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Breaking the Rules: A Rebuttal of Normal-Tension Glaucoma

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Abstract

Glaucoma is a disease of the eyes generally characterized by high intraocular pressure, optic nerve death, and visual loss. Open-angle glaucoma and angle-closure glaucoma are the two main forms of the disease. However, there is one form of open-angle glaucoma that cannot be described by the above abnormalities. This form is known as normal-tension glaucoma, and while it is characterized by optic nerve death and visual loss, it does not display an abnormally high intraocular pressure. Indeed, as this thesis argues, normal-tension glaucoma should not be labeled as a glaucoma disease at all.

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Introduction

Glaucoma is a disease of the eyes that can lead to partial or total blindness in one or both eyes. Blindness can occur over an extended period of time, or it can occur in one violent flash, with the cause of glaucoma being the primary factor in determining the time frame. The cause of glaucoma is one of many criteria which dictates into which specific category, out of dozens, the disease will be classified. In addition to causation, there have to be certain other criteria fulfilled before eye problems can be described as belonging to the general glaucoma family. Today's definition of *glaucoma*, however, is becoming too broad for one disease to encompass because a vast number of characteristics are being attributed to glaucoma. It is reaching the point that if a physician encounters problems with a patient's eyes that resemble glaucoma, but does not know the cause, the physician will attribute another characteristic to glaucoma to meet the patient's problems. One case in point is a form of glaucoma known as normal-tension glaucoma, which is classified as a form of open-angle glaucoma. Open-angle glaucoma is one of the two primary branch points of the glaucoma families, with the other branch point being angle-closure glaucoma. Normal-tension glaucoma, however, lacks the most distinguishing characteristic of all other forms of glaucoma, the elevation of intraocular pressure. Normal-tension glaucoma shares only two basic features with all of the other glaucomas, a death of nerve fibers in

the optic nerve head and a loss of vision (Werner, 1995). There are many other eye diseases which lead to a loss of vision, so the only characteristic physicians are using to classify normal-tension glaucoma is the death of nerve fibers. Physicians cannot even determine the cause of this nerve fiber death, whereas, for all of the other glaucomas, elevated intraocular pressure is the attributed cause. The purpose of this study is to show that normal-tension glaucoma is not a glaucoma but a separate and distinct disease.

In order for one to see why normal-tension glaucoma should not be considered a glaucoma, one must first understand the pathologies of open-angle glaucoma, angle-closure glaucoma, and of normal-tension glaucoma. Another important concept to be familiar with is that of aqueous humor, because it plays a major role in all forms of glaucoma except for normal-tension glaucoma. Understanding these concepts will allow one to discern that normal-tension glaucoma is not a glaucoma.

Aqueous Humor

Aqueous humor refers to the clear liquid that fills the anterior and posterior chambers of the eye. Its purpose is to nourish the lens, cornea, and trabecular meshwork[1], as well as to maintain the intraocular pressure of the eye so that the eye can keep its shape. Aqueous humor is produced by the ciliary processes of the ciliary body[2] and secreted by the nonpigmented epithelial cells of the ciliary body into the posterior chamber. The posterior chamber lies behind the iris, the pigmented muscle of the eye which determines the amount of light which enters the eye by relaxing or contracting. From the posterior chamber, the aqueous humor flows through the central opening of the iris, known as the pupil, and into the anterior chamber. The aqueous humor then drains through the trabecular meshwork into Schlemm's Canal[3] and returns to the bloodstream of the episcleral vein (Figure 1).

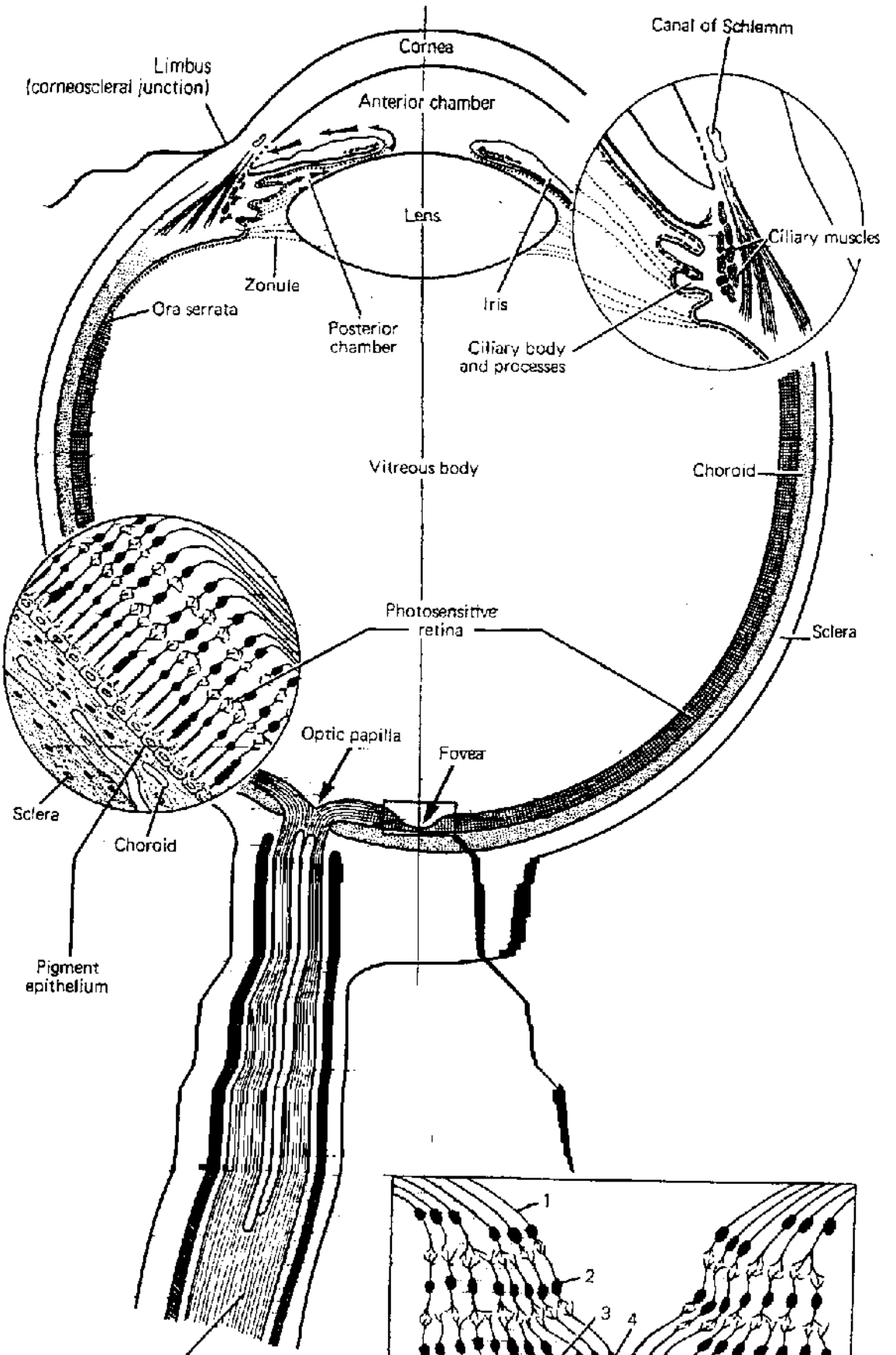
As mentioned above, aqueous humor has two purposes, nourishment of tissues of the anterior segment and maintenance of intraocular pressure. The aqueous humor provides the proper nutrition for the lens and the cornea because they do not contain

[1] A web-like conglomeration of epithelial cells which cover the exit of the aqueous humor from the anterior chamber of the eye.
[2] An anterior extension of the highly vascularized middle layer of the eye, the choroid.

blood vessels. The avascularity of these tissues is important because they would not be clear if blood vessels were to pass through them; light would be scattered and absorbed, and this would impair vision. Examples of the nutrients the aqueous humor provides the lens and the cornea through diffusion include glucose, oxygen, potassium, and some amino acids. Also, the aqueous humor removes wastes such as carbon dioxide and lactate through diffusion as the humor circulates.

The maintenance of intraocular pressure is of paramount importance for the discussion of glaucoma. Intraocular pressure is the force that gives the eye its shape, and the normal range for this pressure is 10-20mmHg . The pressure is created by the amount of aqueous humor present in the anterior and posterior chambers and by the amount of vitreous humor or gel present in the vitreous cavity. The vitreous cavity is the space located behind the lens and in front of the retina[4], and it is the largest cavity of the eye. The pressures created by the contents of these cavities exert forces on all inner surfaces of the eye, thus holding its form. Problems occur when there is a rise in intraocular pressure. An increase in pressure generally arises from a decreased outflow of aqueous humor, causing the aqueous humor to exert pressure on the vitreous gel, which in turn exerts pressure on the optic nerve. Such pressure could damage the optic nerve and produce vision loss.

[3] A vessel solely for the transportation of aqueous humor.
[4] A layer of nervous tissue responsible for the transmission of light images to the optic nerve. It is located on the inner surface of the posterior wall of the eye


Canal of Schlemm
Cornea
Limbus
(corneoscleral junction)
Anterior chamber
Lens
Ciliary muscles
Zonule
Ora serrata
Posterior
chamber
Iris
Ciliary body
and processes
Vitreous body
Choroid
Photosensitive
retina
Sclera
Optic papilla
Fovea
Sclera
Choroid
Pigment
epithelium
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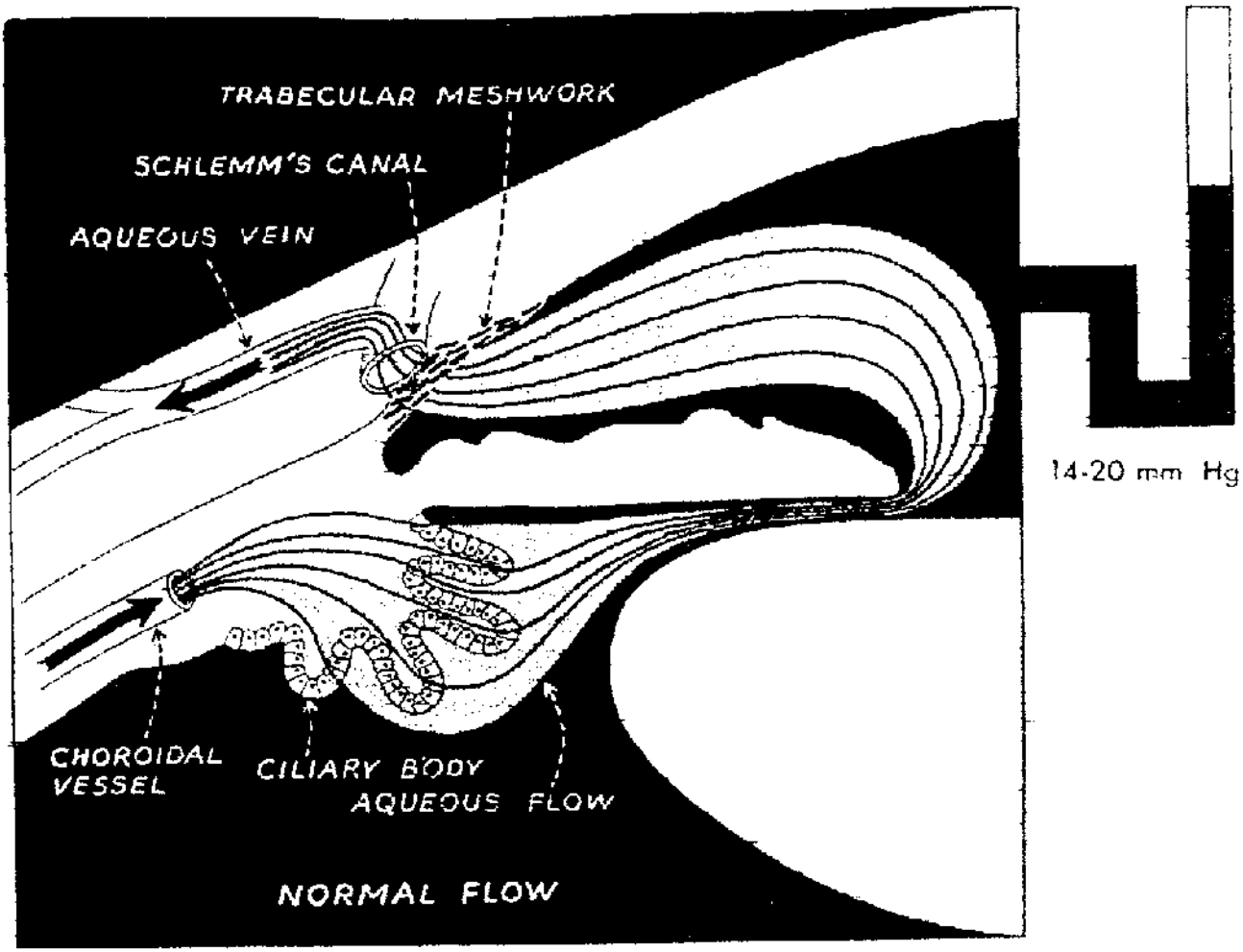

Figure 2. The arrows on this diagram represent the normal flow of aqueous humor within the eye (Kolker and Hetherington; 1983).

Open-Angle Glaucoma

Open-angle glaucoma is a disease of the eyes in which a high intraocular pressure is caused by a blockage of outflow and leads to a death of nerve fibers in the retina and optic nerve and, therefore, a loss of vision. Open-angle glaucoma is often called the "sneak thief of sight" because one usually does not experience symptoms until there is a decline of vision. Vision loss starts with the peripheral vision and gradually moves inward. In 1990, there were 13.5 million people in the world who suffered from open-angle glaucoma, and three million of these people were completely blind (Quigley, 1996).

The most important features of open-angle glaucoma are the pressure build-up in the eye and a normal iridio-corneal angle (Figure 3). A pressure of 24mmHg or above usually means that glaucoma is present (Ritch and Lowe, 1995). According to Brubaker (1995), the anterior chamber, located between the iris and the cornea[5], begins to experience an excess of aqueous humor and then pushes on the posterior chamber. The posterior chamber, which is located behind the iris and in front of the lens, experiences an elevation of pressure and eventually begins to push on the vitreous humor of the vitreous cavity. This pushing causes a build-up of pressure in this very large space between the

[5] The clear, protective surface of the outer eye.

lens and the retina. The vitreous humor in turn exerts pressure on the optic disk, which lies in the middle of the retina. The elevated pressure leads to death of nerve fibers of the optic disc, which is the meeting place of the retinal neurons and the optic nerve. This in turn causes visual loss because the nerve fibers of the retina receive light and transmit signals to the optic nerve and then to the brain for the processing that creates vision.

The optic disk has a small depression in the middle where nerves do not totally fill the disk, and this depression is termed the *cup*. The size of the optic disc and of the optic cup can be measured, and in a healthy eye, the cup-to-disk ratio[6] is 0.3, but in a glaucomatous eye this ratio jumps to 0.7 (Quigley, 1993). The larger ratio is a sign of the death of nerve tissue because elevated intraocular pressure causes neurons to collapse and die. Measuring the cup is another reliable way of determining if a patient has glaucomatous damage.

In general, two basic mechanisms can cause an excess of aqueous humor in the anterior and posterior chambers: the overproduction of aqueous humor or a reduction of the outflow of aqueous humor. There is no known reason for the overproduction of aqueous humor, but a reduction in the outflow is caused by several problems. Aqueous humor leaves the anterior chamber through the trabecular meshwork, and the cells of the trabecular meshwork seem to help facilitate the movement of aqueous humor out of the anterior chamber into Schlemm's canal, which then empties into the venous system (Wilson and Martone, 1995)[7]. Many times in glaucomatous eyes, the trabecular

[6] The area of the cup divided by the area of the disk in millimeters squared.

[7] Although the function of the trabecular meshwork is not known, there are hypotheses relating to its function. One hypothesis, for example, states that serum albumin, which is secreted at the anterior root of the iris, acts as an escort through the trabecular meshwork for a lens fiber protein called (next page)

meshwork seems to show a significant loss of cells as compared to the eyes of asymptomatic people who are the same age (Wilson and Martone, 1995). Since the trabecular meshwork seems to facilitate the movement of aqueous humor, a loss of cells would slow the transport of aqueous humor, hence a back-up of fluid and elevated pressure. Another cause of increased pressure, which will be discussed later, is cells or tissues clogging the trabecular meshwork blocking outflow. The trabecular meshwork can also become damaged from such trauma as a sharp blow to the eye, leaving it distorted and less conducive to outflow.

Open-angle glaucoma is divided into two classes, the first of which is primary open-angle glaucoma. Primary open-angle glaucoma affects 2.25 million Americans age 45 or older (Quigley, 1993). It is a disease characterized by high intraocular pressure, decreased aqueous humor outflow capacity, optic disc cupping, and a normal iridio-corneal angle[8]. These are idiopathic, but they do lead to visual field defects. Possible causes of this disease, as mentioned above, include decreased capability of the trabecular meshwork and an overproduction of aqueous humor. It is thought that when a person grows old, the trabecular meshwork loses cells, a loss which inhibits the meshwork function and leads to this decreased outflow of aqueous humor. These are also the reasons why elderly people demonstrate the greatest prevalence of primary open-angle glaucoma.

Secondary open-angle glaucoma is characterized by an abnormally high intraocular pressure and an open iridio-corneal angle as well. This is similar to primary open-angle

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alpha-crystalline (Doss et al., 1998). Alpha-crystalline has the ability to form micelles if concentrations reach 3.5-5mg/mL, but serum albumin prevents the achievement of these concentrations.

[8] The angle created by the junction of the iris and the cornea.

glaucoma, but the secondary glaucomas have known causes attributed to the decreased outflow capacity and trabecular meshwork abnormalities. There are four general examples of these causes: cells or tissues becoming stuck in the trabecular meshwork, traumatic experiences of the eye, fibrovascular proliferation of the trabecular meshwork, and abnormalities in the episcleral vein[9].

Pigment dispersion syndrome is a secondary open-angle glaucoma, and it is characterized by one abnormality, a loss of pigment from the iris (Wilson and Martone, 1995). This disease occurs in those who have a slightly concave iris that rubs on the zonules[10] directly behind and release pigment. The pigment is released into the aqueous humor from the iris, and can travel and be deposited into the trabecular meshwork, on the corneal endothelium[11], and on the posterior lens. If it is deposited in the trabecular meshwork, outflow capacity is hindered and causes a rise in intraocular pressure. The iris appears to have spokes from where the pigment was lost because of dilation of the pupil. Pigment dispersion does not necessarily result in glaucoma. Some people do develop it, some never develop it, and some can show no signs of glaucoma until twenty years after the pigment dispersion is recognized.

Another form of secondary glaucoma is exfoliation syndrome, which results from the deposit of fibrillar material on the iris, trabecular meshwork, zonules, ciliary body, orbital blood vessels, and the corneal endothelium. The fibrillar material is actually flakes from the lens (Figure 4). Again, if the fibrillar matter is deposited in the trabecular meshwork, outflow capacity is lessened and intraocular pressure is increased. If glaucoma

[9] The episcleral vein is a blood vessel which collects the aqueous humor from Schlemm's canal.
[10] A suspensory ligament of the lens.
[11] A layer of squamous epithelial cells involved in the active transport of ions.

does develop, it is similar to primary open-angle glaucoma.

If a person has cataracts, there is a potential for phacolytic glaucoma. When lens fibers are opacified in a cataract, proteins of high molecular weight are precipitated. The trabecular meshwork can become clogged with these proteins if they are released into the aqueous humor. An inflammation then occurs which causes macrophages to further clog the trabecular meshwork. Again, outflow is hindered and intraocular pressure rises.

Traumatic events, such as chemical burns or a sharp blow to the head, can cause an elevation of pressure. If a traumatic event occurs, there is the possibility for damage to the trabecular meshwork or the episcleral vein. Damage to these anatomical features would lead to decreased outflow of aqueous humor and to this elevation of pressure. Many times these deformities can be repaired through surgery.

When a person suffers from an eye ailment such as an infection, this ailment can lead to inflammatory response by the immune system. If this problem is severe or left untreated, damage to the trabecular meshwork can occur. During the inflammatory response, fibrous materials tend to grow through trabecular meshwork, and these fibrous materials cause a decreased outflow capacity. Intraocular pressure will rise and cause optic nerve death.

Angle-Closure Glaucoma

Angle-closure glaucoma is a disease most generally characterized by a decreased angle between the iris and cornea, obstructing the outflow of aqueous humor into the trabecular meshwork. This iridio-corneal angle closure can cause a mild to sharp increase in intraocular pressure and, in some cases, can result in rapid blindness. Those cases of angle-closure glaucoma which result in a rapid loss of vision are deemed acute angle-closure glaucoma. In angle-closure glaucoma, the iris can be positioned touching the cornea, over the trabecular meshwork, or touching both. Adhesions called synechiae[12] can form between the iris and cornea during the time while the iris is pushed forward, further complicating the problem.

Angle closure can result from several problems, one of the most prevalent being a shallow anterior chamber as defined by being 2.5mm in depth or less. A person can have a shallow anterior chamber through inheritance and have no visual problems until the onset of glaucoma. Also, through inheritance, a condition known as hyperopia or farsightedness may develop. If a person is a hyperope, the eye is mishaped in a manner that will not allow proper focus upon objects, because the focal point of light is behind the retina

[12] An adhesion between the root of the iris and the cornea.

instead of on the retina. This abnormal shape also causes the anterior chamber to be more shallow. In later life, an individual can develop angle closure problems because of a thickening of the lens. The lens is made of crystalline fibers which form on the edges, and as one grows older, the fibers compress to the middle, making the middle of the lens thicker and less flexible. This thickening results in problems which include the need for glasses and a decrease in the volume of the posterior chamber. The need for glasses is due to presbyopia, a decreased flexibility in the lens, which makes the process of accommodation[13] more difficult. The decreased volume of the posterior chamber is troublesome because, although the volume of the posterior chamber decreases, the production of aqueous humor does not. Pressure is created in this decreased space and causes the iris to jut forward and reduce the iridio-corneal angle. There is now a decreased outflow capacity, which further compounds the problem by causing aqueous humor to back up into the posterior chamber and increase the pressure even more. As the problem worsens, the intraocular pressure continues to rise and crush the optic nerve, thereby causing blindness. Having a shallow anterior chamber, however, does not always result in angle-closure glaucoma. Developing angle-closure from a shallow anterior chamber depends mainly upon the rate at which the lens thickens, and most people never reach the thickness that leads to angle closure before they die.

Another possibility for angle closure with a shallow anterior chamber is the overproduction of aqueous humor. The overproduction would cause an increase in pressure in the posterior chamber just as the thickening of the lens would. The mechanism of angle closure would also follow the same path as mentioned above.

[13] A changing of the shape of the lens so as to keep the focal length constant, creating clear images.

Pupillary block can also result in angle-closure glaucoma. The pupil allows the passage of aqueous humor from the posterior chamber to the anterior chamber, as well as the passage of light into the vitreous cavity and onto the retina as mentioned above. The cause of pupillary block glaucoma is paradoxical because it is usually caused by medications used to treat angle-closure glaucoma. Some of these medications, such as miotics, treat angle-closure glaucoma by relaxing the iris. The reasoning behind this treatment is if the iris is relaxed, it will stretch out and become slightly thinner and increase the iridio-corneal angle. However, by relaxing the iris and shrinking the pupil, the passageway for aqueous humor between the posterior chamber and the anterior chamber is also lessened. The trabecular meshwork needs a few days of medicinal treatment before it can return to normal outflow capacity. Coupled with decreased pupil size, these ailments can possibly cause the aqueous humor to back up into the posterior chamber. The posterior chamber becomes pressurized and begins to exert force on the iris and causes it to protrude forward, closer to the cornea, further reducing the passageway for the aqueous humor. Pupillary block glaucoma usually does not occur in patients with normal anterior chambers because the accumulation of aqueous humor can be compensated for allowing more time to meet outflow needs while the trabecular meshwork expands to normal size. If the eye-care practitioner requires follow-up visits for at least three days to observe intraocular pressure and iridio-corneal angle, pupillary block glaucoma can be stopped by changing the patient's medication.

One form of angle-closure glaucoma has not been mentioned, but it is one of most acute forms, malignant glaucoma (Simmons and Maestre, 1995). Malignant glaucoma usually results in the loss of vision of one or both eyes. It mainly occurs as a side effect in

patients who are having eye surgery, but in rare cases, it can also appear spontaneously even if the person has not had surgery. Researchers have not discovered the exact way in which this happens, but the most widely accepted hypothesis states that the surgery can alter the integrity of the eye's structure, causing a collapse of the anterior chamber followed by a forward protrusion of vitreous gel. This gel blocks the flow of aqueous humor from the ciliary body into the posterior chamber. Aqueous humor is then diverted into, beside, or behind the vitreous cavity (figure 6), forcing the vitreous gel forward and also causing a slight dehydration of the vitreous gel. The flow of aqueous humor is now completely diverted into the vitreous cavity, and there is no way for the aqueous humor to escape. The rapidly increasing pressure crushes the optic nerve. Clinical observations suggest that the block of the anterior movement of aqueous humor is at the junction of the lens equator, anterior vitreous face, and ciliary process.

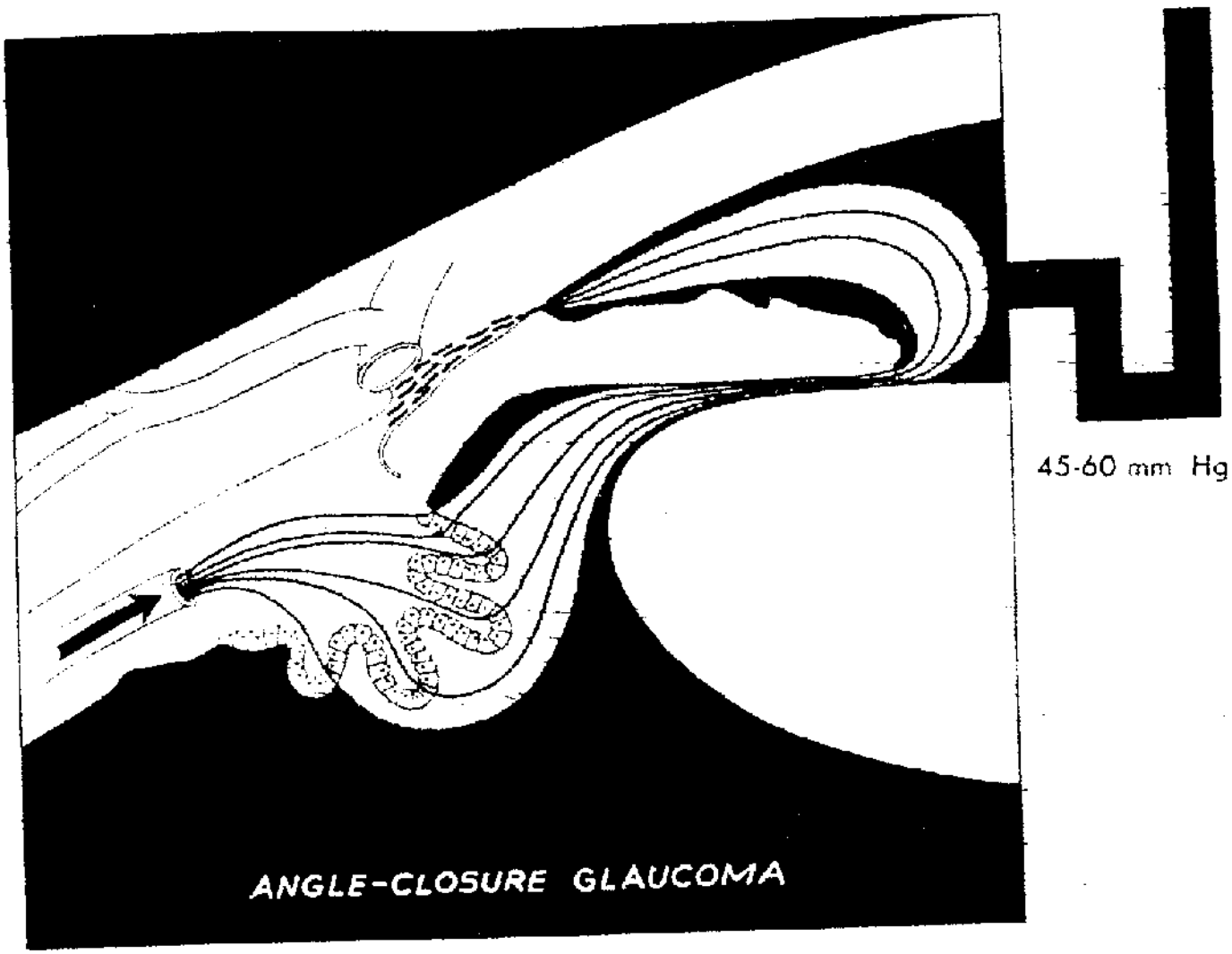

Figure 5. This diagram represents angle-closure glaucoma. Notice the narrow angle between the iris and cornea. Also, the tonometer to the right shows abnormally high pressure (Kolker and Hetherington, 1983).

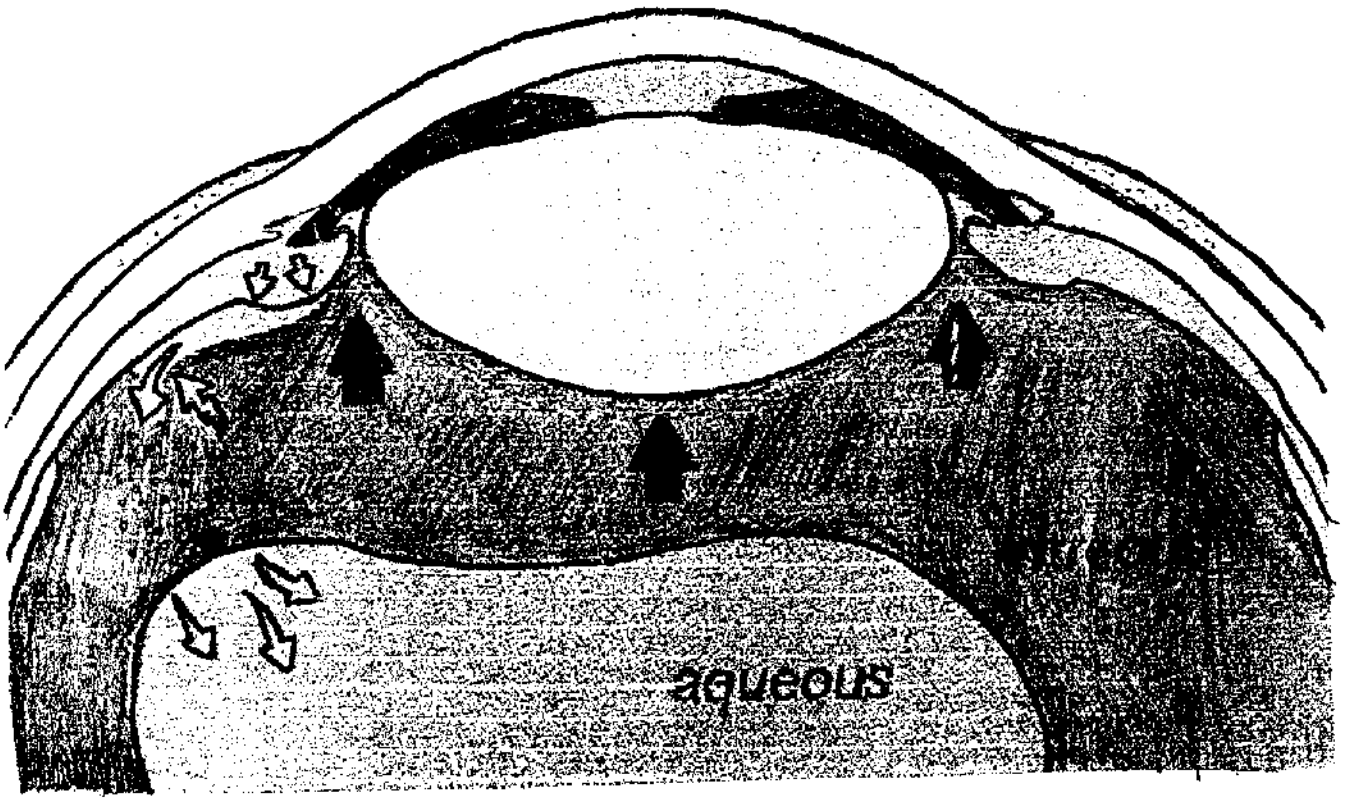

Figure 6. This diagram represents malignant glaucoma. Notice the dark arrows which represent pressure exerted on the posterior chamber by the vitreous humor amd the light arrows representing the misdirection of aqueous humor (Kolker and Hetherington, 1983).

Normal-Tension Glaucoma

Normal-tension glaucoma is a form of glaucoma which has caused much debate in the eyecare field. There is no characteristic elevation of intraocular pressure above the normal range, but glaucoma-like damage still occurs. Normal-tension glaucoma is defined by a cupping of the optic disk, loss of retinal nerve fibers, and a loss of vision. The debate results because glaucoma without elevated intraocular pressure defies what was once a standard by which glaucoma was diagnosed. Glaucoma was first recognized as a disease in 1818, but the only characteristic that physicians used to determine onset of the disease was elevated eye pressure (Werner, 1995). In 1857, a physician named von Graefe presented the notion of glaucoma without high intraocular pressure, but he was opposed so vehemently by his colleagues that he rescinded his idea. Because of the invention of tonometers, instruments that measure intraocular pressure, researchers have been able to measure the pressure more accurately and in many more patients than before. Normal-tension glaucoma has been accepted by many physicians since about the middle of this century because of these more frequent low-pressure readings with the association of other symptoms of open-angle glaucoma. Many, however, still do not accept the idea that normal-tension glaucoma is even a form of glaucoma and often refer to normal-tension

normal-tension glaucoma is even a form of glaucoma and often refer to normal-tension glaucoma as "pseudoglaucoma," which means false glaucoma (Werner, 1995).

In order to diagnose the disease of normal-tension glaucoma before a patient goes blind, an eye specialist must know other distinguishing characteristics of the disease. The most distinguishing characteristic is increased cupping of the optic disk and is found in eyes with normal-tension glaucoma as well as eyes with open-angle glaucoma and angle-closure glaucoma. Indeed, measuring the cupping of the optic disk is the usual method of discovering normal-tension glaucoma, and, in the early stages of glaucoma, the disease often goes undetected because there is no elevation of pressure and only slight loss of vision. The effect of the cup-to-disk ratio as compared with open-angle glaucoma is debated. Some studies have shown that the same cup-to-disk ratio in a patient with normal tension as compared with primary open-angle glaucoma causes an equal amount of visual loss (Jones et al, 1997). Other studies have indicated that although a person with normal-tension glaucoma may have the same cup-to-disk ratio as a person with primary open-angle glaucoma, the former will have less visual loss (Nicolela and Drance, 1996). It is widely accepted that the larger cup-to-disk ratio correlates with a loss in the visual field in normal-tension glaucoma no matter if this ratio is the same as that in other forms of glaucoma.

The onset of normal-tension glaucoma is also detected by the use of a visual field test (Werner, 1995). A loss of vision is usually what alerts patients that they need to seek help and indicates to the eyecare specialist that a visual field test is needed. A visual field test allows for the eyecare specialist to determine where the patient has trouble seeing when looking straight ahead. There is much disagreement as to whether there are specific

areas in which loss of vision occurs in normal-tension glaucoma as compared to other forms of glaucoma, but there is one guarantee: if the patient has any form of glaucoma which is left untreated, the patient will go blind.

Conclusion

Throughout this discussion of the different forms of glaucoma, there has been one recurrent theme, elevated intraocular pressure. Excavation of the optic disk and loss of visual field have also been characteristic features of glaucoma, but elevation of intraocular pressure and its cause have been the main focuses of attention. Almost every textbook discussion of glaucoma focuses the bulk of attention on the elevation of intraocular pressure (Kolker and Hetherington, 1983; Newell, 1992), so why include a disease with normal intraocular pressure within the definition of glaucoma? Optic nerve death and visual loss are common between normal-tension glaucoma and other forms of glaucoma, so if not high intraocular pressure, what does cause these common effects of normal-tension glaucoma and all other forms of glaucoma?

One explanation for normal-tension glaucoma that is gaining popularity is that nocturnal low blood pressure may not allow for proper blood supply and may cause nerve death in the optic disc. Studies have been performed to test this hypothesis using 24-hour blood pressure monitoring of a control group and of a normal-tension glaucoma group (Meyer et al., 1996; Muzkya et al., 1997). Meyer et al. found that the controls and patients with normal-tension glaucoma had relatively similar blood-pressure values during

the day; however, during nocturnal hours the findings were quite different. A significantly greater drop in blood pressure was detected at night in those patients with normal-tension glaucoma as compared to the controls. The work by Meyer et al. was further supported by a study performed by Muzyka et al. in 1997. This study also used 24-hour monitoring of arterial systolic and diastolic pressure. The group added one more element to their study, a group of primary open-angle glaucoma patients. The results of this study showed that the primary open-angle glaucoma patients, normal-tension glaucoma patients, and the controls all had blood pressure drops at night, but just as Meyer et al. had shown, the normal-tension glaucoma patients had a significantly larger blood pressure drop than the primary open-angle glaucoma patients or the control patients. Studies by Graham et al. (1995), Hayreh et al. (1994), and Bechetoille and Bresson-Dumont (1994) have all further confirmed that nocturnal hypotension is a risk factor for glaucoma damage.

Other theories about the causes of normal-tension glaucoma damage suggest that vascular resistance, or impaired ocular blood flow, of the ophthalmic artery (Yamazki and Hayamizu, 1995) or of the posterior ciliary arteries (Cellini, 1997) may be the culprits. Recent research has indicated that patients with normal-tension glaucoma experience an increased level of endothelin-1, which may be responsible for reduced blood flow to the eye (Cellini, 1997; Sugiyama, 1995). Endothelin-1 is a vasoconstrictor peptide produced by endothelial cells of arteries. It is suspected that the endothelial cells associated with arteries supplying the retina and optic nerve have somehow lost the ability to regulate themselves and overproduce endothelin-1 (Cellini, 1997; Gass, 1997). Endothelin-1 would then cause the arteries to constrict and reduce the blood supply to the retina and optic nerve, hence produce nerve death, cupping of the optic disk, and visual loss.

Sunil Shah (1999), a researcher at Royal Bolton Hospital and the University Department of Ophthalmology, Manchester, suggests that glaucomatous damage with no elevated pressure may be the result of a mistake in the pressure reading by the tonometer. He believes that an abnormally thin cornea could cause the pressure reading by the tonometer to be low. The applanation tonometer and the indentation tonometer are the two types of instruments used to measure intraocular pressure. The applanation tonomenter measures the force required to flatten an area of cornea 3.06 mm in diameter. The indentation tonomenter works by placing a known weight on the cornea, measuring the indentation, and measuring the intraocular pressure from this indentation. In Dr. Shah's study, he used pachymetry to measure the thickness of 396 patients' corneas. Of these patients, 113 had clinically normal eyes, 157 had primary open-angle glaucoma, 25 had normal-tension glaucoma, and 101 had ocular hypertension. He found the mean central corneal thickness to be 554.8um in the normal eyes, 550.1um in the primary open-angle glaucoma eyes, 514um in the normal-tension glaucoma eyes, and 577.9um in the eyes with ocular hypertension. Dr. Shah believes that the tonometers give a falsely low reading for eyes with normal-tension glaucoma because the thinner cornea offers less resistance than a normal cornea. He also believes that the eyes with ocular hypertension have false high readings because the abnormal thickness of their corneas give more resistance to the tonometer. Dr. Shah's work was further supported by Morad et al. (1998), who came to the same conclusions.

Another hypothesis about the pathogenesis of normal-tension glaucoma relates to vascular resistance of the ophthalmic artery. Yamazaki and Hayamizu (1995) cite vascular resistance of the ophthalmic artery as the culprit behind optic nerve death and visual loss

in normal-tension glaucoma. Yamazaki and Hayamizu offer no hypothesis on the actual cause of this ophthalmic artery resistance, but previous work by Sonnsjo and Krakau (1993) may shed some light on this idea. They believe that morphological changes in the retinal veins caused by endothelial proliferations cause increased vascular resistance and glaucomatous damage. These endothelial proliferations could also be the active force of opthalmic artery resistance as suggested earlier by Yamazaki and Hayamizu.

Others have hypothesized that normal-tension glaucoma damage may be related to defects of the lamina cribosa. Iwata (1992) and Kolker and Hetherington (1983) both believe that a weakness in the lamina cribosa would cause distortions and twisting, leading to mechanical optic nerve damage. Iwata also suggests that abnormal metabolism of the lamina cribosa in producing extracellular matrix causes an anatomical defect that produces the weakness. The Iwata study also showed fragmentation of collagen, a change of proteoglycans, and reduced amounts of elastin in the lamina cribosa of monkeys with advanced experimental glaucoma.

Again the question can be raised, why should a disease without an abnormal intraocular pressure be considered glaucoma? Every form of glaucoma other than normal-tension glaucoma exhibits a high intraocular pressure, and the main focus of treatment is the relief of this intraocular pressure. Efforts to explain the cause of optic nerve death in normal-tension glaucoma have focused on factors which do not affect other forms of glaucoma. Based on optic disk damage and visual field defects, normal-tension glaucoma is obviously a similar disease to the other glaucomas, but the cause seems to be different; therefore, it should be classified as its own unique disease.

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