УДК 617.7-007.681

Glaucoma: what every patient should know. Part 1. What is Glaucoma and how did you get it?

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Conflicts of Interest and Source of Funding: none declared.

Abstract

The first part of the article aims to give a patient a general idea of glaucoma as a complex disease. It provides a comprehensible description of eye's anatomy, histology and physiological processes. It also explains pathological processes associated with glaucoma, why a patient is prone to take no notice of the changes and what symptoms to look out for. Stating that all forms of glaucoma are related to some degree to the pressure inside the eye, the article dwells further on the concept of intraocular pressure, its normal ranges and what happens if they are exceeded.

The second part describes the various types of glaucoma and how they differ. The author emphasizes that there are almost no life-style choices that are known to be big factors in leading to either form of glaucoma. The most important things that determine glaucoma risk are how the eye was built and how it responds to changes in its environment, because the death of ganglion cells in both open-angle and angle closure glaucoma results partly from weaknesses in the tissues around them and partly from defects in the ganglion cells themselves as well as under-responses or over-responses in the normal defense mechanisms.

The article explicates the idea of contributing risk factors and considers the contributing risk factors for open-angle glaucoma. Main contributing factors of open angle glaucoma — such as age, elevated eye pressure, ethnicity, hereditary background, myopia, low blood pressure, exfoliation and pigment dispersion — are specified and given further explanation. Controversial risk factors (corneal thickness, heart disease, anti-cardiolipin antibodies, migraine and Raynaud's phenomenon) as well as things that do not present risk of glaucoma development, contrary to common opinion (gender, diabetes, hypertension, diet and alcohol) are also listed.

KEY WORDS: glaucoma, pathological processes, intraocular pressure, ganglion cells, risk factors.

Глаукома: что необходимо знать каждому пациенту. Часть 1. Что такое глаукома и откуда она берется?

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Авторы не получали финансирование при проведении исследования и написании статьи. Конфликт интересов: отсутствует.

Резюме

В первой части статьи дается общее представление о глаукоме как о комплексном заболевании. Доступным для пациентов языком описывается анатомия, гистология и физиология глаза. Объясняется, какие патологические процессы связаны с глаукомой, почему многие пациенты склонны не замечать ассоциированных с заболеванием изменений и на какие симптомы стоит обращать внимание. Автор отмечает, что развитие всех форм глаукомы связано с изменением внутриглазного давления, объясняет, как оно формируется, указывает пределы его нормальных значений и что происходит при их превышении.

Во второй части статьи описываются различные формы глаукомы. Автор делает акцент на том, что развитие любой формы глаукомы зависит не от образа жизни и привычек человека, а от индивидуальных особенностей строения глаза и его способности адаптироваться к изменению окружающей среды, поскольку гибель ганглионарных клеток сетчатки частично обусловлена слабостью окружающих тканей, частично — дефектом самих клеток, а также недостаточными и чрезмерными реакциями защитных механизмов глаза.

Также в статье перечисляются основные факторы риска развития открытоугольной глаукомы, такие как возраст, повышенное внутриглазное давление, национальность, наследственность, миопия, артериальная гипотензия, эксфолиативный синдром и перераспределение пигмента. К каждому из факторов риска дается подробный комментарий. Перечисляются спорные факторы риска (толщина роговицы, сердечно-сосудистые заболевания, антитела к кардиолипину, мигрень и феномен Рейно) и аспекты, которые, вопреки широко распространенному мнению, факторами риска не являются (пол, наличие диабета, артериальная гипертензия, диета, алкоголь).

КЛЮЧЕВЫЕ СЛОВА: глаукома, патологические процессы, внутриглазное давление, ганглионарные клетки сетчатки, факторы риска.

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What is Glaucoma?

Take Home Points

- **Glaucoma often has no symptoms**
- **Nerve cells in the eye die slowly**
- **Vision off to the side is affected first**
- **Once vision is lost, it can't be regained**
- **Glaucoma is related to eye pressure**

Most likely, you were told you had or might have glaucoma at a routine exam of your eyes and had no idea that anything might be wrong. Most common types of glaucoma give no indication that they're there (the medical term for this is that the disease is asymptomatic). There are two main types of glaucoma: open-angle and angle closure glaucoma. Half of the people in the developed world with these types of glaucoma don't know they have the diseases, while in the developing world most cases are unfortunately undiagnosed and untreated. This is partly because some people don't go for eye exams. It is also because not all eye doctors recognize glaucoma when they examine the eye.

When you look at something, the light strikes the surface of your eyes and a description of what you see is transmitted to your brain. Your eye has several major parts that assist in this job. Each of the parts is made up of cells, the building blocks of your body. These cells have different specialized jobs; some hold your body together like bricks and mortar, while others send messages to each other like a cell phone sending through towers to another cell phone. Cells that send messages (called retinal ganglion cells, because they are found in the part of the eye called the retina) are particularly important in glaucoma because it is these cells that are damaged in the disease. When light comes into the eye, the light is received first in cells called rods and cones. These cells (also called photoreceptors, because they receive the light) send information about what you are seeing to a second layer of cells, and finally layer 2 cells light up layer 3, the ganglion cells.

Ganglion cells are the cells that die in glaucoma. Once they die, they are not replaced by new cells. This is not true in your skin or even on the front surface of the eye, the cornea, both of which make new cells all the time. But ganglion cells are truly a part of your brain even though they are somewhat outside the brain in the eye. There is a good reason why brain nerve cells don't make new ones normally. We must think of how complex the brain is. There are 1 trillion nerve cells in the human brain and each has about 100 connections or synapses to other nerve cells (100 trillion, or 100.000.000.000.000 for those who like zeroes). In addition, ganglion cells in the retina are surrounded by supporting neurons called amacrine cells and other supporting cells called glia. In the eye there are 3 kinds of glia: astroglia, because they are shaped like pointy stars; microglia because they are small; and Müller cells because Dr. Müller got them named for himself. From the time the retina begins to develop in the womb until around the time of birth, nerve cells are turning into the various types that will be present in the adult (about 10 kinds in the retina). And, up until the age of 6 years of age, the eye's nerve cells are still forming their final permanent connections to other nerve cells in the eye and to partner cells in the brain. Some eye nerve cells connect to other nerve cells at both ends, picking up information from a previous layer and passing it along to the next layer. The ganglion cells that die in glaucoma are that kind of double-ended neuron.

Even more amazing, ganglion cells pick up all the information from all the other nerve cells in the retina and carry it out of the eye on their one fiber through the optic nerve head to the next way-station in the brain (the llateral geniculate). From there, there is another relay to the back of the brain where more complex visual processes go on. The ganglion cell's fiber is amazingly long. If the cell body in the retina were the size of a basketball, the fiber would be as long as a football field (the actual fiber is about 2 inches long). On its way, this fiber has to pass through the wall of the eye to get into the brain. The optic nerve head, where the fiber leaves the eye is the ganglion cell's Achilles heel, a spot where the stress of the eye wall and the need for good blood supply in a tight spot can kink it and disrupt its communication. We have known for a long time that the normal flow of chemicals within the ganglion cell fiber is blocked in glaucoma just where fibers leave the eye, and that this is an important way the ganglion cell is injured and dies.

So, once a large number of ganglion cells die from glaucoma, the patient's peripheral vision is affected seriously. How many have to die to really cause vision loss? Glaucoma Center of Excellence research shows that it takes the loss of about 30% of the ganglion cells to reach the point where the doctor's tests (visual field tests) show that the patient's vision is definitely abnormal.

Glaucoma creeps up on us without notice because of several features. First, it involves the slow loss of retinal ganglion cells. Because these cells carry the visual messages through which we see, losing them causes our vision loss. But ganglion cells die so gradually in most glaucoma that we don't notice the loss. We begin life with around one million ganglion cells and barring major eye disease, 75% of them last until we are 90 years old. Glaucoma speeds up the rate at which they die. Each ganglion cell has its own location in the eye to receive light signals over a tiny area that is up to one millimeter wide. Signals travel from the ganglion cells to the brain along a fiber nearly two inches long. As the tiny fibers of each ganglion cell leave the eye, they are vulnerable to being injured at their exit point, the optic nerve head.

The second reason glaucoma is a silent disease is that the ganglion cells most likely to die are those that provide us with our side vision. Only late in the disease does it attack our center vision, where we have our 20/20 reading ability. We don't rely as much on our side vision as we do the center vision. When we are reading or watching TV or surfing the net, our attention is focused on the object in front of us, not things off to one side. This means that the vision loss from glaucoma is not noticeable in its early stages. Close

your left eye and hold this book (or computer) at a normal reading distance of about 14 inches. Look at the right page with your right eye, where the words are in bold print. The typical place for early glaucoma damage to cause you not to see is on the left page, where some of the print has been removed as an illustration. Since we normally pay most attention to directly where we're reading, most of us would not notice anything wrong if this part of the vision were missing.

Another reason that glaucoma's damage is not noticed early on is that it typically affects only one eye at first. The other eye is still fully functional. Both eyes get similar information about the world, and the brain converts the two separate signals into a single picture. With both eyes open, as we view the world, any object is seen by both eyes and its image is sent to the brain by both. If the brain gets the image from either eye, we see it and we think nothing is missing. In fact, loss of the image from one eye does cause a loss of the ability to see things in three dimensions. This ability helps us to tell how far away from us something is in space and is called stereoscopic vision. So, we can lose a lot of vision from one eye, but if the other eye is unaffected by glaucoma, we don't notice. Clinical research from our Wilmer Institute Center for Glaucoma Excellence shows that the typical person with glaucoma loses twice as much vision in the worse-affected eye compared to the better eye, but if left untreated, eventually both eyes become abnormal and this really decreases our ability to enjoy life.

Fourth, we're pretty adaptable creatures, and we alter our behavior to take account of the damage, even without knowing it. When investigators evaluate how much glaucoma damage it takes to affect patient's daily activities, they find that damage has to be pretty bad before it is recognized as a problem. Yet, when the actual functional capability is measured, in such things as reading, walking, and driving, it is clear that persons with significant glaucoma damage read more slowly, walk more carefully, bump into things more, and give up driving sooner than others.

One fundamental fact is that vision lost from glaucoma does not come back and no present treatment can restore it. Some parts of your body, such as your skin, can recover from damage because those organs can build new cells to replace damaged cells. This is not true for nerve cells in the brain or the eye. The ganglion cells that are damaged in glaucoma cannot be fixed or replaced once they are damaged. The layer of nerve tissue in the eye that contains the ganglion cells (the retina) is a very complicated network of 10 types of cells. Ganglion cells are the only ones to die from glaucoma, but their loss causes rearrangements in the retina and up in the brain's relay centers to which they go. To put back function, we will need to insert new nerve cells in their place, to reconnect the new cells to the cells that are still there, and to make those connections work with the existing connections in the way that they did originally. While our laboratory, along with others, has taken the first steps in this process, it is a long way to go to successfully restore vision in a human eye.

One final important fact is that all of the forms of glaucoma are related to some degree to the pressure inside the eye. The eye is something like a camera, with lenses at the front (called the cornea and the lens) and the film or the digital receiving surface at the back. For clear vision, we need the image placed on the retina and not moving, since if it is not stable, it would seem blurred. The eye is filled with fluid which must be kept within a narrow range of pressure, like the air pressure inside of a bicycle tire. The fluid inside the eye is not the fluid we make when our eyes tear (or whey we cry). Tears come from glands outside the eye and are not directly related to glaucoma. Like a bicycle tire, the eye must have the correct pressure inside to work properly. The balance between fluid flowing in and out of the eye maintains a higher pressure inside the eye than outside. This pressure difference produces stress in the eye wall (sclera), keeping it tense and stable so that the retina's image is clear.

The normal eye pressure is about 15 millimeters of mercury. This is enough pressure to make the images stable on the retina by keeping the wall of the eye firm. The wall of the eye is made of 3 layers: the white outer layer or sclera, the middle layer containing blood vessels (the choroid), and the retina with its nerves. Pressure is maintained by having fluid come into the eye at one location (the ciliary body) and leave through the main outflow zone (the trabecular meshwork). The continuous flow of this fluid (the aqueous humor) also nourishes the structures inside the eye that have no blood supply of their own.

Whether the eye pressure is a bit lower or higher, there is always some physical tension (called stress by engineers) in the sclera. The higher the pressure, the more is the stress. Because the fibers of ganglion cells must go through the sclera at the optic nerve head to go up to the brain, they are damaged by this stress.

Ganglion cells are damaged by prolonged eye wall stress and this is the cause of damage to your vision in glaucoma. This means that the higher the pressure, the greater the chance for glaucoma. However, not everyone's eyes react to pressure in the same way. The fibers in some people's eyes can tolerate greater amounts of pressure that others. If my eye has a thinner wall than yours, or is bigger in diameter, it will have more stress from the same amount of pressure.

So, glaucoma can happen at any pressure, as long as the effects of stress are sufficient to kill ganglion cells. In fact, half of those with the most common type of glaucoma, called open angle glaucoma, always have a normal level of eye pressure. In their eyes, the stress of normal pressure (combined with other features) is enough to kill ganglion cells. Therefore, it is not necessarily "elevated" pressure that is the enemy in glaucoma. All present treatment for glaucoma is designed reduce the damaging level of pressure found in the untreated person, lowering it to a safer level that will allow no further damage.

Experts say that glaucoma has started as a definite disease in a person when one of the eyes has suffered actual structural and functional damage. This damage

shows up as specific abnormalities on standard examination tests. Before this point, there are many persons who are suspected to have glaucoma but have not met the official damage criteria, and they are called glaucoma suspects. In the offices of many eye doctors, these strict definitions are not obeyed — some doctors use the term glaucoma more broadly to mean anyone whom they intend to treat.

The next sections describe the various types of glaucoma and how they differ.

How did you get glaucoma?

Take Home Points

- **You did not do anything wrong to cause it**
- **There is more than one "cause" for glaucoma**
- **In general, your personal habits, diet, and exposure to the world don't cause glaucoma**
- **Features called risk factors for open-angle and angle closure glaucoma are somewhat different**
- **Stress in the eye wall damages nerve fibers as they leave the eye, even at normal eye pressure**

Common factors in open-angle and angle closure glaucoma

In this section, we'll talk about the causes of two main types of primary glaucoma, open-angle and angle closure. The things that are known to cause each of these two disorders are a bit different. But, the damage in both of them happens in the same general way after they get started, and many of the treatments are similar. For any complicated disease like glaucoma, there are no easy answers. It doesn't come from only one thing or a single abnormality. To speak of one cause of a disease is simply not possible. The eye has many interconnecting parts, and each cell that makes up those parts is almost infinitely complex in the interweaving electrical and chemical pathways that help the cell to survive. And, as we will see, there are equally intricate pathways that tell the nerve cells to kill themselves under conditions where the disease is active. (Yes, they actually commit suicide).

One of the first questions we are often asked is: "what did I do that caused glaucoma?" To a large degree, the answer is "nothing" — there are almost no life-style choices that are known to be big factors in leading to either form of glaucoma. We will talk about personal behaviors that can help a bit with your glaucoma in the section "How should you change your life"? For example, we know that cigarette smoking and over-exposure to sunshine can be big contributors to two other eye diseases in older persons — cataract and age-related macular degeneration. But, smoking and sunlight are not at all related to glaucoma. Instead, it seems the most important things that determine glaucoma risk are how the eye was built and how it responds to changes in its environment.

The death of ganglion cells in both open angle and angle closure glaucoma results partly from weaknesses in the tissues around them and partly from defects in the ganglion cells themselves. It also results from under-responses or over-responses in our normal defense mechanisms. These factors can gang up to produce glaucoma by having several things go wrong at the same time. In fact, glaucoma probably happens only when more than one process is malfunctioning. Each of the single things that are part of the disease package is called a contributing risk factor. Together, all the contributing factors that wind up causing the glaucoma make up sufficient cause for it to occur. The mixed bag of contributors to the sufficient cause can be different among people — even among members of the same family each of whom has glaucoma.

One major cause of the death of ganglion cells in both major types of primary glaucoma is how the wall of the eye responds to eye pressure. We showed earlier how it can be worse in glaucoma to have a big, thin-walled eye than a smaller one, since the stress in the eye wall is higher. The fibers of ganglion cells get injured when the eye wall stress affects the optic nerve head and presses on the fibers passing through it. Not just the nerve fibers are hurt going through the nerve head. Nerve fibers are supported by other kinds of cells and tissues, including the small blood vessels that nourish the fibers at this site. Eye wall stress also affects these cells badly. So the behavior of the eye wall is translated into vision loss by physical stress at a critical place. Eyes that are bigger have more stress, explaining why very near-sighted people with longer eyes get more open angle glaucoma. Even normal-sized eyes whose wall responds badly to stress can kill fibers — in them it happens at eye pressures that most of us tolerate with no damage. This is one explanation for how persons with normal eye pressure can get open angle glaucoma; their eye wall delivers more stress to the nerve fibers at normal pressure than most persons. The critical tissues in the nerve head called the lamina cribrosa probably stand up to the eye wall stress better in some of us and worse in others — causing more glaucoma damage when the lamina is weaker. In persons with angle closure glaucoma, the eye is smaller, which ought to be protective from wall stress, but their eye pressures are typically higher than normal and that produces enough stress to damage fibers and their supporting cells.

A lot of other factors are known to contribute to ganglion cell death and therefore to cause glaucoma's vision loss. We know this by studying human eyes of persons who had glaucoma and who donated their eyes after their death to an eye bank. We are often asked by glaucoma patients if it is worthwhile for them to be an eye donor. After all, their eyes are damaged, so surely they aren't useful. Most donated eyes are used to transplant the clear cornea to someone who needs a new one. Eyes from people with glaucoma are not useful for that kind of transplant, but donated glaucoma eyes are vitally important to study how glaucoma does its damage. Many studies have also been conducted with animals in whom glaucoma develops spontaneously or in whom a glaucoma-like condition is produced in one eye.

From the human glaucoma eyes and animal research, we have learned that glaucoma causes harmful chemicals to be released by cells at the optic nerve head and in the retina, where the ganglion cell body lives. The blood nourishing ganglion cells and their fibers can fail to provide enough oxygen or the energy producing compounds that drive normal processes. We will come back to more of these contributing features to ganglion cell death in the section Are there treatments other than lowering eye pressure?

We'll now consider the contributing risk factors for open angle glaucoma and angle closure glaucoma separately from each other, since in many ways they are different.

Things that make open angle glaucoma more likely

- **Older age**
- **There is more than one "cause" for glaucoma**
- **Higher eye pressure (even if it is in the normal range)**
- **Family background (ethnicity) — more common in African, Hispanic**
- **Having blood relatives with it**
- **Being near-sighted (myopic)**
- **Having lower blood pressure (but not high blood pressure)**
- **Having conditions called exfoliation and pigment dispersion**

Other than senior discounts, there are few advantages of getting older and one of the many disadvantages is a greater chance of glaucoma (of all types). While open angle glaucoma sometimes occurs early in life, by far most examples happen after age 60 and the number affected increases at an increasing rate with older age. By age 90, nearly one in ten persons has it. Scientists have lots of suspicions about the many reasons older age would make glaucoma more likely, but it's obvious that humans systems are more likely to fail with every passing decade.

The higher the eye pressure, the greater the chance for open angle glaucoma. About half of cases occur in persons whose eye pressure without treatment is higher than the normal range. Their tendency to get glaucoma probably comes from abnormal outflow of the aqueous humor in the front of the eye. Since water can't get out fast enough, pressure is not only higher than normal, but it fluctuates up and down more than in non-glaucoma persons. Both a higher average pressure and a pressure that varies more are factors known to contribute to open-angle glaucoma. Millions of persons have eye pressure higher than normal and never develop open-angle glaucoma. They are called ocular hypertensives and we discuss them in the section Why isn't glaucoma either there or not there — what makes you an open angle glaucoma suspect? Many ocular hypertensive glaucoma suspects fortunately lack some of the other contributing risk factors for open-angle glaucoma, or their eyes possess better defense mechanisms against the stress induced by elevated eye pressure. They stay suspects and never get glaucoma. Meanwhile, about half of those with open angle glaucoma never have eye pressure above normal. This situation was once called "low tension" or "normal tension" glaucoma. Probably their eye wall delivers more stress to the optic nerve head than other eyes at normal eye pressure. This causes death of ganglion cells at eye pressures that most persons have their whole lives without damage. Fortunately, lowering eye pressure is beneficial even in these normal pressure glaucoma patients.

When you have several known contributing risk factors for open angle glaucoma, the collection of factors can be more serious together than they would be individually. For example, among those with a tendency toward glaucoma, it is bad to have low blood pressure and bad to have higher eye pressure — and doubly bad to have the two together. For blood to nourish the optic nerve head and retina, it has to get to the eye, and with low blood pressure coming in and higher eye pressure keeping the blood out, the perfusion pressure is too low. One has to have pretty low blood pressure (or very high eye pressure) to get into a danger zone here, but specialists now keep better track of both blood pressure and eye pressure along with the general doctors who care for open-angle glaucoma patients. While blood pressure that is too low may be harmful in glaucoma, we still recommend that high blood pressure be controlled as needed to protect your overall health. Care should be taken not to over treat high blood pressure in persons with glaucoma.

The lower the eye pressure, the better for open angle glaucoma. Some things that make it lower are aerobic exercise, avoidance of corticosteroid medications (even inhaled or nose sprays with steroid), and avoidance of drinking many caffeine-containing drinks per day.

Where your family came from in the world also affects the chance for open-angle glaucoma. We now recognize that there is no clear way to test the genes of a person and to properly label them as derived from Africa or Asia or Europe. What is often called "race" is a very complex set of features and the census bureau and scientists studying disease resort to asking someone to state what they call themselves — so-called self-described ethnicity. When you look at the whole population together, we are becoming more related to one another as the world's communication, immigration, and intermarriage increase. Yet, interestingly, when we do a study of how many people have open-angle glaucoma and we compare those who self-describe as African-derived (black) and European-derived (white), the rate of glaucoma is 3-4 times higher in the African-derived. The rate of open angle glaucoma is nearly identical for African-derived Baltimore City residents and villagers in central Tanzania in Africa. This seems to tell us that tendency to open-angle glaucoma is inherited in a way that doesn't depend heavily on diet, environment, daily or cultural activities, since these things are so different between these two populations of African-derived

people. These two groups must share some inherited genetic similarities. The studies of Hispanic persons also show a higher rate of open-angle glaucoma. While we must assume that this is a real worry for this group, the question is even muddier as to whether Hispanics are as homogenous in genetic inheritance terms as other ethnicities. After all, in some studies, people were included as Hispanic because of the language spoken, not their family derivation. We have a colleague who was born in Central America and speaks Spanish as his primary language; he would be Hispanic if studied in Mexico City, yet both his parents came from Central Europe, and if they hadn't moved, he would be classed as European-derived in a study done in Austria. This issue is complicated, indeed!

Many diseases, including glaucoma and breast cancer, can occur more frequently in certain families. These unlucky families have an unusual version of a particular gene that is passed from parents to children and greatly increases the risk of getting the disease. Our genes contribute to open-angle glaucoma, and having a close family member affected increases the chance of getting it by 10 times. So, among European-derived adults over age 40, the rate of open-angle glaucoma is 2 in 100. But your chance increases to 20 in 100 if your Mom or Dad, brother or sister, or your adult child had or has glaucoma. We often hear "but, no one in my family ever had glaucoma — so why do I have it if it's inherited?" Even though some families have increased risk for glaucoma, people with no family history also get it. Genes aren't the only reason people get glaucoma. Or, perhaps the reason "no one in the family had it" is that they were never examined, or they died prior to getting it, or they didn't tell anyone else in the family that they had it.

Those with family members who have glaucoma still have a very good chance of NOT getting glaucoma (80%), but, they should be examined regularly, because otherwise they won't know that they have it until it has done serious damage. Routine eye exams can help to avoid unnecessary vision loss in family members who are at risk. On the other side of the coin, we frequently hear from patients that their Mom had glaucoma, only to find out when records of Mom's care are produced that she had cataract, or used daily eye drops for another problem, like dry eyes. In one study, more than half of those who said that they have glaucoma, in fact did not have it — and this was a study of nurses! It is even more important to have regular eye exams for glaucoma if your family member not only had it, but lost vision from it. The tendency to have worse glaucoma is probably inherited, too. At this time, there are 3 known genes in our human DNA that have mistakes called mutations which increase the chance of open angle glaucoma. These make up only a small fraction of all those with glaucoma and at present there is not a good reason to do testing for gene defects as a method to screen for who is going to develop it.

In the section How did you get glaucoma?, we explained that people with near-sightedness (myopia) are more likely to get open-angle glaucoma. Myopia means you need glasses to see well at distances like 20 feet, but see things held close to your face fairly well without glasses. Myopic eyes are more often longer and have thinner walls. Both features make the stress from any eye pressure worse in causing glaucoma damage. Having laser treatments to change the need for glasses doesn't improve this risk, and those considering such refractive surgery should have careful discussions with the surgeon before doing so for two reasons. First, some forms of refractive surgery use an instrument that raises the eye pressure very high for some minutes. This could theoretically be dangerous for the glaucoma patient. Second, performing these refractive procedures changes the measurement of the eye pressure, typically making it seem lower than it is. We can correct for this best by knowing what pressure was just before and just after the laser refractive procedure. The bottom line is that those who have worn glasses since teen age for myopia should have annual evaluations for glaucoma in adulthood.

Two conditions that make open angle glaucoma more likely are exfoliation syndrome (also called pseudoexfoliation syndrome) and pigment dispersion syndrome. Exfoliation eyes produce a white-dandruff like material that can only be seen inside the front of the eye on the iris and lens. This material is produced by many cells in the body, but mostly causes trouble in the eye. Part of its damage comes from the exfoliation material blocking up the outflow of aqueous humor, so that the eye pressure is both higher and more variable than normal. Both higher pressure and more variable pressure are bad for eyes at risk for glaucoma. Second, there is some evidence that exfoliation eyes are more susceptible to glaucoma because either the structure of the eye or its blood vessels are weaker in exfoliation. We can see exfoliation in detailed eye exams in many persons who don't yet show damage from glaucoma. They are best advised to have more frequent exams than others with less glaucoma risk.

The second internal eye condition that makes open angle glaucoma more likely is pigment dispersion syndrome, which happens in some myopic eyes. Their iris rubs on the structures just behind the iris, the supporting fibers that attach the lens to the eye. Pigment rubs off the back of the iris and blocks the outflow of aqueous humor when the pigment is carried to the trabecular meshwork. Eye doctors can see the places where pigment has rubbed off and the places it deposits on the inner eye, so before there is glaucoma damage it is possible to begin monitoring those with this condition more closely. While exfoliation is more commonly seen in the typical older glaucoma patient, pigment dispersion can begin to cause glaucoma in the 20s and 30s. The features that make pigment dispersion more likely are having a larger eye (being near-sighted) and having an iris that is less in its overall volume. At present, there is controversy about whether making a hole in the iris keeps the pigment from rubbing off in pigment dispersion. If it did, then laser iridotomy treatment would be helpful. A recent controlled clinical study found no benefit of iridotomy for pigment dispersion eyes.

Controversial risk factors for open angle glaucoma

- **Corneal thickness**
- **Heart disease**
- **Anti-cardiolopin antibodies**
- **Migraine**
- **Raynaud's phenomenon**

A recent study found that when the thickness of the cornea is measured by a test called pachymetry those with thinner corneas are more likely to go from suspect status to having evidence of open-angle glaucoma damage. When we measure eye pressure, the instrument doing the measurement, the tonometer, pushes against the cornea. The higher the eye pressure, the harder it pushes back against the tonometer, giving a higher pressure reading. If the cornea is thin, the instrument will think that the pressure is lower than it really is because it is easier to flatten. So, part of the reason why eyes with thin corneas were more likely to develop glaucoma was that their eye pressure was really higher than the measured number. There is some controversy about whether eyes with thin corneas are more prone to glaucoma even after we take account of the falsely low pressure that is measured. It would make sense that such eyes would be more at risk if having a thin cornea meant that the eye wall all over was thin or that the optic nerve head was more susceptible to pressure. However, this hasn't been shown to be the case (yet).

For many years, it was said that persons with various kinds of heart disease and blood vessel abnormalities were more likely to get glaucoma or to have worse glaucoma when they get it. This is logical, since as we already mentioned, having a low perfusion of blood into the eye (low blood pressure combined with higher eye pressure) is a contributing risk. But, some very extensive studies actually have failed to show that many aspects of cardiovascular disease make glaucoma more likely. This includes things like having had a heart attack, having migraine headaches, and having a constriction of blood vessels in the hands called Raynaud's phenomenon. It may well be that small numbers of persons do have vascular disorders that make glaucoma worse. For example, a recent study found that glaucoma got worse much faster in people who have something in their blood stream called anti-cardiolipin antibodies. But, less than 5 in 100 glaucoma patients had these antibodies.

Things that aren't risk factors for open-angle glaucoma

- **Sex (biological gender)**
- **Diabetes**
- **Hypertension**
- **Diet**
- **Alcohol**

Men and women get open-angle glaucoma at about the same rate. To determine such things, it is important that research studies look at the whole population by some random sampling, as is done in voter's polls before elections where a representative sample is questioned. Otherwise, persons who are more likely to go to the doctor will be found to have a disease more often and it will be incorrectly assumed that they have it more. Women tend to go to doctors in the United States more than men, and women live longer. So doctors who do such studies adjust their estimates by doing random sampling, and by taking account of how many persons at a certain age have the disease. This is called age-specific rates or prevalence.

Some of the most surprising findings about contributing factors to open angle glaucoma have come from recent studies on diabetes mellitus. For years, textbooks taught that diabetes made glaucoma more likely. To be sure, diabetes is a major cause of vision loss, especially when proper diet and exercise recommendations are not followed. But, against the prevailing ideas, more and more studies are showing that having diabetes does not make you more likely to get open-angle glaucoma.

Just like diabetes, all the experts formerly said that having high blood pressure was associated with more glaucoma. And, as large studies that examined the question were done, this link became so weak that most studies show no relation at all. In part, it depends on how the study is done. Studies in which glaucoma is defined by having only high eye pressure tend to find that hypertension is related to glaucoma. The more modern open-angle glaucoma definition recognizes that eye pressure can be high or low in untreated open-angle glaucoma. When this definition is used, there is no contribution of hypertension to open angle glaucoma. There is clearly some link between the level of blood pressure and the level of eye pressure, as the Glaucoma Center of Excellence investigators showed in a large study of healthy adults. They go up or down together to some degree because the systems that control both pressures are similar parts of our unconscious nervous system. Get stressed and both blood and eye pressures tend to rise. Again, it would be foolish to allow yourself to have uncontrolled blood pressure, since that raises the risk of heart attack, stroke and kidney disease.

From a glaucoma viewpoint, there are no dietary or drinking habits that increase the risk of the disease. Drinking a bottle of water very quickly does raise eye pressure, so we recommend you drink slowly to avoid this. Eating a diet with lots of fruits and vegetables is a good health habit. Many studies show that drinking alcohol and caffeine in moderation does not make glaucoma more likely. No nutriceuticals (herbs and the like) have been shown in any decent study to improve the risk of glaucoma. That doesn't mean that you can eat, drink, and be merry, since if you do, you won't live long enough to get glaucoma.

To be continued in the 2-nd part.

Поступила 07.06.2014

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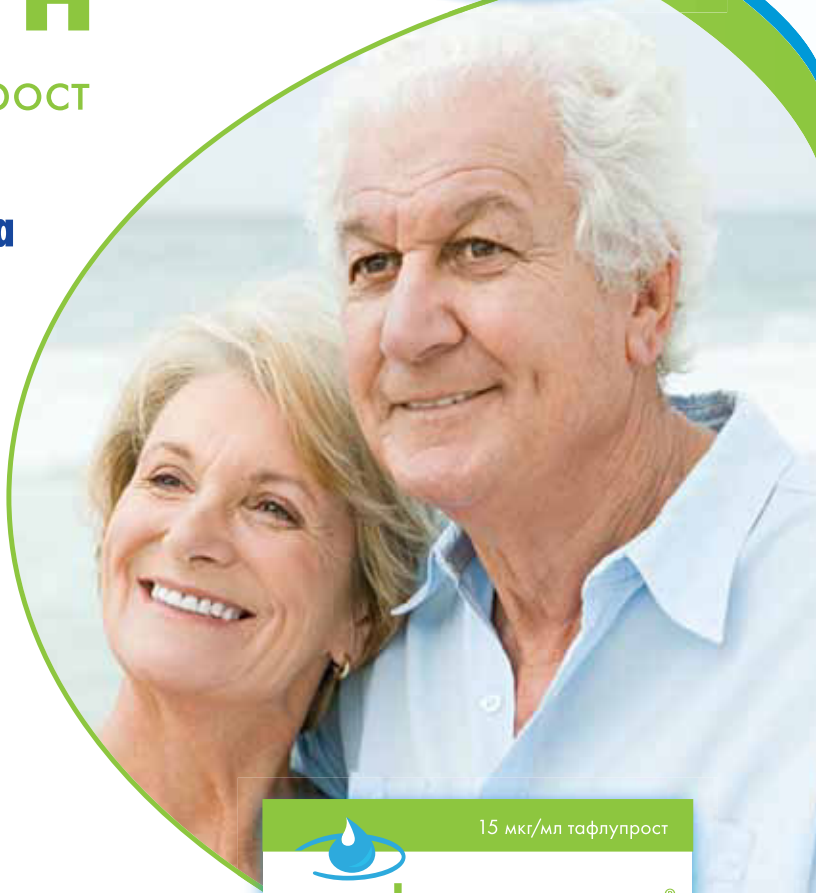

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Краткая информация по применению (перед применением необходимо ознакомиться с полным текстом Инструкции по медицинскому применению): **ТАФЛОТАН®. Рег. номер:** ЛП-002287. **МНН:** Тафлупрост. **Состав:** 1 мл глазных капель содержит: ***Активное вещество:*** Тафлупрост - 15 мкг; ***Вспомогательные вещества:*** Глицерол, натрия гидрофосфата дигидрат, динатрия эдетат, полисорбат-80, натрия гидроксид и/или хлористоводородная кислота для коррекции pH, вода для инъекций до 1 мл. **Код АТХ:** S01EE05. **Фармакологические свойства:** Механизм действия: Тафлупрост – фторированный аналог простагландина $F_{2\alpha}$. Кислота тафлупроста, являясь его биологически активным метаболитом, обладает высокой активностью и селективностью в отношении FP-простаноидного рецептора человека. Сродство кислоты тафлупроста к FP-рецептору в 12 раз выше, чем сродство латанопроста. Тафлупрост снижает внутриглазное давление (ВГД), усиливая увеосклеральный отток водянистой влаги. Клинический эффект: Снижение ВГД начинается в течение 2-4 часов после первой инстилляции препарата, а максимальный эффект достигается примерно через 12 часов. Продолжительность эффекта сохраняется, по меньшей мере, в течение 24 часов. Тафлупрост эффективен в качестве монотерапии, а так же обладает аддитивным эффектом при применении его в качестве дополнительной терапии к тимололу. **Показания к применению:** Для снижения повышенного внутриглазного давления у пациентов с открытоугольной глаукомой и офтальмогипертензией. В качестве монотерапии у пациентов которым показаны глазные капли, не содержащие консерванта; пациентам с недостаточной реакцией на препараты первой линии терапии; пациентам не переносящим препараты первой линии или имеющим противопоказания к этим препаратам. В качестве дополнительной терапии к бета-блокаторам. Тафлупрост предназначен для пациентов старше 18 лет. **Противопоказания:** Гиперчувствительность к компонентам препарата. Женщинам с детородным потенциалом не следует применять Тафлотан®, если они не используют адекватные средства контрацепции. Тафлотан® не следует применять во время беременности, за исключением случаев, когда нет других вариантов лечения. Тафлотан® не следует применять в период грудного вскармливания. **Способ применения и дозы:** Рекомендуемая доза – одна капля Тафлотан® в конъюнктивальный мешок пораженного глаза один раз в день, вечером. Содержимого одной тюбик-капельницы достаточно для закапывания в оба глаза. При применении нескольких офтальмологических препаратов местного действия, интервалы между их применением должны быть не менее 5 минут. **Побочные эффекты:** В исследовании фазы III при сравнении тафлупроста 0,0015 % без консерванта с тимололом гиперемия глаз отмечалась у 4,1% (13/320) пациентов, получавших Тафлупрост. Следующие побочные эффекты, связанные с лечением были зарегистрированы в ходе клинических исследований: Офтальмологические: ***Часто встречающиеся (от ≥ 1/100 до < 1/10)***: зуд глаз, раздражение глаз, боль в глазах, гиперемия конъюнктивы/глаз, увеличение длины, толщины и числа ресниц, синдром «сухого глаза», ощущение инородного тела в глазах, изменение цвета ресниц, эритема век, поверхностный точечный кератит, фотофобия, повышенное слезоотделение, затуманивание зрения, снижение остроты зрения и повышенная пигментация радужной оболочки. ***Не часто встречающиеся (от ≥ 1/1000 до < 1/100)***: пигментация век, отек век, астенопия, отек конъюнктивы, появление отделяемого из глаз, блефарит, воспаление передней камеры, ощущение дискомфорта в глазах, флёр передней камеры глаза, пигментация конъюнктивы, конъюнктивальные фолликулы, аллергический конъюнктивит, и атипичное ощущение в глазу. Нарушения нервной системы: ***Часто встречающиеся (от ≥ 1/100 до < 1/10)***: головная боль. Нарушения кожи и подкожных тканей: ***Не часто встречающиеся (от ≥ 1/1000 до < 1/100)***: гипертрихоз век. **Особые указания:** До начала лечения пациенты должны быть предупреждены о возможности чрезмерного роста ресниц, потемнения кожи век и усиления пигментации радужной оболочки глаза. Нет опыта применения тафлупроста в случаях неоваскулярной, закрытоугольной, узкоугольной или врожденной глаукомы. Рекомендуется соблюдать осторожность при лечении тафлупростом пациентов с афакией, артифакией, поврежденной задней капсулой хрусталика или имплантацией хрусталика в переднюю камеру глаза, а так же пациентов с установленными факторами риска развития кистоидного макулярного отека или ирита/увеита. Нет никакого опыта применения препарата у пациентов с тяжелой астмой. В связи с этим пациентов этой группы следует лечить с осторожностью. Тафлупрост не оказывает влияния на способность управлять автомобиль и работать с механизмами. Как и при применении любых других офтальмологических средств, после инстилляции препарата может возникнуть кратковременное затуманивание зрения. В этом случае пациент должен подождать пока зрение полностью восстановится, и только после этого управлять автомобилем или эксплуатировать механическое оборудование. **Форма выпуска:** Капли глазные 0,0015%. По 0,3 мл в тюбик-капельнице. 10 тюбик-капельниц, спаянных в виде пластмассовой ленты, в пакетах из ламинированной фольги. 3 пакета вместе с инструкцией по медицинскому применению в картонной пачке. **Срок годности:** 3 года. После первого вскрытия пакета – 4 недели. Не использовать препарат после истечения срока годности, указанного на упаковке. **Хранение:** Хранить при температуре 2 – 8 °С в недоступном для детей месте. После вскрытия пакета с тюбик-капельницами хранить тюбик-капельницы в пакете при температуре не выше 25 °С. После однократного использования тюбик-капельницу следует выбросить вместе с имеющимся остатком. **Условия отпуска:** По рецепту. **Производитель:** Сантэн АО, Нииттюхаанкату 20, 33720 Тампере, Финляндия.

1) Риск развития гиперемии конъюнктивы 4,1%: SPC Taflotan®, 2013. **2)** В рандомизированных контролируемых исследованиях Тафлотан® снижал ВГД на 6,9 – 9,7 мм рт.ст. [vd]: **a.** Uusitalo H et al. Acta Ophthalmol 2010; 88:12-9. **b.** Traverso C et al. J Ocul Pharmacol Ther 2010;26:97-104. **c.** Konstas AGP et al. Br J Ophthalmol 2013;97:1510-15. **d.** Chabi A et al. Am J Ophthalmol 2012;153:1187-96. **3)** Erb C et al. Adv Ther 2011;28:575-85.

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Подготовлено: Июль 2014. Только для медицинских и фармацевтических работников.