final trials on humans are about to begin in the US.

A new solid state refractive laser may bring refractive correction to many more Asian people.