Introduction

The emmetropization process involves monitoring the ocular growth to match the refractive power of the eye. Myopia occurs when the ocular axial length exceeds the value corresponding to the refractive power of the eye. This chapter will report the current understanding of the emmetropization process and present recent findings of myopia research.

Eye development and emmetropization

The ocular refractive status refers to the locus of the optical focus in relation to the retina during minimal accommodation. In the ideal eye the distance from the cornea to the retina (i.e. axial length) are in concordance with the total refractive power and the light entering the eye will form a sharp image on the retina, that is an *emmetropic* eye. In a *hyperopic* eye the light is focused behind the retina which is due to a too low refractive power alternative a too short axial length. In a *myopic* eye the light is focused in front of the retina, which can be due to either a too high refractive power alternative a too long axial length. The axial length of the eye ball in an adult is approximately 24 mm and to focus the light onto the retina the optical power has to measure approximately 60 dioptres. The refractive elements of the eye are the corneal surface, which accounts for approximately 42 diopters of the total refractive power and the crystalline lens, which accounts for approximately 18 diopters. In a newborn full term child the axial length is shorter (~17 mm) and the refractive power higher (~85 dioptres). The cornea counts for ~50 diopters and the crystalline lens 35 diopters. The eye bulb reaches almost full axial length at 3 years of age but the ocular growth does not cease until 14-15
years of age. The eye thus only grows approximately 1 mm from 3 years of age to early teenage. When growing, the relation between ocular axial length and ocular refractive power has to be adjusted simultaneously to maintain a well working optical system. This mechanism is referred to as the *emmetropization* process.

Emmetropization regulates the shape of the refractive media, by detecting the refractive error of the eye at rest and initiating ocular changes to minimize the refractive error. In experimentally induced focusing errors by means of positive or negative lenses, the net result of the initiated ocular changes was that the eyes become approximately emmetropic with the lenses in place (Schaeffel et al. 1988). When the lenses were removed, the eyes showed a refractive error in the opposite direction, hyperopic after imposed myopia and myopic after imposed hyperopia. After removing form deprivation filters in chick eyes, the myopia quickly decreased to negligible levels, provided that optical correction was not introduced and that the treatment was initiated at a sufficiently early age (Wallman & Adams 1987).

When inducing monocular deprivation in animals the occluded eye ball became longer than normal. The difference in length was over 1 mm and the sclera of the on the posterior wall of the occluded eye was thinner. This effect was found to be largest on younger animals (Wiesel & Raviola 1977). Even a modest degree of constant form-deprivation using partially occluding filters would trigger an axial length growth inducing myopia. The denser the filter is the larger the myopia became (Smith & Hung 2000). The fovea is not essential for normal refractive development as foveal ablations has no apparent effect on emmetropization. However, the peripheral retina, in isolation, can regulate emmetropizing responses and produce anomalous refractive errors (Smith et al. 2007). Hyperopia is more common than myopia in early infancy, and most individuals undergo emmetropization to a refractive state of low hyperopia rather than precise emmetropia (Irving et al. 1996). A few are born myopic and this has to be reversed before reaching young adulthood because the eye ball can grow, but it can not shrink.

**Current research in myopia**

While hyperopia is considered relatively harmless, myopia is clearly linked to eye health hazards. Myopia is considered to be the leading cause of visual impairment (World Health Organization, 2000). Immense effort is put into understanding the underlying mechanisms of myopia progression and the biological, neurophysiological and environmental bases for
myopia development. The goal is to find predictors to show who will develop myopia and to begin prophylactic treatment in them to minimize or hinder its progression.

The prevalence of myopia is increasing globally and myopia has reached epidemic proportions in parts of East Asia with up to 70% to 90% of 17- to 18-year-olds in the region affected (Lin et al., 2001; Saw et al., 2005; Zhao et al., 2000). A Swedish prevalence study in 12-13 year old school children from 2000 showed myopia in 49.7% (Villarreal et al. 2000). Previous prevalence studies in Scandinavia revealed considerably lower values for myopia. In Denmark, 1983, Fledelius reported a prevalence of 30% myopia in individuals 16 years of age and older (Fledelius 1983). In Finland, 1980, Laatikainen found a prevalence of 29% in the 14- to 15-year-olds (Laatikainen & Erkkilä 1980).

During the last decade the understanding in the mechanisms of myopia development have increased through ocular biometry, i.e. measurements of the intraocular parameters affecting the refractive state of the eye. From the CLEERE multicentre study in US it seems clear that both early-onset myopia (childhood) and late-onset myopia (15-18 y) typically involve excessive enlargement of the eye where the axial length is prolonged in the absence of compensatory lens changes (see table 1 below for details).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aged 6 years</th>
<th>Aged 14 years</th>
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<tbody>
<tr>
<td>Spherical equivalent refractive error (D)</td>
<td>+0.85 ± 0.86</td>
<td>-0.28 ± 2.48</td>
</tr>
<tr>
<td>Corneal power (D)</td>
<td>43.67 ± 1.48</td>
<td>43.37 ± 2.48</td>
</tr>
<tr>
<td>Anterior chamber depth (mm)</td>
<td>3.54 ± 0.25</td>
<td>3.66 ± 0.29</td>
</tr>
<tr>
<td>Vitreous chamber depth (mm)</td>
<td>15.50 ± 0.61</td>
<td>16.44 ± 1.19</td>
</tr>
<tr>
<td>Crystalline lens power (D)</td>
<td>24.23 ± 2.16</td>
<td>22.38 ± 2.09</td>
</tr>
</tbody>
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Table 1. Summary of the main findings of the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study, a US multicentre 6-year study on normal ocular growth in 2583 children aged 6-14 years (Zadnik et al., 2003)
Myopic eyes are larger in all three dimensions (i.e. equatorial, anterior-posterior, and vertical axes). Twin and family studies indicate a genetic predisposition to myopia (Goss & Wickham 1995) and a parental history of myopia is well known to be a high risk factor for developing myopia. The prevalence with two myopic parents is 30% to 40%, whereas it is reduced to 20% to 25% in children with one myopic parent, and to >10% with no myopic parent (Mutti et al. 1996). Anterior and vitreous chamber depths are larger as the risk (the number of myopic parents) of myopia increases.

Although the eye growth ceases at around 15 years of age, between 8 and 15 % of the myopes develop their myopia between 15 and 18 years of age (i.e. late-onset myopia) with slow progression to levels rarely exceeding 2 D. The environmental risk factors most often cited include education, urbanization and near work but the nature of their interaction with genetic factors remains unclear (Saw 2003). Late-onset myopia has been attributed to near work, especially when the work has a high level of cognitive demand. The influence of electronic displays on myopia progression is still not clear and a better understanding of the interaction of accommodation and the oculomotor system to these displays need to be consolidated, especially as a new generation of 3D displays is forthcoming. Interestingly, sustained accommodation has been shown to reduce intraocular pressure by up to 2.4 mm/Hg and there is recent evidence for a relationship between IOP and myopia in a Japanese population.

Refractive errors in prematurely born children

Low birth weight is one factor influencing the refractive development. Premature infants are more prone to develop myopia from an early age and myopia development can continue up to 2 years of age. The incidence of myopia in preterm infants ranges from 1% to 16% and the children may remain myopic later on in childhood and adolescence. Retinopathy of prematurity (ROP) is a disease affecting prematurely born infants due to an immature eye and incomplete development of the retinal blood vessels. The incidence of ROP among prematurely born infants is approximately 40% (Holmström et al. 1993). If mild ROP is present the incidence of myopia increases to 17% to 50%. The more severe the ROP is the higher the incidence of myopia became. Some populations show up to 100% incidence of myopia in the advance stages of the disease. The biometric components found to contribute to the refractive error in prematurely born children include a shallower anterior chamber and a shorter axial length (15 mm), increased lens power (45 D) and increased corneal refractive
power (54 D). The mechanism of myopia development thus seems different from that in full term children. The available treatment options for ROP are cryo therapy and laser treatment and it is very difficult to differentiate the effects of the disease and the effect of the treatment on myopia. Treated infants have a higher incidence of myopia than non-treated infants. At the same time, the more advanced stages of ROP are more likely to need more treatment.

Research on myopia prevention

Today the best single predictor for developing myopia is cycloplegic refraction. Children with hyperopia of 0.75 D or less at a mean age of 8.6 years have been shown to have a sensitivity of 86.7 % and specificity of 73.3 % for developing myopia (Zadnik et al. 1999). The question is how refractive errors should be treated while the eye still is growing. There is unfortunately no straightforward answer on that question. The clinical tradition recommends under-correcting myopia and fully correcting hyperopia in children before entering puberty. The philosophy is to reduce the accommodative demand in order to not induce transient myopia and in the long run manifest myopia. One theory of myopia progression is based on the observation that myopic children have a higher lag of accommodation than non-myopic children. The hyperopic retinal blur that results from a high lag of accommodation during near work is hypothesized to cause an increased rate of axial length growth. However, several studies could not find any change in axial growth when prescribing near reading addition, which minimizes or eliminates the lag of accommodation. The CLEERE study suggests that high accommodative lag is a by-product of myopia, rather than the causative factor. Pharmacological treatment by Pirenzepine, a muscarinic receptor antagonist, shows promising results in reducing the myopia progression. In a recent US study a significant 0.27 D reduction in myopia progression was found after the first year of treatment and a 0.41 D overall reduction after the second year (Siatkowski et al. 2004). Development of new pharmacological agents for controlling scleral growth is today a topic for discussion. This is an exciting and hopefully promising treatment option for the future.

Several challenges for myopia research society still exist. The current treatment options are more based on a clinical experience than scientifically proven evidence. The majority of myopia research performed is based on animal studies. Human research is required to fully understand the interaction of genetic and environmental risk factors for developing myopia.
Further, better tools for measuring near work exposure are required in order to fully understand the effect of near work on myopia.

Conclusions

A clear optical image is of main importance for a normal ocular development. The emmetropization process regulates ocular growth and is based on defocus of the peripheral image on the retina. Neural mechanisms involving the fovea or the visual cortex do not seem to take part in the process. Myopia due to excessive axial length of the eye has increased globally and has become a major concern with regard to ocular health. Great efforts have been made in trying to understand the mechanisms of ocular growth and how to retard myopia progression.

References


