

EHLERS-DANLOS SYNDROME - The Role of Collagen in the Eye

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ABSTRACT

Ehlers Danlos syndrome (EDS) is a group of heritable connective tissue disorders characterized by hyperextensible skin, hypermobile joints, and connective tissue fragility.¹ These symptoms are believed to be the result of gene mutations affecting the structure or assembly of different collagen types. The eye is made up of 80% collagen. Therefore, it is recommended that individuals with EDS be seen at least annually by an optometrist or ophthalmologist for a full evaluation of their eye health. This article attempts to explain common ophthalmologic findings and their symptoms. The symptoms discussed in this article occur in the normal population and are not exclusive to EDS. However, due to the involvement of collagen and its role in the eye, individuals with EDS may have a higher incidence of ophthalmic implications, especially in the Kyphoscoliosis Type of EDS (formerly known as Type VI).¹ Additional research in this area is needed. This article is based on two presentations by Dr. Stephanie Kirschbaum to the Northern California Branch of the Ehlers Danlos National Foundation.

ROLE OF COLLAGEN IN THE EYE

The human eye is primarily made up of connective tissue. The sclera (the tissue that makes up the white of the eye) is all collagen and represents 80% of the eye. The cornea (clear tissue at the front of the eye) is mostly collagen as well.⁴ Since EDS is a collagen defect and the eye is primarily made of collagen, individuals with EDS in particular may experience ocular changes.^{1, 4} An optometrist or ophthalmologist should be consulted for a comprehensive eye exam to establish the patient's baseline medical data. This first exam should include a complete history and examination of all parts of the eye. Dilation of the pupil will allow for thorough examination of the internal parts of the eye. With annual follow-up exams, an eye physician should be able to identify any ocular changes. The presence and nature of any pain, discharge, redness or changes in visual acuity require further evaluation. Any disturbance in vision demands an explanation. If retinal changes occur, follow up frequency should be at least every six-months. For floaters (floating spots behind the lens of the eye, usually harmless and not visible during normal visual activities) suggested follow-up frequency is every three months. Patients experiencing flashes of light should report this immediately to their

primary eye care physician.

Many factors may effect ocular changes; genetics, nutrition, computer usage, environment and overwork. The strength and sensitivity of the collagen in the eye appear to be responsive to overuse. Overuse or overworking of the eyes can be defined as excessive reading, television viewing, or computer screen use without blinking or looking away every few seconds and taking a break from the activity after one hour. While reading, that would translate into looking away after every page and putting the material down after an hour to focus on another activity for a few minutes.

Many articles identify ophthalmologic findings of individuals or small groups of patients with an Ehlers-Danlos syndrome diagnosis.^{1, 2, 3, 4, 5, 6} Findings identified in these articles are:

Epicanthal Folds	Keratoconus
High Myopia	Blue Sclera
Lens Subluxation	Retinal Detachments
Angioid Streaks	Strabismus
Carotid-cavernous sinus fistulas	Photophobia
Posterior Staphyloma	Glaucoma
Cataracts	Macular Degeneration
Dry Eyes	

Note that these findings also occur in the normal population and that no research to date compares their occurrence within the general population to that of individuals with EDS. Major diagnostic criteria for the Kyphoscoliosis Type of EDS include scleral fragility and ocular rupture.¹

EPICANTHAL FOLDS

An epicanthal fold is an extra fold of skin covering the inner corner of the eye. They are caused by the hyperextensibility of or an excess of eyelid skin. The excess skin causes a fold in the area closest to the nose. Epicanthal folds are commonly found in the Classical Type of EDS⁴ and people of Asian ancestry.

KERATOCONUS

The cornea is the clear membrane at the front of the eyeball. Keratoconus is a type of abnormal corneal curvature that occurs when the cornea becomes cone-shaped.^{2, 4} It usually happens during the second or third decade of life and will cause images to be distorted. It is believed to be more common amongst people with lots of allergies (atopic). Gas permeable contact lenses are helpful. As a last resort, corneal transplant is required. Keratoconus can lead to blindness.^{2, 3}

HIGH MYOPIA

High Myopia is characterized by nearsightedness where items in the distance become blurry. The nearsightedness results because the eye is too long or the cornea is too steep so the focus point of light rays entering the pupil is in front of the retina. Corrective lenses are an effective treatment for high myopia.^{2, 3}

BLUE SCLERA

The sclera is the white of the eye or the thick outer coat of the eyeball. =20A bluish appearance is attributed to a thinning of the sclera. The thinning is most noticeable at the limbus (where the cornea meets the white of the eye) thus creating the a blue "halo" at the limbus. The blue halo becomes less prominent with aging and the normal decrease in scleral transparency. Blue sclera is considered to be a prominent feature of osteogenesis imperfecta and EDS.3, 4, 6

LENS SUBLUXATION

The lens, located behind the pupil, bends light rays as they enter the eye so that they focus on the retina in the back of the eyeball. The signals travel to the brain where they are translated into images. The lens is suspended by ligaments and may sublux, or come loose, sometimes falling into the posterior of the eye, causing an inability for light to focus in the eye. The lens is made up of epithelial cells that grow in many layers, like an onion. It grows throughout a person's lifetime. With normal aging, thickness and loss of resiliency can cause focusing to be more sluggish. This is known as presbyopia, or the need for magnifying glasses after age 40.2, 3, 4

RETINAL DETACHMENTS

The retina is the innermost layer of the eye upon which light rays are focused. As the eye lengthens or expands, the retina is more loosely attached than in infancy. A piece of the retina may detach itself and be trapped within the vitreous or the inside gel of the eye. A retinal detachment may be preceded by a shower of sparks, floaters, or lightening flashes then a 'curtain' falls across the visual field. **THIS IS AN EMERGENCY.** Floaters are trapped debris, usually a clumping of protein, in the vitreous gel of the eye. Most people have floaters which prove to be harmless, but they should always be reported to the eye care professional to be certain.3, 4, 6

ANGIOID STREAKS

Angioid streaks are cracks in the Bruch's membrane, the basement or "anchoring" membrane of the retina. The "streaks" usually radiate from the optic disc and appear as changes in the color of the retina. Through aging, the Bruch's membrane thickens, but if there is a defect in any of the collagen layers of the membrane, streaks appear. It is as if one dipped an uninflated balloon in paint and let it dry. As the balloon is inflated, cracks appear in the paint. Angioid streaks are common to many systemic disorders including Sickle cell, epilepsy, Marfan syndrome, Paget's disease, and EDS.3, 4, 6

STRABISMUS

A strabismus occurs when the resting eye is in a position other than at the center. A group of six muscles hold the eye in place and enable it to move around. Both eyes normally move in concert with one another. If any one of the muscles is weaker than the others, the eye will drift or cross. Loose tendons and ligaments around the eye create hard working muscles that get tired. Over active muscles will not work efficiently. Multifocal lenses (bifocals or trifocals) can help to balance the muscle activity associated with changing focus from faraway to close up and back to distance, as when driving. Prism in prescription glasses can be helpful in directing light to the correct spot on the retina. Avoid intentionally crossing the eye or moving one eye out of synch from the other. Surgical repair of a strabismus may be further complicated because sutures are difficult to place in thinned sclera. Surgical repair may not have lasting effects if the cause is a non-uniform elasticity of the tendons and ligaments associated with the eye muscles.3, 4

CAROTID-CAVERNOUS SINUS FISTULAS

A carotid-cavernous sinus fistula is very much like an aneurysm. It is the rupture of a blood vessel which bleeds into a sinus cavity and/or some part of the eye. The blood flow can cause serious structural damage to the eye.=20 **THIS IS AN EMERGENCY.** Individuals report hearing their pulse in their temple and having a frontal headache on one side or the other. A doctor will look for it by placing a stethoscope over the temple and listening for a 'whooshing' sound. Carotid-cavernous sinus

fistulas commonly found in Vascular, formerly called Type IV EDS, but all types and the normal population are susceptible as well.^{3, 4, 5}

PHOTOPHOBIA

Photophobia is an intolerance to light or glare. Light-eyed people are more susceptible to this kind of glare. It may be relieved by tinted, glare-resistant or dark UV protected glasses. Sudden photophobia should be reported to an eye care professional immediately.

POSTERIOR STAPHYLOMA

Posterior staphyloma is a stretching or distortion in the back of the eye. Scleral tissue "bubbles" which results in a significant myopic shift (increased nearsightedness.)⁴

GLAUCOMA

Glaucoma is an increase or change in the intraocular pressure which leads to vision impairment ranging from slight changes to blindness, as well as a progressive loss of peripheral vision. Glaucoma is irreversible if it is identified too late in the progression of the symptoms. It is believed to be caused by nearsightedness, heredity, injury, diabetes, vascular and mechanical irregularities.^{2, 3, 4}

CATARACTS

A cataract is a cloudy lens. The lens tissue discolors naturally as a result of sclerosis, or hardening, as one matures. It becomes more golden in color as it thickens which also decreases vision. Premature cataracts can occur from UV exposure, diabetes or nutritional factors.^{3, 4}

MACULAR DEGENERATION

Macular degeneration occurs when the macula atrophies causing pigment changes and a decrease in keen vision to occur. The macula, the strongest part of the retina, contains the highest concentration of vision receptors. There are two kinds of macular degeneration: wet and dry. In wet macular degeneration the underlying retinal blood vessels break or leak. Dry macular degeneration is a deterioration or "wearing out" of the retina. High risk factors include chronic UV exposure, smoking, inadequate nutrition, and heredity.^{3, 4}

DRY EYES

Dry eyes result when the normal coating of tears on the eye is diminished. This can result if one doesn't blink regularly or under dry environmental conditions. Dry eyes should not be treated with bottled eye drops that have a preservative in them. Instead, drink plenty of water, blink frequently, use a warm compress on eyes and/or use eye drops that do not have a preservative. Preservative free eye drops come in packages of single use containers.³

KYPHOSCOLIOSIS TYPE EDS

Kyphoscoliosis Type EDS is caused by a reduction in the normal activity of the enzyme lysyl hydroxylase which is required for the assembly of collagen fibrils. This type of EDS may include the progressive loss of pigment tissue in the eye. Improper drainage of the fluid of the eye may lead to increased intraocular pressure which promotes the incidence of glaucoma. Scleral fragility and ocular rupture are possible with this type of EDS.^{1, 3, 4}

SUMMARY

Since the eye is primarily collagen, anyone with a preexisting collagen disorder or defect must pay particular attention to any and all ocular changes. A yearly eye exam is as important as a yearly physical. The presence and nature of any pain, discharge, redness or any changes in visual acuity require an immediate evaluation. Begin with a thorough medical eye exam performed by an optometrist or ophthalmologist to establish a baseline eye health profile. If changes in vision or eye health occur, consult your eyecare professional as soon as possible.

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