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# Current Concepts in Myopia Control

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**ABSTRACT**

*Current animal and human models of myopia progression show that beside genetics, there are several environmental factors that contribute to the axial elongation process, the underlying cause for progressive myopia. During last years, extensive research in this field revealed some apparently independent mechanisms, which play an important role in myopisation. Understanding of these processes led to the introduction of novel techniques in optical corrective approach, pharmacological interventions as well as suggestions in environmental control. Many of these methods were proven effective for specific cases; however follow up sometimes shows efficacy drop and the catching up of myopia on longer term. In the present paper an overview of pharmacological and optical corrective options as well as environmental manipulation for the purpose of myopia control is presented and their efficacy is discussed.*

***Key words**: refractive error, myopisation, myopia control, retinal defocus, near point stress*

## Introduction

Progression of myopia is the most frequent vision-related problem in second to third decade of human life. Myopic person is highly dependent on his or her visual aid and needs relatively frequent change of prescription. Excessive growth of the eyeball in progressive myopia is also associated with structural changes of the posterior pole, including choroidal and retinal degeneration and the risk of retinal ablation. Increased prevalence of cataracts and primary open-angle glaucoma is also noted in highly myopic patients.

During last years, new data showing significant increase in myopia prevalence were published[1]; at the same time, some new concepts about myopia progression were introduced. Current animal and human models show that not only genetic factors are responsible for axial growth; there is also strong evidence of several environmental factors, which regulate eye length. While over 30 myopia-associated genes (MYP genes) were identified until 2012, it is debated, how many of them are truly responsible for myopisation. Moreover, it is postulated, that most of them are only associated with poor emmetropisation process, which causes myopia under certain environmental conditions to grow. This should especially be true for the late onset myopia; early onset myopia, which typically ends up in higher degrees of »minus«, is believed to be more genetically determined. The genetics part will not be discussed further in this paper, since it represents a relatively new area of research, in terms of myopia control, and there are no practical applications in humans yet.

Already decades ago, extensive near work was deemed a major environmental factor associated with myopia. While near point stress and sustained near work are still considered important, their influence seems to be rather complex. Research revealed several mechanisms, which regulate axial length of the eye, and only some of them are associated with near work.

## Influence of Light Spectrum on Myopisation Process

Several studies confirmed that children, who spend more time outdoors, reach lower levels of myopia. A particularly comprehensive one was the Orinda study[2], which also showed that the risk of becoming myopic is positively correlated with the number of myopic parents.. On the other hand, parental risk factor could partially be counterweighted by the time spent outdoors. It was also shown, that it is not the outdoor physical activity, which plays a role in protection from myopia, nor the typical absence of near work, but the light intensity and spectrum[3]. Higher levels of illumination (typically over 5.000 lux) and the natural spectrum of wavelengths compared

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to typical skewed indoor light profile (more long wave light) apparently contribute most to this effect. A study by Donovan et al.[4] found also that myopia progresses significantly more during winter months compared to summer months, however, it is still discussed, whether this could be attributed to more time spent outdoors during summer, or to less near work typically exhibited during that period. Another recent study by Sherwin et al.[5] used conjuctival ultraviolet autofluorescence as a biomarker of outdoor light exposure. The authors found that higher levels of cumulative UV light exposure had even stronger protective effect against myopia then the »hours per day« spent outdoors.

The protective effect of the sunlight on myopia growth is more evident at an early stage of developing refractive error; once children do become myopic, it becomes less potent. This fact raised some speculations about the possible positive influence of short wavelength – and UV light; when children start wearing glasses, less UV light enters the eye. Certainly, the amount of UV light that reaches the phakic eye's retina is very small even without wearing glasses, and there is no evidence of whether any of the retinal receptors are able to respond to it in terms of axial length regulation. Recent research shows though that intrinsically photosensitive retinal ganglion cells containing melanopsin regulate circadian cycles including increased dopamine levels and melatonin suppression in the retina, when light levels are high. These cells have peak response to short wavelength light of 470 nm. Low dopamine levels were previously found to correlate with myopisation in monkeys[6], and high dopamine levels were reported to have protective effect on myopia development[7]. This would imply that the timing of optimal illumination could be one strategy by which myopia can be slowed down. There is a need for further research in order to clarify the complex influence of light intensity, its spectrum, and possible circadian disturbances on myopia development.

## *Axial elongation mechanisms attributed to retinal defocus*

Normally, the non-presbyopic eyes adjust to near task by accommodating to the object's plan. However, this adjustment is somewhat inaccurate – the focus typically lags behind the retina by about 0.5 D for a 2.5 D demand, which represents a hyperopic defocus. Mutti et al. and some other authors found that children having progressive myopia do experience larger lags of accommodation[8]. Hence, major plans for optical intervention were directed towards manipulating the lag, as discussed later.

Animal models have shown that the axial growth of the eye is guided by several independent mechanisms, some of them being of local retinal character. Experiments with monkeys have shown that deformation of sclera, due to imposed defocus, can occur even in a hemi-field-way. When the visual field of the monkey's eye was partially occluded, deprivation myopia with scleral stretching developed only in corresponding area of the globe[9]. Furthermore, it was shown in monkeys that foveal input is not essential in regulation of eye length; it is more the periphery of the retina that is responsible for this[9]. Since accommodation is led almost exclusively by foveal nerve fibers, one could conclude that accommodation itself is not the triggering mechanism of axial elongation.

In animal studies it was shown that even with optic nerve cut, the eye is still susceptible to imposed defocus and will grow in the length if focus is lagging behind the retina. This means that visual feedback is not the only mechanism by which the eye regulates its shape.

It was long not clear, however, how retina is able to detect the sign of defocus since the same extent of positive or negative defocus makes the same blur at the retinal plan. Fischer et al.[11] and Bitzer and Schaeffel[12], have shown in chicken that retinal amacrine cells are able to detect and report the sign of defocus via expression of transcription factor ZENK. Knowing that peripheral defocus is of greater importance for the axial length guidance, many attempts were made later on to influence the image shell on the retina in terms of maintaining central focus at the fovea and at the same time shifting the peripheral focus inwards the eyeball. This was done via modifications of optical devices – first with conventional, then concentric progressive addition glasses, and later with dual-focus contact lenses.

## *Spectacles: bifocal and progressive addition lenses (PAL)*

Beside their general use for correction of presbyopia, bifocal and PAL glasses are infrequently used in children with accommodative insufficiency, accommodative infacility and near esophoria to reduce near point stress and / or facilitate binocularity. Already decades ago, there were some indices that this sort of lenses might inhibit myopisation and practitioners occasionally prescribed them in young progressing myopes; alternatively, sometimes a separate pair of glasses with decreased amount of minus was prescribed for near work. The COMET study[13] has finally shown that children with larger lags of accommodation can indeed benefit from PAL lenses. The group fitted with these lenses increased in myopia less than the group of their counterparts fitted with single vision (SV) lenses. Later a discussion arose, whether the effect of the addition in lower portion of the lens was due to decreasing the lag of accommodation, or it was the peripheral defocus of this part of the lens that made the myopia slow down – under assumption that children actually used the far portion of the lens when reading. The aim of the COMET 2 study is to clarify this issue, but it remains clear that, as shown in COMET 1, near phoria is an important factor, as it can cause a greater than normal lag of accommodation and thus represent a source of visual stress and possibly a factor in myopia growth. Therefore, some authors introduced experiments with bifocal lenses combined with prisms[14]. The results showed a slight benefit of prismatic support to the convergence with base-in prisms, which is not entirely consistent with the idea of decreasing esophoria. In this particular study, myopia in the group with prismatic bifocal glasses increased least, following by the group with conventional bifocals, and the group with single vision lenses. Interestingly, in early onset myopic group of children, the extent of lag of accommodation was not associated with the rate of myopia progression, but children wearing PALs still profited from them[14] – they progressed by 0,35 D, while children wearing SV lenses progressed by 0.52 D per year.

Beside conventional PALs, a different type of multifocal glasses was developed to address the peripheral focal plan. These concentric PALs, the so called »radial refractive gradient spectacle lenses«, feature a circular plus power addition in the periphery, in order to shift the image shell in the peripheral retina to the hyperopic side; the central part of the lens consists of single vision optics and serves viewing at all distances. The influence of these lenses on myopia progression was proven statistically significant[16], however, clinical relevance remains questionable. The distorted vision on secondary gaze through these lenses leads to poor acceptance by the patients, so this type of glasses did not find application in clinical praxis yet. On the other hand, the principle was successfully applied in contact lens design.

### *Dual-focus contact lenses*

Soon after the introduction of peripheral defocus theory, attempts in contact lens design were made in order to achieve the altered image shell with peripheral focus at the myopic side (inside) the retina. Standard bifocal contact lenses were not suitable for this purpose, since they form two foci, the far and the near, in the center of visual field simultaneously; the use if either is determined by neural discrimination and cortical selection of the user. On the other hand, bifocal lenses for myopia control are made with relatively large central part including distance refraction with the add part pushed further out to the periphery. This part is not intended for near vision use under any circumstances; it only serves to achieve the peripheral myopic defocus while the eye is fully accommodating to near objects. This lens design is adapted to relatively large pupils of young myopes and cannot compare to standard bifocal soft contact lenses, which usually use the »center – near« concept. Several successful implementations of dual-focus lens designs were reported in studies[17,18], and several patents on the lens design were announced. The approach with this type of visual correction is very new, and there have not been any long-term results presented yet. Some statistics have shown that dual-focus lens effect on myopia progression diminishes with time; at the International Myopia Conference in 2010, the early marketing of dual-focus contact lenses was criticized, as there was still a lack in follow-up for this procedure.

Actually, any type of conventional minus-powered single vision contact lenses causes blurred myopic defocus at some degree of excentricity due to transition from optical zone to the peripheral part of the lens; this was recently proven by Backhouse et al.[19]. However, the effect in this case is design dependent, and the extent of defocus is largely variable, depending on the size of the patient's pupil and anterior chamber depth. This might explain why the results of numerous studies, comparing the correction of vision with standard SV spectacle lenses and standard SV contact lenses in regards to myopia progression, are so inconsistent.

### *Ortho-K contact lens fitting*

Ortho-K is a contact lens wearing regime, where RGP contact lens with specific, pseudo-flat fit design, are worn overnight to flatten the central part of the cornea. Therapeutic effect is observed after the removal of the lens, typically lasting the whole following day.

Already at the introduction of Ortho-K contact lens fitting procedure, it was found that this technique could inhibit myopia[20]. This and later studies however found that after concluding therapy, myopia catches up. As the discussion of image shell form at the posterior pole gained attention and peripheral hyperopic defocus became an important factor in the explanation of axial growth, Ortho-K effect was found to have similar effect to dual-focus contact lenses due to its modification of peripheral focus. Extensive research in this field was done by Queiros et al.[21].

### *Effectiveness of undercorrecting myopia*

The concept of undercorrecting myopic patients to halt myopia is probably the oldest and the simplest one. It was supported by the theory that accommodation itself is the triggering mechanism for shortsightedness. In order to decrease accommodative effort at near, a decreased amount of myopic correction was prescribed, leaving the far vision slightly blurred. While this approach does make sense in elder presbyopic patients, several studies have proven it to be ineffective or even counter effective in young population, when trying to get myopia under control[22,23]. This suggests that the eye, which is becoming myopic, does not use foveal input for emmetropisation process. These facts further support the theory of the role of peripheral retinal defocus in the development of myopia.

Today, it is generally accepted that the prescription of exact amount of spherical and cylindrical power with binocular refractive balance makes most sense for the aspect of myopia control. If patients show large amounts of accommodative lag and / or near esophoria, PAL or bifocal lenses can be prescribed to reduce the near point stress.

### *Pharmacological interventions to regulate axial elongation*

For decades, muscarinic antagonists were used as myopia growth inhibitors. Among them, atropine solution was found to be particularly potent, but it was never widely used for this purpose due to its significant side effects. Some studies have shown that myopia growth is halted completely by continuous atropine therapy; however, its cessation caused a significant rebound effect and most subjects undergoing this kind of therapy caught up in myopia with the control group within a year or two[24]. Until recently, it was believed that atropine affects myopisation via inhibition of accommodation. However, this view has changed. According to retinal defocus hypothesis, the eye, which is about to become myopic, responds to the imposed hyperopic defocus by releasing certain messengers, which pass from the retina to the sclera to promote the softening of scleral collagen, so it can stretch backwards to catch the focal plan. It is assumed that atropine, as a potent unspecific muscarinic antagonist, inhibits this mediation. This effect has been studied extensively during the last few years in order to identify the messengers and the pattern of mediation. While the full mechanism has not been explained yet, the alternative action has been proven: there are factors in the retina, which normally prevent axial growth, but can be blocked chemically, making the eye respond to the imposed defocus. Important results were presented by Penha et al., 2011[25], showing that in chicken, intravitreally injected insulin is able to pass the retina and choroid, and affect the scleral tissue. Animals receiving these injections have grown more myopic when their eyes were fitted with minus lenses. The effect in this case is attributed to the inhibition of ZENK factor, which prevents the axial growth.

In humans, also less potent muscarinic receptor antagonists than atropine have been used with similar success. Pirenzipine was found to have inhibitory effect in child myopia too[26], but still, it was never used widely due to the adverse effects. Lately, also diluted 0.01% atropine was used for anti-myopia treatment[27], surprisingly reaching similar efficiency compared to 1% atropine; however, no side effects like follicular conjunctivitis and dermatitis, reported in previous studies, occurred. During this treatment even the mydriasis and cycloplegia were absent, which further supports the new hypothesis about the mechanism of action of atropine in myopia inhibition.

## Conclusion

There is certainly enough evidence that myopia is not simply a genetically determined condition. In human and animal models, it was shown that there are several environmental factors, which affect emmetropisation. Time spent outdoors, specific light spectrum, time spent in reading, hyperopic retinal defocus during near work, and intrinsic factors as near esophoria or great lag of accommodation are considered responsible for the disruption of emmetropisation processes and for the promotion of myopia progression.

In this paper, some actual principles of ecological, optical and pharmacological interventions are presented, giving the practitioner an overview of possibilities for slowing down the patient's myopia progression at least by some degree. According to the review of the literature, few advices regarding myopia can safely be given to the patient: First, before onset and in the beginning stage of myopia, staying outdoors reduces the risk of progression of myopia; second, the sustained near work should be avoided – one should interrupt it with short pauses. Here the rule of 20 – 20 – 20 can be applied (each 20 minutes take a distant look at 20 feet for 20 seconds). Last, practitioners should not forget to assess near point vision of young progressing myopes accurately – accommodative posture, lag of accommodation, and binocular vision / phoria – to get an overall impression of subject's visual response to near tasks. In the case of great lag and / or near esophoria, bifocal or PAL lenses can be prescribed. Even though we might not succeed in getting myopia under control, we can at least reduce near point visual stress and offer the patient a more comfortable vision during near work.

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## DANAŠNJI STAV U TRETMANU MIOPIJE

## SAŽETAK

Današnji stav o progresiji miopije, kako na modelu životinje, tako i na modelu čovjeka, jeste da postoje kombinirani utjecaji genetski i vanjski faktori na aksijalno izduženje bulbusa. Najnovija istraživanja pokazuju da ne postoji međusobna uzročnost u progresiji miopije. Jedan noviji tretman kod miopske progresije jeste i farmakološki pristup sa instilacijom kapi na duže vrijeme. U ovoj studiji je opisan tretman kontroliranog zaustavljanja rasta miopije, kako farmakološki, tako i optičkom korekcijom.