THE NEW ARMENIAN MEDICAL JOURNAL
Vol.7 (2013), No 4, p.61-67

REVIEW

MYOPIA: ETIOPATHOGENESIS AND SOME PROBLEMS OF CLINICAL ASSESSMENT

BAZINYAN L.E.

Ophthalmology Clinic, Yerevan State Medical University, Yerevan, Armenia
Department of Paediatric Ophthalmology, Yerevan State Medical University, Yerevan, Armenia

Received 7/21/2013; accepted in final form 12/28/2013

ABSTRACT

The paper presents historical and contemporary views on the etiology and pathogenesis of myopia and myopic eye disease based on the analysis of data available from myopia relevant literature arranged chronologically.

As obvious from the data cited, clinical examination on the state of accommodation in persons with myopia is widely and variously implemented in modern practice of ophthalmology, whereas until present the intravital characterization of the state of eyeball fibrous capsule in subjects with myopia might be done only indirectly and with greater approximation.

The author comes to the logical conclusion on the necessity to wider apply modern high-precision methods of investigation on scleral rigidity for adequate clinical characteristics of the myopic disease course.

Keywords: *nearsightedness (myopia), myopic disease, pathogenesis, fibrous capsule, hydro- and hemodynamic parameters.*

Nearsightedness (myopia) is the most common pathology associated with the organ of vision. It belongs to the most frequent causes of disability. In this sense, it is difficult to overestimate the role of research dedicated to the early diagnosis of myopia transition from a "simple" refractive anomaly into the complicated course – the so-called myopic eye disease. The biomechanical, biochemical and morphological properties of sclera play an important role in myopia course [*Iomdina E., 2000*]. There are three main pathogenetic links of myopia associated with the weakening of accommodation, hereditary predisposition, and weakening of the sclera. The first written record of myopia description is found in Aristotle (384-322 BC), who noted that at weakness of the screwed up eye a person brings the object that he wants to see closer to the eye. Aristotle was the first to use the word "miops" (literally meaning: "to close eyes winking"), from which the modern term "myopia" was derived. More or less successful attempts to explain the origin of myopia were initiated in 1611, when the famous astronomer J. Kepler gave a correct description of the visual act and dioptrics of the eye pointing to the fact that at myopia the image of the examined subject is obtained not on the retina, but in front of it [*Radzikhovskiy B., 1963*]. It has been suggested that the cause of specific image formation in the myopic eye is the excessive distance between the lens and retina, as well as its too much convex shape or the greater curvature of the cornea. Further studies revealed both widespread myopia among schoolchildren and the increase of its frequency with increasing length of learning at school, contributed to the emergence of multiple hypotheses linking myopia development with the eye strain. As believed, the stress of accommodation leads to increased intraocular pressure (IOP), and, in turn, to stretching the eye membranes. The idea that formation of myopic refraction occurs mainly due to stretching of the weakened sclera under the influence of IOP existed already in the last century and is shared by many researchers nowadays as well.

Among others, A. Kushel (1923), V.P. Filatov and V.V. Skorodinskaya (1955) suggested that weakness of the sclera in patients with myopia is a

ADDRESS FOR CORRESPONDENCE:
Yerevan State Medical University after M. Heratsi
60/1 Abovyan Street, 0025, Yerevan, Armenia
Tel.: (+374 060) 621 396; (+374 91) 478 710
E-mail: lilit-bazinyan@mail.ru

manifestation of the weakened supporting connective tissue of the body, which might be also expressed in the form of flat feet, gastroptosis, scoliosis [*Avetisov E., 2002*]. W. Comberg (1951) believed that stretching of sclera weakened under the influence of various unfavorable factors resulted from the summation of short-term increases in IOP during blinks and eye movements at reading [*Avetisov E., 2002*]. In 1966, B.L. Radzikhovskiy supposed that derangements of trophic tissues of the eye under the influence of various factors underlay scleral weakening and development of myopia. According to proposed hypothesis, from the pathogenetic point of view, all forms of myopia (congenital, school-related, the so-called malignant) are homogeneous. The whole point is for how long and to what extent the tissues trophism is deranged [*Avetisov E., 2002*].

A number of hypotheses assign to accommodation the determining role in myopia genesis: school mild-degree myopia is caused by adaptation of the visual analyzer, its accommodative apparatus for primary work in close quarters and the loss (or weakening) of the active function of accommodation into the distance. T. Sato (1957) believed that the basis for myopia development was prolonged tension of accommodation under the influence of visual work in close quarters. In his view, this leads to the steady strengthening of the refractive power of the lens, through which the myopic refraction is formed. Myopia, by T. Sato, is a morphological consequence of accommodation spasm [*Avetisov E., 2002*].

A common feature of the earlier proposed hypotheses of myopia accommodative origin is as follows: in these hypotheses the mechanism of emmetropic eye transformation into the myopic one is directly associated with changes occurring in the eye upon accommodation (supposed increase in IOP, tension of the choroid, delay of lens flattening, blood stasis, etc.). Thus, as obvious from the foregoing, the normal physiological act is recognized as the cause of abnormal eye development.

E.S. Avetisov put forward a new hypothesis for the origin of myopia associated with the visual work in close quarters. According to this hypothesis, the emmetropic eye becomes myopic not due to accommodation, but because it is difficult to accommodate for a long time; moreover, the causal factors leading to myopia are far beyond the eye. The essence of the hypothesis is as follows. The environmental aspect of considering visual organs in various animals allowed to establish the adaptive nature of refraction, i.e., such formation of the eye as the optical system, which ensures optimum visual orientation of the precise animal species due to the nature of its vital activities and the habitat.

Obviously, it is not accidental, but evolutionary and environmentally conditioned that in modern humans there occurs refraction predominantly close to emmetropia providing best advantage for clear vision of both distant and near objects. In most adults the naturally approaching refraction to emmetropia is reflected in high inverse correlation between the anatomical and optical component of an eye: during its growth a tendency is manifested to combine greater refractive power of a visual apparatus with a shorter anterior-posterior axis and, conversely, the less refractive power at the longer axis. Hence, the growth of the eye is a finely regulated process. Under the growth of the eye one should understand not a mere increase of its size, but a directed formation of the eyeball as a complex optical system under the influence of environmental conditions and genetic factors.

Of two components – anatomical and optical – the anatomical component is significantly more "mobile" one. It is known that after the birth refractive power of the eye decreases rapidly and by the age of 5 years it practically reaches the final value, whereas the anterior-posterior axis may increase after the first decade of life. Precisely, the regulating effect of the organism to formation of eye refraction occurs primarily through the anatomical component.

At the weakened accommodative ability any concentrated and sustained visual activity in close proximity becomes an unbearable load to the eyes leading to changes in the optical system of the eye in order to adjust for a work in close quarters without the stress of accommodation. This is mainly achieved through moderate lengthening the anterior-posterior axis of the eye. Such rearrangement of the eye obviously takes time, and this can explain the fact that the intense visual work at close range usually begins in children aged 6-8 years, while myopic refraction is mainly formed by the age of 11-12 years.

The following important fact should be emphasized. Weakened accommodation creates a func-

tional readiness, predisposition to the formation of myopic refraction. This predisposition is realized only under certain conditions of the visual work, if they make unaffordable demands on the individual capabilities of the accommodative apparatus and the eyes generally. Therefore, the eye prone to myopia, at a moderate visual load during high school years can remain hypermetropic or emmetropic and later become myopic in the performance of work requiring eye excessive strain when looking at the fine details of objects at close range. This is the way "professional" myopia forms; in its genesis this latter in no way differs from the "school" myopia [*Avetisov E., 2002*].

Considering the pathogenesis of myopia, M.S. Remizov and B.I. Gildina (1971) attached great importance to the accommodation strain. As one of the probable reasons for accommodation strain leading to its weakening authors considered the uneven contraction of ciliary muscle fibers necessary for self-correction of corneal astigmatism [*Avetisov E., 2002*]. Several studies showed that weakness of the accommodation apparatus might be a result of impacts produced by common whole body disorders and diseases to the ciliary muscle. O.N. Saveliev (1975) found that the decrease in blood inorganic phosphorus concentration indicating a disorder of calcium-phosphorus metabolism adversely affected the efficiency of ciliary muscle, the relaxation of which might serve as a basis for myopia development [*Avetisov E., 2002*].

The prevalence of myopia in different ethnic groups supports the role of genetics in the development of myopia. Recent research has identified genes that can weaken the connective tissues and thereby cause the development of myopia.

In sclera of myopic people degenerative and structural changes occur. It is established that elongation and residual deformation of the eye sclera in adults with high myopia is much higher than in emmetropia, especially in posterior area of the eyeball. Heterogeneity and anisometropia characteristic of normal scleral tissue become even more pronounced at myopia [*Rada J. et al., 2006*].

Electron microscopic studies revealed changes in the microstructure of the sclera at myopia [*Kuznetsova M., 2005*]. Myopic disease ranging from its mild degrees is accompanied by changes in the connective tissue scleral membrane: the lesions of collagen fibers and extracellular matrix are worsening with the progression of myopia. At high-degree myopia the activation of fibroblasts resorbing debris of destroyed fibrils is detected. Transformation of fibroblasts into myofibroblasts was observed [*Kuznetsova M., 2005*].

Unlike glaucoma, in myopia the reduction of strength-related properties of sclera occurs. This is due to the fragmentation and swelling of collagen fibers, changes in their structure, less distinct collagen bundles splitting up. At the same time, destructive changes in the collagen framework of sclera in the form of splitting fibrils into subfibrils are detected even at low degree of myopia. At the average degree of myopia an infringement of collagen bundles, their dissociation and splitting were revealed, while at a high degree myopia – deep discomplexation of the sclera elements with the collapse of the split subfibrils and changes of collagen complexes [*Kuznetsova M., 2005; Hakobyan A. et al., 2008*]. However, changes of the extracellular matrix make the basis of destructive changes in the collagen framework of the sclera. They are manifested by identified free glycosaminoglycans (GAGs) and their content reduction in the sclera with increasing refraction, while in glaucoma the level of GAGs in sclera increases. All this is reflected in the biomechanical properties of the myopic sclera, which is losing its strength, becomes extensible through the accumulation of residual microstrain due to periodic overloads, in particular, daily, orthoclinostatic, pulse, converged, respiratory, muscular, etc. fluctuations in IOP [*Hakobyan A. et al., 2008*].

The first sign of myopia is reduction in distance vision that, as a rule, rises up to a normal level at applying to eyes negative optical lenses. Initially, the decrease in visual acuity might be temporary, reversible. Schoolchildren with initial myopia often complain of rapid fatigue of eyes at visual work in a close distance, they point out to difficulties in seeing anything written on the blackboard and ask to change their place to one of the first desks in the classroom. When reading or writing, these children lean low over a book or notebook; in the cinema and theater they tend to take place closer to the screen or stage. Frequently, short-sighted subjects narrow the eyes to reduce the size of pupil and circles of scattered light on the retina and thus slightly improve eyesight.

As a rule, at the initial stage of myopia development visible changes in the fundus are not revealed except for rare cones around the optic nerve. Some cases of congenital and hereditary myopia with more or less pronounced changes usually specific to high degrees of myopia make exception [*Avetisov E., 2002*].

Myopia of weak or medium degree is formed more often and remains life-long. It normally does not cause violations of visual functions and is not accompanied by pathological changes in the eye media and membranes. In fact, this form of myopia is not a disease of the visual organ.

The progression of myopia can cause serious irreversible changes in the eye and a significant loss of vision, which, due to eye-glasses, improves only to a small extent or is not improved at all. Dark adaptation is disturbed, visual field losses may appear. Changes are often observed in the posterior part of the eye, which is subjected to tension, they primarily affect the area of the optic nerve. Earlier available cones or those arising anew are gradually increased and embrace the optic nerve in the form of a ring that more often is irregular in shape. Sometimes the disk itself is changed: it looks elongated, increased or decreased, more flat, acquires grayish shade [*Avetisov E., 2002*].

At very high degrees of myopia in the posterior area of the eyeball the true protrusions – staphylomas – might be observed. They are limited by an arcuate line concentrically arranged towards the optic nerve disk, through which the vessels of the retina are bent.

Due to the increasing atrophy of elements in vascular and retinal membranes the degenerative changes are becoming more extensively spread. At first there appear whitish-yellow stripes, then – round or irregularly shaped *foci* of white lesions, frequently with clumps of pigment. These lesions coalesce and affect a large area of the fundus. Because of depigmentation and disappearance of the layer of small and medium-sized vessels the fundus becomes unevenly dyed or acquires albinotic appearance with sparse choroidal vessels. In some cases, increased pigmentation of choroid prevails. Accumulations of pigment in intervascular spaces in the form of elongated spots or triangles can create the picture of "parquet-like" fundus [*Avetisov E., 2002*].

The decrease in visual acuity is especially significant, if the atrophic process captures the macular area. Already in the early stages of myopia progression macular reflexes are distorted or disappear, this area is sometimes darker. Then twisting narrow light stripes, small atrophic whitish or pigmented *foci* appear. Progressive changes in the retina, especially at the extreme periphery of the fundus (focal hyperpigmentation, thinning, cystoid degeneration, splitting, minor defects and disruptures) can contribute to retinal detachment [*Avetisov E., 2002*].

A patient's striving to bring closer to eyes the object of visual work so that to make its image on the retina larger and clearer leads to increased convergence, a significant increase in the load on the internal rectus muscles. This can cause fatigue and asthenopia effects. If the muscles cannot cope with such hard work, the binocular vision is disturbed and exotropia occurs. The reduced need for accommodation, as a result of which the stimulus to convergence is also weakened, contributes to emergence of exophoria and exotropia [*Avetisov E., 2002*].

As appears from the above, the accommodative factors of myopia "launch" are widely investigated and studied intravital; nevertheless, it is difficult to state the same about the clinical evaluation of the consistency of eye fibrous capsule. The latter is particularly important in predicting the course of myopia – first of all, the process of transition from "simple" ametropia to the myopic disease. Obviously, it is precisely at this stage of myopia pathogenesis that one can talk about more or less pronounced efficacy of existing therapeutic actions aimed at preventing the myopia development. In this sense, the study and evaluation of sclera rigidity properties essentially make, though indirect, but currently the only available diagnostic method of investigation, which provides an opportunity for dynamic assessment of the elastic-viscous properties of the outer capsule of an eye in myopes alongside with myopia progression.

Under the rigidity of the eyeball specialists understand the elastic-viscous properties of the outer membrane, due to which the size and shape of the eyeball are maintained, even with significant fluctuations in IOP.

The fibrous outer membrane is divided into cor-

nea and sclera. The sclera makes 5/6 of the entire external membrane of the eye. The water content in sclera reaches 65-69% and its main component, collagen fibers, constitute 75% of sclera dry weight, while protein accounts for about 10% and mucopolysaccharides – 1% [*Kon I., 1997; Tuchin V. et al., 1997a*].

Scleral stroma consists of fibrous structures (collagen and elastin fibers) and the base cementing substance provided by neutral and acid mucopolysaccharides. It is a hard enough fibrous tissue, which is mainly composed of collagen connective fibers packed in bundles in the form of rectangular *lamellae* [*Cox J. et al., 1970; Bendek G., 1971; Graig A., Parry D., 1981; Worthington C., Inouye H., 1985; Farell R. et al., 1990; McCally R., Farell R., 1990; Rol P. et al., 1990; Komai Y., Ushiki T., 1991; Rol P., 1991; Meek K., Leonard D., 1993; Vaezy S., Clark J., 1994; Nemati B. et al., 1996; Kon I., 1997; Newton R., Meek K., 1998a;b*]. Collagen fibers are surrounded by an amorphous base material that contains glycosaminoglycans, proteins and protein-polysaccharide complexes and makes the so-called intercellular matrix. The state of these substances determines tissue turgor and regulates its permeability for water and molecules of other substances.

Bundles of collagen fibers are interwoven and form a complex architectonics of the sclera that is specific to each of its department. The close interlacement of collagen structures of the sclera provides it with strength and elasticity [*Tuchin V. et al., 1997b*].

The thickness of the sclera varies depending on the individual features of the person and in different parts of the eyeball. The greatest thickness of sclera is in the posterior part (up to 1.1 *mm*); in the anterior direction the sclera becomes thinner, and at the site of attachment of rectus muscle tendons it becomes thicker (0.6 *mm*) again. In the passage of the optic nerve, the hole is covered with a cribriform plate, which is the thinnest part of sclera [*Eroshevskiy T., Bochkareva A., 1983*]. The thickness of sclera undergoes changes throughout a person's life-span. Until the age of 20 years sclera thickens; since 20 to 50 it remains relatively constant, and after 50 years of age the trend appears to thinning [*Avetisov E. et al., 1979; Savitskaya N. et al., 1982*].

The rigidity of sclera is a measurable physical parameter of the eye and expresses its elastic properties [*Friedenwald J., 1937*]. The first clinical method for investigation of eye rigidity was proposed by Roemer in 1918 [*Nesterov A. et al., 1974*], who conducted experiments on isolated eyes and found that the increase in pressure during tonometry was associated with an additional stretching of the eye membranes due to displacement of fluid from the deformed area. On this basis Roemer proposed an equation, according to which there is a linear relationship between changes in pressure and volume of the eye, but the rigidity index proposed by Roemer is not currently in use.

Later on, in 1937, J.S. Friedenwald, using data of other authors proposed a formula for rigidity coefficient determination; two tonometers, of larger and lighter weight (10 *g* and 5.5 *g*) are used to determine this coefficient. The value of coefficient depends on the elasticity of membranes, but not on the IOP. According to J.S. Friedenwald, the coefficient of rigidity in humans varies from 0.006 to 0.037 (on average: 0.0215) [*Nesterov A. et al., 1974*]. Measurement error for the coefficient of eyes rigidity varies from 20% to 100% of the measured value, depending on the size of ophthalmotonus and the type of tonometer used. The systematic error in the study of eye membranes rigidity depends on changes in blood flow of the intraocular vessels, individual variations in the volume of the eyeball and the initial value of IOP.

The most modern method for determination of the fibrous membrane rigidity uses the analyzer of hydro- and hemodynamics of eyes "GlauTest-60 Eye Tonograph" (Russia) (hereinafter: tonograph), which is designed to determine the IOP considering the effects of elastic-viscous properties (rigidity) of the eyes corneoscleral capsule, intraocular fluid and blood circulation parameters in the eye.

The tonograph calculates the entire set of tonometric, tonographic and sphygmometric indicators required for early diagnosis of diseases associated with disorders of hydro- and hemodynamics of the eye. The operation of tonograph is based on tonography impression method of measuring displacement of the cornea under the influence of applied force and the set of diagnostic indicators characterizing circulation of the aqueous humor and blood in the eye calculated according to J.S. Fried-

enwald's formulas [*Friedenwald J., 1957*].

Thus, we can conclude that:

- *first*, modern ophthalmic practice has a sufficient number and variety of studies describing the characteristic changes of the vision in myopia and myopic disease;
- *second*, in spite of the mentioned diversity of investigation methods the study on rigidity properties of the sclera should be considered as unreasonably forgotten, though, as clear from the above data, it is a rather informative method to judge on the myopic disease resistance of the eye membranes. Obviously, the mentioned allows recognizing the relevance of research aimed at evaluation of certain stages of myopia and myopic disease in combination with other states, through the study on rigidity of the eyeballs and the trends in their changes.

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